Proceedings of the Workshop on the Control of Existing Chemicals Under the Patronage of the Organisation for Economic Co-operation and Development

June 10–12, 1981
Berlin (West)
Reichstagsgebäude

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Preparatory Committee:
Friedrich Schmidt-Bleek (Chairman), Christa Morawa (Co-Chairman), Dagmar Biehn, Wolfram Haberland, Albrecht-Wilhelm Klein, Heinz Jochen Poremski, Peter Rudolph.

It was assisted by:
Chris Charlesworth, Rolf Johannes Engelhardt, Helga Müller

Editor:
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Printed by:
Mercedes Druck
Blücherstraße 22
D-1000 Berlin 61

Participants of the Workshop in front of the conference site, the Reichstagsgebäude, Berlin (West)

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Opening address by Paul Lemerle

Deputy Secretary General, Organization for Economic Co-operation and Development

I want to begin by saying what a great pleasure it is for me to be here in Berlin today, in a city that I have always enjoyed visiting and for which I have all free men's feelings. It is also my pleasure to thank the German authorities, on behalf of the OECD, for arranging this Workshop on the Control of Existing Chemicals. It is an honour for me to be invited to join Dr. Hartkopf in opening this workshop.

It is not the first time that an OECD activity has been initiated through discussion in Berlin. In May of this year, as you all know, the Council of the OECD took a major decision under which test data on chemicals produced in one OECD country will be accepted as valid in all other OECD countries for purposes of assessment of chemicals, or for other reasons relating to the protection of health and the environment. In adopting this decision on "the Mutual Acceptance of Data in the Assessment of Chemicals", the Council also adopted two recommendations which seem to me quite far-reaching. The first provides recognition for a major international set of methods for testing chemicals – the OECD Test Guidelines. The second provides an agreed set of principles to assume high quality results in the testing of chemicals – the OECD Principles of Good Laboratory Practice. Well, some of the seeds of this decision were sown by a working group here in Berlin in September 1977. I am sure this precedent augurs well for the success of this workshop.

Mr. Chairman, it seems to me that there are three aspects of the control of chemicals in our society which are of particular importance. *In the first place*, policies of prevention are always more cost effective in the long run, both to industry and to society in general. *Secondly*, the beneficial aspects of the use of chemicals in our society should not be clouded by the inadvertent impact some of them may have on health and the environment. *Lastly*, permit me to say, the OECD is in a unique position to act as the forum for the harmonization of chemicals control. Let me elaborate a little on these points.

Since 1960, the chemical industry has grown at about twice the rate of the overall industry sector. It is a dynamic industry and it plays a critical role in economic growth and industrial development, not only within OECD but also throughout the world. In 1978, the chemical industry of OECD member countries manufactured products worth over 350 billion dollars, an estimated two-thirds of world production. At the same time, the chemical industry directly employs more than 4 million people, and its products ensure the livelihood of many, many more in those "downstream" industries whose very existence depends on the products the chemical industry manufactures.

These products are now an essential part of both our economic and our social life.

However, because of some unfortunate experiences with the serious effects of certain chemicals released into the environment, governments and industry alike have become increasingly concerned about the potential unintended consequences which the use of man-made chemicals could have on human health and the environment. The numbers are striking. Of some 4 million known chemical substances, approximately 70,000 are produced in commercial quantities and it is estimated as many as 1,000 new substances reach the market every year. There is mounting evidence that a small percentage of these substances, acting separately or together, can have serious long-term effects on human health and on the environment. This is a small percentage of a large quantity, which means that there must be a significant number of chemicals already in use in our societies that could cause harm.

The challenge, therefore, which government and industry together have set themselves, is to develop policies that enable societes to reduce the negative effects of using chemicals, while continuing to reap the benefits from their use. Each nation needs controls that enable its chemical industry and its government to anticipate and prevent the more serious problems from ever occurring, without unduly inhibiting the industry's growth and development. Of course, I do not need to remind you that prevention is preferable to and cheaper than cure.

This brings me, then to my own subject: OECD's role in chemicals control, and the need for international harmonization in the control of chemicals.

The chemical industry is perhaps one of the most international of industries: it trades extensively all over the world. The volume of this trade is huge; in 1979, chemical exports of OECD countries amounted to 108 billion dollars while their chemical imports were worth 83 billion dollars. Much of this trade was between OECD countries.

I am sure we all appreciate that a set of unco-ordinated control strategies put in place by the OECD Member countries would have significant implications for the international trade in chemicals. It has therefore been of the highest importance that national actions be harmonized to introduce as few distortions to trade as possible. Indeed, a harmonized approach to chemical control strategies is already helping to avoid the emergence of non-tariff barriers and other distortions to trade.

It is also now evident that chemicals, once free in the environment, have no respect for national boundaries, and can travel extensively to even the remotest parts of the globe. The consequence of this is to magnify the potential ill-effects of the use of some chemicals and to render control of their use by any one country more difficult.

I believe there has been general recognition that international co-operation is also important in helping to avoid wasteful and costly duplication of effort in the necessary testing and assessment of chemicals, and that it can and will enable a more efficient use to be made of our valuable and limited scientific and human resources, both in the public and in the private sector.

These then are primary objectives of the OECD Chemicals Programme, and they have been the driving force for the major effort which has been made within OECD to arrive at a harmonized approach to chemicals control. It is also very important to remember that because these have been the objectives of the Programme, it has benefitted from the active support of industry, as well as governments and communities.

The results to date of the work within OECD have been quite encouraging. Tackling first the control of new chemicals, several years of work, to which all Member countries contributed, has now begun to bear fruit. I am of course referring once more to the Council Decision of 12 May last on the Mutual Acceptance of Data.

In reaching its Decisions and Recommendations, the OECD Council particularly praised the experts and governments involved in the Chemicals Programme. More than 300 experts, drawn from government, industry and academia, have worked together over a three-year period in a unique exercise in technical co-operation. The Council noted that OECD Member countries have had not only the expertise but also the incentive to develop this activity because they comprise the world's major producers, traders and consumers of chemicals. In addition, the setting provided by the OECD allows the necessary complex policy analysis to take place in such a way as to advance simultaneously environmental, industrial, economic and trade objectives. Thus, the measures adopted should protect human health and the environment from chemical

hazards while ensuring that international trade in chemicals is not unnecessarily disrupted.

Of course, there are many areas in the control of chemicals, other than those presently being worked on within the OECD, where international harmonization would be beneficial. The various OECD committees have been aware of this and the subject has been discussed for several years now. The result of these discussions has been for the committees to choose the control of existing chemicals as one of several areas which needs priority attention by OECD, and for the German Authorities to offer to host this Workshop as a point of departure for the ensuing work on harmonizing the control of existing chemicals.

No-one will claim that the questions surrounding the control of existing chemicals are simple. Nevertheless, there is a pressing need for answers, and your agenda over the next three days provides the occasion for significant progress to be made in clarifying a number of important issues. I therefore take this opportunity, Mr. Chairman, Ladies, and Gentlemen, to wish you every success for the work you are about to undertake. We in OECD can only benefit from such success.

Opening address by Jean-Paul Parenteau

Chairman of the OECD Chemicals Group, read by Pascal Deschamps

M. Parenteau regrets very much that a too full agenda does not permit him to attend the Workshop on the Control of Existing Chemicals.

The Chemicals Group, in its usual sessions as well as in its High Level Meeting of May 1980, has set a high priority on the work on existing chemicals control.

This is a very important question. Probably it was essential to stress in the last years on the control of new chemicals, to have a better control on the future, taking account of innovation in the chemical industry. But it remains that existing chemicals (many of them existing since many years) form the most important part of the chemicals in contact with man and environment.

Fortunately most of them seem to have proofed their innocuity by a long use apparently without problems – yet progress of scientific knowledge and disease identification have led to some questions, and a more systematic action seems necessary.

The selection of products to investigate is nevertheless very difficult to solve and appears as full of dangers. The way is narrow between too *a systematic approach*, leading to useless studies and expenses out of proportion to the expected advantages, in a period of economic crisis where governmental or private resources are requested from everywhere, including other environmental problems, and *what we designate in French by the "ostrich policy"*, that we can't accept.

More it is essential to take account of work and selection made in other international programmes on chemicals, as this one carried out by WHO.

OECD seems to me a particulary adapted forum for this work, as also for conducting the following action that issue from it:

- Cooperation between the countries to share the studies on selected products, in order to avoid duplications of testing and waste of resources.
- Search of international agreements on the broad outlines of rules and restrictions to edict in the different countries, in order to avoid trade barriers and measures insufficently founded on a scientific point of view, which might result from premature national decisions.

The Chemicals Group looks with great interest to this workshop for help to define on a precise basis its future programme.

I am sure that the organisation of this meeting by the UMWELTBUNDESAMT, which on behalf of the Chemicals Group I am glad to thank warmly for this essential action, will be, in consideration of its wellknown efficacity and strictness, the guarantee of the success of this meeting, for which I express my most sincere wishes.

Dr. Günter Hartkopf

Staatssekretär, Federal Ministry of the Interior, Our Challenge: Existing Chemicals

1. Introduction

With great pleasure and deep satisfaction I bid you a cordial welcome in Berlin, also on behalf of the Federal Minster of the Interior, Gerhart Rudolf Baum, who in the Federal Republic of Germany is responsible for environmental protection. And, I am sincerely happy that it was possible to assemble here in Berlin so many well-known and knowledgeable international experts in chemicals control! It seems to me of particular significance that the audience represents virtually all segments of society which can and, I hope, will contribute to effective proposals for solutions regarding the control of existing chemicals.

Before beginning to share with you what I believe to be the major issues of this conference and our major points of concern, I should like to give credit and thanks to the OECD for taking the initiative early to co-ordinate various national efforts toward harmonized chemicals control in the industrialized countries. For the first time an overall programme was launched to find agreements on all major facets of the problems surrounding man-made chemicals. And, even more important, almost all major industrialized countries, producing and exporting countries alike, agreed upon designing and implementing this harmonization programme.

You have gathered here in Berlin to address one of the most difficult and pervasive environmental problems of our time: *tens of thousands* of different *man-made chemicals* are out there in factories, in hospitals, in food, clothing, kitchens, in the air, in lakes and streams, everywhere. These chemicals were invented to help us feed the hungry, to help us stay healthy and enjoy life more and make us live longer. Chemicals have been and still are beneficial to man. However, this is not their only characteristic. They have been Janus-faced from the very beginning. Their disadvantages are not advertised on glossy paper. Still, they are today no longer – as during the past 100 years – dismissed from our consciousness.

And yet, as it is true with so many man-made "benefits" to modern life, no one has yet found enough time, money and courage to have a *hard* look at the darker side of the equitation: *at what real costs are all these chemicals among us?* What are, behind the widely known advantages, the quiet, subtle damages and changes inflicted upon man, plants, animals, what are the long-term changes in soil, in the air, in water, how are these changes related to each other – changes that nobody wanted, but have been put up with nevertheless.

It has been a hallmark of the policy of all industrialized nations in the world for many decades only to *react* to *obvious* changes and damages. We reacted to individual problems caused by individual chemicals. Minamata and Love Canal, Seveso and Flixborough have opened our eyes: today the necessity of anticipatory tests is generally acknowledged in view of the fact that we have to deal with *manifold potential* problems.

It is the intent of this conference to take stock of the potential magnitude of the problems posed by *man-made* chemicals and possibly identify first alternatives for their *solution*. But I think it is only fair and realistic when I point out at the outset of your work here in Berlin that this conference can be *but a very first beginning*. No one should expect too much, too soon. In fact, a sin that has been committed for a century cannot be redeemed in a conference. Remission of sins takes longer, anyway.

The OECD has sponsored this conference, the Federal Republic of Germany has particularly vigorously supported harmonizing efforts in the area of chemicals control within the family of OECD Member Countries. It does not detract from the merits of the organizer if the efforts made to prepare this workshop are to be considered as only one step of a long ladder. We must not overlook that the problems relating to chemicals control go far beyond the OECD countries. We all know already of examples of why the global involvement in solving these problems is absolutely essential: The chlorofluorocarbon/ozone question is not a problem that concerns only the United States or Japan or the Federal Republic of Germany. Agricultural chemicals are not just exported to developing countries, and pose problems there, many of these chemicals are promptly returned in the form of residues in fruits and other food items when these are exported to the very countries which the chemicals originated from. Trade and transport of chemicals do not stop at any political boundary. Sooner or later most chemical products find their way into and across all countries. They touch us all and everything around us. And once they are released from the production sphere we have lost control in almost all cases. Then it is too late to stop the chain of events which environmental chemicals are part of: distribution in the environment, persistence, accumulation and, of course, effects upon air, water, soil, biological targets and complex functional inter-dependencies.

2. Why International Co-operation is Essential

Let us explore a little further the question why effective control of chemical products can ultimately not be exercised by any individual country alone:

There are crude estimates that up to ten per cent or more of the chemicals marketed today may pose a danger to man and the environment. This means that *„Candidate Lists of Suspicious Molecules"* may eventually reach some 3000 or 5000 or more entries. Our environmental experts tell me that they have spent a good deal of time and money recently to assemble "Base Set"* or MPD** data dossiers for some 50 "well known" industrial chemicals. One imagine – 50 out of some 50 000 or a grand total 0.1 per cent of all existing chemicals are now officially on file and known to us to the same extent as we are demanding for all new chemicals in the future according to the European Control Legislative on dangerous substances*. This is not to neglect the fact that presumably only few substances are really dangerous and that considerably more knowledge has been accumulated for certain classes of substances, specifically those which were designed as active ingredients in drugs and pesticides. But even counting all of these, thousands of chemicals remain, about which very little is known – at least to the *competent* authorities.

Industry knows more about their products, there are indications that they do. I therefore urge their representatives here to show us ways of sharing this information with us. In suggesting this, I am not asking that industry simply turn over wholesale its computer files on data. But I suggest very strongly that a dialogue be started during this conference on ways and means to put existing knowledge to its best possible use, thereby taking confidential data into account. We can all not afford to dispense with data knowledge already available or to accept to do expensive double work.

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* Laboratory testing results according to Annex VII of the Directive 79/831/EEC (6th Amendment)

** "OECD Minimum Pre-Market Set of Data" essentially corresponding to Annex VII of Directive 79/831/EEC

There may then be a few hundred existing chemicals for which sufficient data are available to perform adequate hazard assessments. It remains to be seen whether these hazard assessments will have to be performed separately for environmental hazards and for health risks.

It would seem further that the great majority of entries for *Candidate Lists of Suspicious Molecules* would have to be investigated in the laboratory before regulatory actions could be considered.

How much does all this cost? $ 50 000 for each chemical? One million? More? And then: Do we have enough laboratories and experts – not only toxicologists – to cope with this problem? *And: how much time can we spend on dealing with these problems before public patience with good reason wears thin? When will another chemicals accident globally shake public confidence again?*

It should be quite obvious from the conditions I have just mentioned why we feel that a state *cannot* effectively deal with these problems *on its own*. But there are very good additional reasons why sharing the burden internationally is the prudent route to take: Suppose one country were in a position – from a personnel and financial point of view – to shoulder the burden alone – would the resulting knowledge be accepted in other countries? Experience would indicate some doubt here.

Would furthermore, if no international co-operation existed, the *selection* of particular laboratory studies for a given chemical by one country be accepted as the best choice by others? Again some doubt is in order.

Furthermore, our problem does not only relate to people. In many places all over the world there are very serious discussions going on about the necessity of sacrificing test animals. It seems to us that seeking international co-operation in solving existing chemicals problems would offer an excellent opportunity to cut down substantially the number of animals that have to be sacrificed in laboratory tests.

Finally, it is predictable that many of the entries of any *Candidate List of Suspicious Molecules* are not produced in one country alone. They are frequently produced by different companies in different countries. So who is to pay for what tests in accordance with the polluter-pays-principle?

In short, we believe that real progress in solving problems associated with existing chemicals depends critically upon international co-operation.

This international co-operation must be well prepared. The major facets of the needs, the possible approaches and the limitations have to be considered carefully before decisions are made.

In this connection it is worthwhile to recall with great thanks that the OECD has already laid part of the foundation for future co-operation:

As we all know, in the past it was not possible to trust that information derived from laboratory data in one country was freely convertible worldwide. For instance, when a fish test was run in Japan with Japanese carps it was not necessarily so that these data were acceptable to European countries. And, vice versa, when a biodegradability test was performed in Germany, there was no guarantee that resulting information could be accepted by Japanese government authorities. The OECD "Chemicals Testing Programme" has meanwhile resulted in a large number of harmonized Test Guidelines and also in Good Laboratory Practice principles. Certainly, GLP and approved Test Guidelines could, and should, be part of the basis of producing acceptable data and information on existing chemicals in the future.

I am very pleased to hear that the OECD Council accepted as a "decision" on May 12, 1981 the concept of the acceptability of data, based upon the Test Guidelines *and* the GLP principles.

Other parts of the OECD's harmonization programme for the control of chemicals should also be analysed with respect to their possible contributions toward a co-ordinated existing chemicals programme. For instance the information exchange and the confidentiality issues would seem to be of considerable interest here.

Similarly, the experiences and achievements of UNEP, FAO, ILO and in particular of WHO and IPCS must be integrated into a future joint effort in coming to grips with the existing chemicals problems.

In this connection I wonder to which extent international agreement exists today with respect to purpose, format and details of reports on individual chemicals? Surely, the scientific parts of *"Chemical Reports"* on substances like benzene and cadmium should *not have to be duplicated over and over again* in various countries – the wheel has not been re-invented several times either. Surely, enough experience exist today to agree on how *"Chemical Reports"* could best be produced by whom and for which chemicals.

3. Some Thoughts on the Programme of this Conference

Topic I:

This brings me to the first of your *four* major conference topics, namely international co-operation for the control of existing chemicals.

You start with the presentation and discussion of the current efforts of international institutions which are involved in solving existing chemicals problems. At the present time this involvement still seems to predominantly take the form of dealing "curatively" with *individual* chemicals or *small groups* of *chemicals*, one at a time, which, for one reason or another, have in the past given reasons for serious concern. Examples may be asbestos, benzene, PCB, and chlorofluorocarbons. It is important to note that, by and large, these chemicals are all among those for which considerable laboratory data and other information is already at hand.

Apart from questions relating to the harmonization of *priorities* in choosing individual chemicals or groups of chemicals by one or the other international institution, I would suggest the following points to be among those which are worthy of your attention:

First: The lists of priority chemicals or groups of chemicals which have already been selected for assembling *"Chemical Reports"*

Second: The presently perceived time frames for the work to be performed

Third: The specific purpose or purposes for which the resulting "Chemical Reports" are intended

Fourth: For whom are these documents intended? For individual governments? The scientific community? Industry? The citizens?

Fifth: Would it be useful to establish and agree on lists of items which should be considered in each "Chemical Report" so as to satify as many needs as possible?

Sixth: Is it conceivable that the workload in preparing "Chemical Reports" could be shared among the international institutions or would it be preferable to concentrate this task somewhere and to finance it jointly?

All in all it seems to us that the purpose of the deliberations under this topic should not only be to illustrate in detail the efforts of the involved international organizations

but also to identify specific areas of concern in which closer co-operation among institutions would benefit the results and would thus lead to a better use of scarce resources.

Topic II:

The next topic relates to the analysis of the regulatory and administrative possibilities of the control of existing chemicals in the OECD Member countries. I hope you will also find it possible to deal with the practical implementation of the regulations in force. This is important because we all know that the mere existence of laws and regulations alone does not necessarily reflect the real extent to which man and the environment are being protected.

For instance, it would be rather interesting, I believe, to attempt a comparison of the man-power and other resources available for *enforcing protective legal instruments* in various countries. I am not at all certain whether we all are devoting sufficient resources in our countries to the regulatory enforcement process with respect to chemicals. In fact, I am sure that this is not the case. And there is another aspect:

Many countries in the Third World would probably welcome some guidance as to the administrative man-power requirements in dealing effectively with the multitude of information provided by a sophisticated industry.

It would furthermore seem to be important to obtain a comprehensive survey as to where the member countries of the OECD stand at the present time with respect to having legal mandates to cope with existing chemicals. Surely information exchange, in particular the mutal exchange of confidential information, would seem to depend upon the respective legal situations.

Irrespective of all technical matters, however, a better understanding of our neighbor's legal and administrative powers – not only those of the OECD countries – as well as his societal and institutional peculiarities and traditions in dealing with chemicals control would greatly help in working together. At least this is our experience within the European Community.

Topic III:

From a *practical* point of view the third topic, the establishment of criteria according to which existing chemicals are to be selected for further tests, which you intend to deal with may be the *most important* one of your conference. It is intended to start by identifying the *lists of existing chemicals* which could form the baseline from which to select entries for *"Candidate Lists of Suspicious Molecules"*.

In this respect I regret that the work on the European Inventory of Existing Chemicals may not be sufficiently far enough advanced to be considered as one of these lists at this time.

Having agreed on a base list from which to pick and choose, the question arises: how does one select, from among 40 or 50 000 chemicals, those which are of most interest: those which are, or seem to be, particularly suspicious? Does that mean that we will have to subject *all* chemicals contained in this base list to laboratory testing in order to provide a *first* meaningful hazard assessment? That, ladies and gentlemen, is the definition for the so-called OECD "Minimum Pre-Marketing Set of Data" (MPD) which costs some US $ 40–50 000 each. The total could thus run to $ 2 billion for this series of exploratory tests alone and would undoubtedly take years to complete. Or is it possible to avoid some or most of this resource input and *still select the truly suspicious*

chemicals for further consideration – without jeopardizing and compromising the protection of man and the environment from dangerous existing chemicals?

It seems to me that the scientific challenge of your meeting has its fulcrum here: given the scarcity of information available on most of the existing chemicals, can one agree upon an array of criteria which can and should be used for this selection procedure and how should these criteria be applied? In which sequence and/or in which combination? It also seems reasonable to assume that the selection of chemicals for their potential *health* risk may have to be performed differently than selecting chemicals which seem of particular interest for safeguarding the *environment.*

It would seem to be most interesting to obtain an indication from the industrial representatives among us, whether they are prepared to search their data files if and when one could agree upon a short list of "Most Wanted Data" for selection purposes?

In this part of the conference we shall hear from representatives of Japan and the United States about their actual experiences with selecting from the existing chemicals those which *they* feel must be investigated further. We are very much looking forward to learning about these practical experiences.

It also seems to be of great importance to touch upon the following areas during the discussions:

First: Data and information by themselves do not necessarily mean reliable data and information. Are there efficient and harmoniseable ways to establish reliability of data and information? What are these ways? What do they cost?

Second: For the chemicals which are already well studied in the laboratory, improved data collection – to establish assessment criteria – and international transfer mechanisms may be desirable!
Here, too, industry could assume a key role.

Third: How could such an exchange of information be organized without running the risk of transferring continuously *large quantities of superfluous information?*
We can gladly do without data dumps guarded at great expense by legions of civil servants.

Topic IV:

This brings us to the fourth topic of our programme, the establishment of the financial resources required for testing and assessing existing chemicals. We would expect that reliable calculations in this area are still unsatisfactory at this time. This is why it seems of particular importance to come to some first estimates of the financial resource needs because the nature and quality of political decisions will critically depend upon those estimates. As I have emphasized earlier, we firmly believe that the costs involved here are of such magnitude that *one country cannot shoulder alone the solution of the problems* associated with existing chemicals. But we are willing to discuss sharing resources and expertise with other countries. We trust that industry will be able to give us good guidance in this areas in their own interest and share with us their considerable experience.

From our point of view it would be particularly interesting to obtain information on:

First: the typical costs of assembling information, performing quality checks and composing *"Chemical Reports"* based upon such information for chemicals which are already well described in literature.
It is our experience that such *"Chemical Reports"* require at least 3 man-

years to complete. Possibly IPCS* and IRPTC** can be of help to identify cost ranges in this area.

Secondly, we are greatly interested in obtaining estimates of

- cost ranges for such entries of the *"Candidate List of Suspicious Molecules"* which need further laboratory investigations before "Chemical Reports" can be assembled.

While you may find it difficult to agree upon cost ranges during your discussions here in Berlin, it would already be very helpful to identify key cost items and obtain indications of ways and means as to how cost estimates can be improved in the future.

4. Conclusions and Outlook

I hope that my considerations have confirmed my initial remark that it would be *unrealistic to expect* from this meeting in Berlin *ready recipes* for actions on "how to solve the existing chemicals problem". However, what I do hope is that you can identify the various *major facets* of the problem which may have to be considered further and analyzed so that realistic solution alternatives can be advanced later. It would also be desirable to obtain suggestions for ways and means to analyze the problems. For instance, you may agree that a comparative legal analysis of the regulatory and administrative powers within the OECD Member Countries, or within other groupings of nations, or even worldwide, is desirable with respect to *existing chemicals.* You may also agree on the need to discuss the items which should normally be considered when "Chemical Reports" are assembled and who should best carry on these discussions. Or you may find it possible to agree on the organizational form best suited to identify and agree upon selection methods for entries to *"Candidate Lists of Suspicious Molecules"*, e.g. the formation of an international Expert Group on *Environmental Selection Criteria for Existing Chemicals* and/or a similar group for health risks.

Finally I would like to ask you as experts for your advice, and I invite you to give this advice to my staff members of the Ministry of the Interior and the Federal Environmental Agency during this conference:

We have planned a preliminary study to address the feasibility of examining the major issues which must be resolved before an international programme on existing chemicals can definitely be put into practice. Some of these issues are of scientific nature, involving testing protocols, laboratory procedures and data interpretation. Others are of an organizational nature, such as the location of testing, sharing of costs among participating countries and firms and the guarantee of the acceptability of the results in various contries.

Probably not all of these issues can be resolved merely through rational analysis. Many of them require careful preparation and consideration among some key individuals in several decision areas in the countries where major production of chemicals is located. Thus, the success of the subsequent programme will problably depend as much on the development of effective co-operation as on careful scientific analysis. A preliminary study therefore seems to be a practical and expedient step to lay the ground for a subsequent study which is to identify and detail alternative solutions based upon international co-operation.

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* International Programme for Chemicals Safety

** International Register of Potentially Toxic Chemicals

The feasibility study is to concentrate on four tasks:

First: identification of the issues which must be addressed,

Second: review of existing programmes relevant to those issues,

Third: identification of experts with the knowledge, skill and experience required in their analysis, and

Fourth: specification of the design for the subsequent study.

The results of this study should become available early in 1982 and could be suitable as a planning basis for a major internationally supported study detailing definite alternative solutions.

Obviously the success of this studies depends critically on the discussions you are about to begin. We intend to share its outcome with all interested countries, hoping to launch the subsequent major study as a truly international effort if you in your capacity as experts think that it is advisable to recommend us this long and certainly rather expensive procedure.

In this opening address, I have done little more than raise uncomfortable questions which will not be easy to solve. It was my intention to make you understand that my government is deeply worried and concerned about the solution of the problems associated with existing chemicals. We are convinced that *only close international co-operation* can at all ascertain acceptable solutions. We take your coming to Berlin as an indication for sharing with us this view, and we should like to interpret the presence of representatives of many countries as willingness to agree upon joint action.

With this in mind, I wish to all of us that during these days here in Berlin the workshop will be successful, mutual understanding will grow and that personal friendship will be deepened.

CHIEF RAPPORTEUR'S REPORT

Norman King

Rapporteur's Report

Introduction

1. The Workshop has been organized by the Federal Republic of Germany with the patronage of the OECD. It is intended as a contribution to the current debate on existing chemicals – a topic identified at the first High Level Meeting of the OECD Chemicals Group as deserving priority attention.
2. In his introductory paper, Dr Hartkopf emphasised the importance of developing strategies to deal with the problem raised by existing chemicals. Ways must be found for developing a more systematic and internationally harmonized approach to such problems. He stressed that we are only at the beginning of the tasks and that the workshop offers a first opportunity to consider the magnitude of the problems and to identify options for future work and actions which might help solve such problems. The international aspects are important both because some of the problems are international and because international cooperation is needed if scarce resources are to be used in the most cost-effective way and if the burden of costs is to be equitably shared. The important role which OECD has already played is acknowledged and it is accepted that OECD will play an important role in the future. Indeed, aspects of the existing OECD Programme are already very relevant to the problems of existing chemicals and the whole programme should be analysed to see how it can be developed to address the kind of problems which are addressed in the Workshop. Other international agencies are also active, notably the International Programme on Chemical Safety (WHO/ILO/UNEP). There is a continuing need to ensure cooperation between the different programmes. Sharing the burden, not duplicating the work, must be the aim.
3. Industry has a part to play. Chemical companies know a great deal about their products and ways of tapping this knowledge and expertise need to be worked out. Again, the aim should be to avoid duplicating work while ensuring that the valid commercial interests of industry are preserved.
4. Testing in animals is expensive and there is the need to improve the reliability of short-term screening tests to minimise the need for expensive long-term studies in animals. This is not only a problem of costs, the very serious problem of animal welfare must not be overlooked. In many countries there is a deep and growing concern about the too ready use of animals in testing chemicals. Cooperation and eliminating duplication of effort are important ways to reduce the number of animals which might otherwise be involved in testing.
5. Turning to each of the four main topics of the Workshop, Dr. Hartkopf offered his views on points which need to be raised and discussed in each session. (The Chief Rapporteur, as far as he has been able, has taken these points into the discussion of each of the topics). He commended the idea that existing chemicals be considered in two broad categories: Class I where sufficient information already existed to allow a proper appraisal of the possible hazards to man and the environment and Class II where insufficient information existed for this purpose.
6. Finally, Dr. Hartkopf sought guidance from the meeting on the feasibility study being considered by his Ministry in collaboration with the Federal Environmental Agency. This is intended to examine the major issues which need to be resolved before any cooperative international programme on Class II chemicals is started.

The Workshop will provide a very valuable input to such a study. A pilot study is already in hand, the results of which might be available early in 1982.

7. The remarks of Mr Lemerle, Deputy Secretary-General of the OECD, complemented those of Dr Hartkopf. In thanking the German authorities for arranging the Workshop, he noted the economic importance of the production of and trade in chemicals and the need for continued efforts to harmonize procedures and actions as a means of achieving cost-effective and efficient chemicals control.

Topic I International Co-operation in Controlling Specific Existing Chemicals

The International Programme on Chemical Safety

8. Dr Parisek described the present and planned activities of the International Programme on Chemical Safety (IPCS). He emphasised that this is a joint programme of WHO, ILO and UNEP. It has seven major objectives:
   (i) to carry out and disseminate evaluations of the effects of chemicals on human health and on the quality of the environment; 15 studies have been completed and 30 are in hand or planned;
   (ii) to develop guidelines on exposure limits;
   (iii) to develop methods that could produce internationally comparable results.
   (iv) to coordinate laboratory testing and epidemiological studies;
   (v) to develop knowledge and procedures for coping with chemical accidents;
   (vi) to promote training and development of manpower in the field of toxicology.

Within this framework, it is up to the Member States to define the problems which are best solved at the international level.

Programme of the European Regional Office of WHO

9. Dr Waddington spoke on the activities of the European Regional Office of WHO in the area of existing chemicals. The programme covers the interest of 35 member states and is centred on the following areas:
   (i) the development of trained manpower, which is a constraint in many countries;
   (ii) contingency planning for chemical emergencies;
   (iii) the development of the health aspects of environmental impact assessment;
   (iv) collaboration and exchange of information concerning the development of methodologies and control procedures.
10. In addition, the European Regional Office has assumed global responsibility, under the IPCS, for manpower development and contingency planning.
11. A series of consultation meetings and meetings of working groups on specific topics relating to this programme is underway and has already generated many useful ideas. Meetings have already been held on priorities, manpower needs, contingency planning, monitoring and epidemiology, toxic wastes, man-made mineral fibres, high-level radioactive wastes, micro-pollutants in river sediments, delayed and chronic effects in the workplace and good laboratory practice.
12. The programme is an applied one, it is not concerned with areas of "high science". Links have been established with OECD, EEC, the IPCS Central Unit and the American Regional Office of WHO.

Programme of the European Community

13. Mr Mosselmans described the work on the control of existing chemicals in the European Community. He stressed that as well as seeking to improve the quality

of life, the Community is concerned with the removal of, and prevention of, barriers to trade within the Community. He spoke principally on 2 themes:

(i) labelling, which is intended as a primary means of passing information to users; directives already exist covering dangerous substances, solvents, paints and pesticides;

(ii) priority chemicals where a series of activities were in hand; new substances will be subject to the "6th Amendment"; the data bank ECDIN is considered a potential management tool for the Commission and for Member States; the Commission's Advisory Committee on Toxicology and Ecotoxicology has been asked to consider how to prioritise existing substances;

(iii) action to control specific chemicals; the 1976 Directive on marketing and use ("PCBs directive") has been applied to a range of substances, in addition there are directives on the biodegradability of detergents, lead in petrol, sulphur in fuel oil; directives on exposure in the workplace; and a limit on the production of chlorofluorocarbons has been agreed.

Existing OECD Programme

14. Dr Crawford described the background to the OECD Chemicals Programme and emphasised that this has always had a dual purpose – to protect man and the environment and to avoid non-tariff barriers to trade. Harmonization is important. "Harmonization" is best considered as developing or re-ordering national policies to achieve shared objectives. It is neither a lowest common denominator approach nor an insistence that the objectives be reached in exactly the same way in all countries.
15. Most of the current work in the OECD Programme is relevant to the problem of existing chemicals. The recent OECD decision on mutual acceptance of data will be just as relevant to data generated in the future on existing chemicals as it will be on new chemicals. The OECD experience in working towards this decision may throw some light on how to best ensure the quality of data already generated – a subject of particular interest when considering existing chemicals.
16. The results emerging from the working group on Key Terms are as relevant to existing chemicals as to new ones. Similarly, the work on confidentiality is relevant although it may be easier to exchange information on existing as opposed to new chemicals; exchange of information is an established part of the programme.
17. The principles of hazard assessment being developed, while aimed at new chemicals, will be applicable more generally. Hazard assessment is an essential part of decision-making but the latter also involves other factors e.g. social, political and economic considerations. These are particularly important in the case of existing chemicals and the possibility arises of work to harmonize approaches to their inclusion in decision-making, e.g. is it possible to agree on a framework/lexicon within which trade-offs could be made nationally? "Visibility" and "Transparency" in decision-making are being demanded to an increasing extent and such a framework may offer advantages in this respect.
18. There is still uncertainty over many aspects of the problem of existing chemicals. There is a need to develop not only criteria for selecting chemicals to test but also for information gathering and assessment. There is a need to develop thinking not only on sharing the cost of testing but more generally on how the burden of work can be equitably allocated. We cannot do everything at once and there is a need to develop priorities and a staged approach.

19. While there is great momentum in the OECD programme, there is much work to be done and certainly plenty of room for cooperation with other agencies.
20. In leading the discussion, the Session Chairman noted that the results of the Workshop will be put to the Chemicals Group and Management Committee in OECD for consideration and the rapporteurs will be particularly concerned in identifying points of principle and areas where further work might be required.
21. In approaching the question of international cooperation in the testing of existing chemicals, it was recognized that the first need is to carry out a critical review of the available information on an existing substance before attempting to identify what further testing may be required. Because such reviews are both expensive and time consuming it is important to share the burden of their preparation. It is important to achieve, as far as possible, the mutual acceptance of such reviews in much the same way as OECD has achieved agreement on the mutual acceptability of data. Agreements on the quality control of data and on those elements which should be included in reviews of possible hazard to man and the environment are important in this context.
22. Within IPCS, agreement has been reached on both format and the parameters to be used for the evaluation of hazard to health in the Criteria Programme. Lead and participating institutions as well as groups of experts are used in preparing these criteria documents. The IPCS criteria programme uses published data which has undergone peer review to assure its quality. Exceptionally, where data is essential but unpublished, the expert groups themselves serve the peer review function. Expert judgement and scoring have been used in the development of lists of chemicals selected for priority evaluation within IPCS but expert judgement tends to predominate. Priority lists of existing chemicals prepared by expert groups such as the IPCS/CEC Joint Task Force (Ispra, November 1980) list should be viewed as dynamic rather than permanent.
23. OECD work in the area of quality assurance of data is recognized and the wide use of OECD guidelines and principles of GLP should reduce the problem of the international acceptability of data in the future.
24. Existing international (and national) lists of priority substances have been drawn up for differing purposes and using a variety of criteria for selecting them. The development of internationally agreed criteria may be an area for future work (see topic III). However, three different kinds of chemicals were noted: –
    (i) those chemicals identified as causing problems; these are candidates for regulatory action;
    (ii) chemicals on which considerable data have accumulated so that assessments could proceed (similar to Class I);
    (iii) all remaining chemicals on which sufficient data are not immediately available. (Class II chemicals as defined previously).

    There might be several hundred substances in categories (i) and (ii) but there would be tens of thousands in category (iii).
25. In developing international programmes on existing chemicals, emphasis had been placed on dealing with the chemicals in the first category and this is likely to continue. However, this does not diminish the need to develop a programme on chemicals in the second and third categories.
26. Recognizing that the WHO criteria documents to date have dealt with health effects the meeting stressed the necessity for reviews of chemicals to deal with environmental exposure and effects as well, noting that this will involve different experts.

27. Hazard assessments must consider not only inherent toxicity but also the exposure potential. National assessments are necessarily confined to exposure situations arising in a particular country. International assessments may, by extending the consideration of exposure, throw additional light on potential problems.
28. The concept of decentralized centres of excellence which would include industry input was discussed as a means of assembling and reviewing available data and developing draft reviews. Advantages might include development of a quick review process. However, it should be recognized that, in part, the reasons for the wide acceptance of WHO documents is that they are not products of any one country or centre. Thus any decentralized concept will have to include procedures for avoiding too narrow a review.
29. Industry also needs to consider selection criteria as review and testing are necessary consequences of product development. Industry could play a major role in providing unpublished information on chemicals to be reviewed. Consideration should be given to developing incentives and mechanisms to facilitate this while protecting the proprietory value of some information although confidentiality may not be as severe a problem with existing chemicals as with new ones.
30. It was the sense of the meeting that there are advantages in international cooperation on this subject. The advantages include: –
    (i) sharing the burden or avoiding duplication of efforts, both of which save scarce resources;
    (ii) possibly drawing information and experience from a larger pool;
    (iii) casting a different light on a problem or approaches to its solution;
    (iv) certain substances require international consideration because of their environmental distribution;
    (v) few chemicals are produced and marketed in only one country;
    (vi) promoting international acceptability of data;
    (vii) avoiding barriers to trade.
31. There are possible problems including: –
    (i) slowness of response/action;
    (ii) varying national views on the significance of a problem, and appropriate policy approaches;
    (iii) fears over a loss of competitive advantage through disclosure of commercially valuable information to foreign competitors.

    Chemical substances which require international cooperation or action are likely to be those which are traded internationally, used in many different countries or have been widely dispersed in the environment.

    In some cases it is adequate to ensure that information generated and actions taken on the national level are adequately reported; in others, concerted international action may be necessary on specific chemicals, as OECD has done with PCBs. The aim should be the elimination of incompatible or duplicative actions by different nations.

Possible follow-up arising on Topic I

32. *(i) A joint meeting of the secretariats of the international organisations concerned with the potential hazards of existing chemicals would be useful. A necessary prerequisite is the careful identification of issues to be addressed. While it is recognized that international organisations work within the constraints of their own governing bodies this should not preclude cooperation*

and complementary programmes. Duplication of programmes must be avoided to ensure the best use of both experts and resources. OECD should consider taking the initiative in convening such a meeting;

(ii) The development of more effective ways to use existing information e.g. by pooling of information and by making it possible to have access to unpublished information held by industry; by ensuring its quality;

(iii) The development of guidelines for critical reviews of selected existing chemicals;

(iv) The development of principles and a mechanism which would lead to the wider availability and utilization of such assessments.

Topic II Analysis of the Legal and Administrative Powers to Control Existing Chemicals in OECD Member Countries

33. Mr Stanley Johnson reviewed the legislation of OECD Countries in the field of existing chemicals (based principally on the questionnaire prepared for the workshop). He indicated that, although there are gaps, the legal authority for governing all phases of the life cycles of existing chemicals exists in most member countries of the OECD. As examples of the gaps, he pointed out that some countries do not have provisions for environmental impact assessment, for reporting of information concerning risks posed by existing chemicals (e.g. Section 8 TSCA), and for applying testing requirements similar to those applicable to new substances to selected existing chemicals of priority concern (e.g. Section 4, German Chemicals Act).
34. Mr Johnson concluded his survey with some suggestions for specific activities on existing chemicals for OECD countries to consider. These are summarized below.
35. OECD should continue and strengthen its role in the area of existing chemicals, in cooperation with the activities of other international organizations not only because of its record in the field of chemicals but also because the vast bulk of chemicals are produced in and traded between OECD countries.
36. As a first step, OECD should organize an exchange of information of chemicals which are candidates for review on an international basis. This survey of existing data should be undertaken with the close collaboration of industry and should result in a "Candidate chemicals list".
37. As a second step, OECD should seek to establish a "Priority list of existing chemicals", i.e. chemicals which are strongly suspected of being dangerous to health or to the environment.
38. For those priority list chemicals that require further testing, the burden of that testing should be borne by industry which would therefore need to be closely involved and would have to work out appropriate systems of cost-sharing.
39. Once the list of priority chemicals has been established, OECD should help evolve appropriate international control strategies for substances on that list. Options range from labelling provisions through restrictions or limitations to prohibitions on marketing, import or use. A major effort should be made to achieve an internationally coordinated approach to each substance.
40. Concurrently with such action on priority chemicals, which must necessarily be limited in number, an attempt should be made to define and agree on selection criteria for reviewing and evaluating other chemicals that are candidates for inclusion on the priority list.

41. To avoid unnecessary expenditure of resources, consideration should be given to compiling a single international inventory of existing chemicals that would serve as the basis for determining "new" chemicals and also as the basic list from which chemicals would be drawn for consideration in accordance with the criteria discussed in the preceding paragraphs.

National Statements

42. Mr Langley (UK) pointed out that the UK has instituted an informal system whereby a small number of substances are selected for critical review. The selection criteria include social and political, as well as scientific, factors. The UK will begin to publish these reviews later this year. Harmonization of *regulatory action* on specific substances may not be feasible nor appropriate because social and political factors are paramount in regulatory decisions. The resources in the UK are largely committed to the review system referred to above and to the implementation of the notification scheme for new chemicals. It will be very difficult, therefore, to release any of these resources for *additional* work on existing chemicals. However, the UK is more than willing to share the results of its programme on existing substances where appropriate.
43. Dr Silano (Italy) explained that his country has a programme for examining selected substances. The assessments are carried out by advisory committees and the results are considered by the appropriate control authorities. Two lists of existing chemicals are currently being developed. The first is relatively short (about 140 chemicals) and includes all available information on each substance and an assessment based on that information. The second is much larger (several thousand substances eventually) and contains information likely to be useful in an emergency.
44. M. Deschamps indicated that the French authorities have the power to do whatever is considered appropriate to review and control existing substances. There is no national programme for formally selecting substances for review – each case is considered on its merits. Developing the minimum pre-marketing data (MPD), which has been accepted by the Chemicals Group and Environment Committee of OECD as the basis for assessing new chemicals, may not be relevant in the case of many existing chemicals. For existing substances, much may be known of use patterns and usually possible long-term effects are the principal concern and the latter are not covered in the MPD.
45. M. Exsteyl stated that in Belgium the national effort on existing chemicals was concentrated on the working environment but such work was a sound basis for extending protection more widely.
46. In introducing the discussion the Session Chairman reminded the meeting of Dr Hartkopf's request for guidance on whether more legal analysis is needed. In this context the following topics are offered as

possible follow-up work arising from Topic II: –

(i) the preparation of matrices of national legal provisions applicable to control existing chemicals at various stages of their life cycle (see appendix to Mr Stanley Johnson's paper);

(ii) comparative case studies of the control of selected existing chemicals, in order to have examples of the implementation and enforcement of laws applicable to existing chemicals in OECD countries;

(iii) the efforts of various OECD countries to integrate the implementation of their legal powers in order to apply these to chemicals in a coordinated way, to a particular chemical, to a particular kind of industry, or in a particular geographic region;

(iv) the extent to which EEC Directives and OECD Council actions concerning chemicals are incorporated into national laws so that their objectives are achieved, and the procedures that exist, or should exist, for assuring that they are incorporated;

(v) the extent to which legal or administrative arrangements concerning the provision of information about new chemicals (including confidentiality) are applicable to existing chemicals;

(vi) the preparation of catalogues of regulated substances, (including pesticides) in OECD countries, or those under consideration for regulation, as a means of developing a candidate chemicals list; the catalogue should cover the action applicable to the chemical, its status, the reasons(s) it is being carried out, or contemplated, and the office to contact concerning the activity;

(vii) the extent to which laws applicable to existing chemicals are susceptible to implementation at the local, state, or national level and how these various levels of government collaborate in the implementation;

(viii) the relative emphasis given to human (including occupational) and environmental health in the laws of OECD countries, both as they are written and as they are implemented;

(ix) the extent to which there are differences in levels of proof of risk required before imposing controls in different OECD countries, and the extent to which varying economic, political and social factors are taken into account in these countries.

47. In dealing with many existing chemicals at the international level the fact that they often represent a significant established economic interest should be taken fully into account. In addition they may already be subject to control in various ways by public authorities and this too must be considered. This requires an intimate knowledge of the varying national political, legal, administrative and economic contexts. The various topics mentioned above, if dealt with in an international perspective, could contribute significantly to our knowledge.

Topic III Identification and Quantification of Criteria for Selecting Existing Chemicals for Gathering Information, Testing and Assessment on a Case by Case Basis

48. This topic was generally considered the most important in the Workshop. There were too many papers to attempt to summarise each one here and it became clear in the discussion that many different and sometimes contradictory views were held. This indicates the need for further work on this topic and this point is picked up in the possible follow-up action at the end of this section of the report. However, some mention must be made of the contributions from the USA (Dr Bracken) and from Japan (Mr Kobayashi) as these countries have unique experience in selecting substances for testing. The scoring system developed by the Interagency Testing Committee in the United States is an attempt to apply agreed criteria relating to potential exposure and potential effects in an equitable and open fashion while including expert judgement as appropriate. The "openness" or "transparency" of the review is an essential feature since industry is charged with any testing requirement which emerges. The Japanese system

places great emphasis on criteria relating to exposure and in particular, on those relating to indirect exposure to man through the food chain. Hence persistence and bioaccumulation are key elements in the information both in leading to selecting for testing and in any testing programme resulting from such selection.

49. In general, the reasons for selecting existing chemicals for review and testing were agreed to be:
    (i) to identify those chemicals which may pose actual or potential risks or injury to human health or to the environment;
    (ii) to identify those chemicals for which available information is either sufficient for the purpose of hazard assessment or insufficient;

    but several factors make agreement on the *selection procedures* difficult. For example, estimates of the number of substances on the market vary from 30,000 to 70,000 and to achieve a manageable number, the selection procedure must be very selective; there are national variations in the patterns of production, use and release into the environment; when deciding whether data are sufficient or insufficient the dividing line may not be precise leaving room for variation in interpretation.
50. The OECD Step Systems Group has defined the hazard of a chemical as "a function of two broad considerations, the potential of the chemical to harm biological systems and its potential for exposure". It follows that the criteria for selection should include the two broad categories of effects on man and the environment and of exposure of man or other "targets".
51. Information on effects is generated in a number of ways including toxicological studies in animals, plants and microorganisms, human epidemiology, occupational health surveys, accidental human exposure, accumulation in biological systems, and structure activity relationships.
52. Information on exposure may be derived from a number of sources including measurement and monitoring of environmental levels (in water, air etc.), quantities of chemicals produced, used and released into the environment, studies and models of behaviour in the environment (transformation and transport processes) and measured levels in man and other organisms (biological monitoring).
53. In addition socioeconomic factors were recognized as a third category of criteria.
54. The social factors include concerns arising from public perception of chemicals and potential hazards, the awareness of particular groups concerning their exposure to chemicals and other political pressures. Economic factors include the consideration of risk/cost/benefit and the implications of control measures (dislocation costs).
55. The relative importance (weighting) of the criteria often reflect national conditions and the purpose for which the criteria are used (e.g. environmental protection, occupational health protection). Criteria have been applied in a formal structured way (e.g. matrices, scoring systems); groups of experts may be used to complement this at appropriate stages. Such criteria may also be applied qualitatively by a group of experts applying their collective judgement. The latter system avoids the problems associated with "weighting" but is often considered less "transparent".
56. Following the selection of an existing chemical for review, the initial step is to consider the available information relevant to the factors, motivating the review action. This information would include the relevant scientific literature and unpublished data held by government agencies, industry etc. This initial step identifies what further investigation and testing, if any, are required to provide the

data necessary for a meaningful hazard assessment. In turn, the overall assessment will clarify the various options for, the nature and the extent of, appropriate control measures.

57. Priority lists based on one or more of the categories of criteria set out above are an often-used device in administration to come to grips with the vast number of existing chemicals. Priority lists have been compiled for a variety of purposes (e.g. lists of carcinogenic substances, list of water pollutants, list of highly toxic chemicals as an aid in contingency planning in the event of an accident).
58. Not surprisingly such lists vary widely. They are rarely static, revisions occurring in the light of new knowledge or with changing emphasis on one or more of the selection criteria.

Possible follow-up arising from Topic III

59. *(i) Further work on identifying selection criteria; although there are divergent views on what are appropriate criteria in different circumstances, it is agreed that the differences should be analysed, the common ground identified and harmonization actively pursued.*

(ii) Although there are differing views on the priority list approach, if it is accepted, then one option which might lead to a more concerted approach in all OECD member countries to the choice of existing chemicals for further study would be to use existing international lists as a starting point e.g. the WHO/IPCS ("Ispra") list might be an agreed starting point for chemicals worthy of and capable of review (Class I chemicals): the TSCA Inventory of chemicals on the market might be the source from which a further selection (of Class II chemicals) might be made.

OECD is considered to be a suitable agency to develop thinking in these areas.

Topic IV Identification of Resource Needs for Testing and Evaluating Existing Chemicals

60. The first presentation (by Dr Welinder) was based, in part, on replies to the questionnaire sent out by the organizers of the Workshop. It deals exclusively with chemicals on which there is considered to be insufficient information (Class II). On the basis of a specific set of assumptions, and using certain estimates of costs and numbers of chemicals, he developed an estimate of the total cost of testing the existing chemicals likely to be of interest. This ranged from about $ 1 billion to more than 5 $ billion.
61. An unpublished survey of the European Chemical Industry, prepared by an OECD consultant, indicates that the $ 400 million spent on testing in 1980 amounted to 3.5 % of the estimated R & D costs of the European Chemicals Industry. Only 15 % of the work was concerned with industrial chemicals, the remainder being concerned with pharmaceuticals, pesticides and food additives. This report suggests that existing testing capacity will not be exceeded before 1984.
62. The second presentation (by Dr McCollister of BIAC) reviewed the activities of eight national and international institutions, both public and private, which are testing existing chemicals, largely on a voluntary basis. Annexes to this paper both list the chemicals selected for testing, and identify the individual chemicals which are being (or have been) tested. Industry already does much testing and has data on existing chemicals which it is willing to make available when a definite need has been established. Information based on experience in use can make up for apparent deficiencies in test data. He stressed the need to employ efficiently the

limited resources available for testing and assessment and pointed out the importance of selection criteria in ensuring that this happens. He suggested that attention should be focussed on the study of chronic, carcinogenic and reproductive effects. In some instances, government may have to sponsor testing.

63. The role of OECD, working closely with other international agencies, might be to consider broad policy questions and the development of "guidelines" for selection criteria but the actual selection of chemicals should be left to national governments and to institutional programmes some of which are already underway with support from the chemical industry. OECD could act as a "clearing house", providing a mechanism for consulting on and consolidating lists of "priority chemicals" exchanging information on selected chemicals and on programmes of review and testing.
64. In a national presentation, the UK reviewed their experience of a 4 stage system of data appraisal. This is considered a necessary prerequisite to any consideration of the need for the testing or for any control action. Each appraisal of an existing substance takes between one and two man years (at a cost of between $ 40,000 and $ 60,000). The UK intends publishing the reports arising from these appraisals. Sharing the burden of such appraisals among countries and a greater degree of mutual acceptance of the results of the appraisals could do much to reduce the costs to individual national agencies.
65. In the general discussion which followed, many points were raised but they centred around three broad themes: the costs of a programme of assessment and testing of existing chemicals, the resources likely to be available and how the burden might be shared.
66. Costs depend critically on the numbers of chemicals selected for review, the depth of that review and on the extent and nature of any testing required. In this context selection criteria are clearly of paramount importance. The cost-effectiveness of collecting existing information as opposed to generating it afresh was questioned where the quality assurance of the data was poor. The development of criteria to be applied in selecting existing data and on ensuring its quality could save time and effort and avoid testing or re-testing. The problem of requiring test data on small volume/low cost chemicals was mentioned. Varying views were expressed on the relevance of the MPD or base set data elements for existing chemicals. The usefulness of general, agreed formats for the presentation of data and for conducting reviews was discussed. Some of the participants considered that these would be useful tools in the analysis of risk (on a national basis).
67. On the resources available for testing, some representatives of industry and of government expressed the view that the statutory testing of new substances left only limited testing capacity for existing chemicals and BIAC asked for the opportunity to review the OECD consultant's report before publication.
68. No clear concensus emerged on cost sharing although international co-operation is seen as an important way in which the costs of assessment and testing might be reduced. The pooling of experience and agreements on mutual programmes to avoid duplication of effort could better focus national efforts on the appraisal of data on existing chemicals while, at the same time, reducing the delay in tackling the back-log of substances and increasing the number of substances appraised. Again, the importance of co-operation between the Secretaries of international organizations was stressed. By running complementary programmes with agreed priorities and methods of working together, they could do much to reduce the burden on national authorities.

Possible work arising from Topic IV

69. *(i) A study of the costs arising from the various options for programmes on the assessment and testing of existing chemicals. This could include an evaluation of the resources needed relative to those thought to be available;*
(ii) Development of guidelines on the selection of priority chemicals for appraisal/testing;
(iii) Development of a format for data appraisal;
(iv) Co-ordination of the efforts of national governments, international agencies and the chemical industry for comparing and consolidating priority lists of existing chemicals for appraisal and testing. In this context OECD might increase its activities as an "information broker" and consider whether mechanisms need to be developed to facilitate the sharing of the burden of appraisal and testing. This might be the basis for a further workshop.

Concluding Session

70. In his concluding remarks, the General Chairman, Mr Menke-Glückert, reminded the Workshop that Dr Hartkopf had seen this as only the beginning of international consideration of the subject. He believed that it had been a good beginning. Many issues had been discussed; some had been clarified while others had been shown to require further work. In particular he attached importance to the need to:
(i) reach agreement on a list of dangerous chemicals falling into Class I (where sufficient information exists to identify and assess problems). The IPCS/CEC ("Ispra") list might be the starting point;
(ii) agree on the scope of reviews of chemicals as a prerequisite for sharing the burden of their preparation;
(iii) establish selection criteria for screening out those likely to be dangerous from the vast array of substances falling into Class II (those where insufficient information exists to review the substances effectively);
(iv) solve the problem of confidentiality.
71. Anyone who may have come to the Workshop with doubts about the need for international co-operation on the problem of existing chemicals or about the willingness of nations to come together to tackle it, should have had those doubts dispelled. Nations and, in particular, international organizations, have a duty to tackle this in the most cost-effective way. No one favours duplication of effort or the development of "information dumps" guarded by armies of civil servants.
72. He foresaw the need for a follow-up workshop perhaps in about a years time and focussing on specific aspects of the problem which had been identified at this Workshop as subjects worthy of further study. The Workshop has produced valuable guidance to the German authorities on the issues which they should address in the feasibility study which they planned to carry out. However, the main impact of the Workshop is the contribution which it will make to the work of the Chemicals Programme in OECD. The proceedings of the Workshop and the proposals for further work which have emerged during it would be a sound basis for the future discussions in OECD. He hoped that the other international agencies would also be able to use this material in planning their programmes.
73. He concluded by thanking, on behalf of the German Authorities, all of those who had participated in the Workshop.

Summary of Possible Work Arising

74. *The OECD should take the lead in organizing a joint meeting of the secretariats of the international agencies with an interest in the problems of existing substances. In particular every attempt should be made to ensure that the International Programme on Chemical Safety (WHO/ILO/UNEP) and the work on existing substances within the OECD Chemicals Programme are complementary. The aim should be to share the burden, conserve scarce resources and provide the best possible service to national governments. (Paragraphs 2, 19, 30, 31, 32, 35, 63, 68, 69, 71).*
75. *There is a need to consider further and, if possible, to develop internationally agreed criteria for selecting substances for review and, as appropriate, for testing. If such criteria can be agreed, they might be applied internationally to identify substances for review/testing. The concept of Class I substances (those where sufficient information exists to proceed with an assessment of hazard) and Class II substances (those where information is insufficient for the determination of potential hazard) may be useful in this respect. (Paragraphs 13, 18, 22, 24, 29, 40, 48–59, 62, 63, 69, 70).*
76. *Contradictory views were expressed as the value of "international priority lists" of substances which indicates the need for further discussion. If the concept is accepted, then consideration should be given to how far work that has already been done on listing existing substances can be used as a basis for the international harmonization of approaches to, and cooperation on, the problems posed by existing substances. (Paragraphs 22, 36, 37, 40, 41, 43, 46(vi), 57, 58, 59, 62, 63, 70.)*
77. *It was recognized that a critical review of what is known about a substance is a pre-requisite before deciding on the need for further testing and the need for control. At present, such reviews tend to be conducted nationally (although the Criteria Programme of the IPCS is relevant). Consideration should be given to the possibility of sharing among nations the burden of such reviews with the intention of working for a greater degree of mutual acceptance of the results. Work may be needed to agree what should be included in such reviews and their format. (Paragraphs 17, 21, 22, 26–32, 36, 42, 43, 44, 56, 64, 66, 69, 70.)*
78. *Principles and mechanisms to allow access to and use of such reviews should be developed. As a first step in sharing the burden of preparing reviews, OECD should consider setting up a "clearing house" where member nations, international agencies and industry could pool resources and experience and, as appropriate, agree on complementary programmes of reviews. Such a clearing house may also be valuable in co-ordinating existing programmes for the testing of existing substances. (Paragraphs 21, 29, 32, 42, 62, 63, 64, 68, 69.)*
79. *The role of industry is important. In the first instance they are responsible for the safety of their products. As a result chemical companies often have a great deal of relevant information about their products but not all of this is published. Ways of tapping the expertise in industry and gaining access to unpublished information need to be worked out. Such mechanisms must allow for the protection of legitimate proprietory value of some information. (Paragraphs 3, 28–32.)*
80. *There are problems over the quality assurance of information generated before systems of good laboratory practice developed. This is particularly so for unpublished information which has not been subjected to peer review. OECD should consider whether principles and mechanism can be developed to improve the quality assurance of such information. (Paragraphs 15, 21, 22, 23, 32, 66).*

81. *There are significant and well-established economic interests associated with many existing substances. In addition, any increase in activity on the appraisal or testing of such substances is likely to require significant resources. These factors underline the importance of sound economic analyses of the various options likely to be considered. An essential part of such analysis should be an evaluation of the resources needed relative to those available. The role of international cooperation and harmonization as a factor in reducing costs should also be considered. No consensus on the problem of cost-sharing emerged and this subject may merit further study. (Paragraphs 30, 38, 47, 54, 60–69.)*

82. *Session II threw up many ideas for further legal analysis. Some of these might be considered within the current Chemicals Programme in OECD; others fit, in whole or in part, within the areas set out above. However, there is scope for a further study which should be seen as under-pinning any work programme developed in OECD. (Paragraphs 33, 46, 47.)*

CHAPTER I

International Co-operation in Controlling Specific Existing Chemicals

Michel Mercier, read by Jiri Parizek

Present and Planned Activities of the International Programme on Chemical Safety (IPCS) on Existing Chemicals

I should first like to underline some points that may sound obvious but which are essential for understanding the character of this Programme. The IPCS is a joint venture of 3 international agencies of the United Nations family, namely, the International Labour Organisation (ILO), the United Nations Environment Programme (UNEP) and the World Health Organization (WHO). This does not mean that it is a joint venture of the secretariats of the 3 organizations, but rather a coordinated effort of their Member States, and it is up to those Member States to decide which aspects of chemical safety call for a coordinated global approach.

As will be explained later, the World Health Assembly, the WHO Executive Board and the IPCS Programme Advisory Committee have all recognized evaluation of the effects of chemicals, on the basis of existing knowledge, as the fundamental issue requiring a global approach, but this IPCS activity – which is of particular relevance to the present meeting – is entirely dependent on inputs from other national or international activities of Member States and on the expertise available in, and the results obtained by, their scientific institutions. It follows that the establishment of efficient information channels is essential for successful implementation of this and other components of the IPCS. For this reason, we are very grateful for this opportunity to present some basic facts on the IPCS.

A. Background of the IPCS

During the last 25 years WHO has been concerned about the evaluation of the health effects of chemicals, as one of the bases for planning and implementing national environmental health programmes. In this connexion, it may be appropriate to quote from a report of the WHO Director-General[1] and list some relevant activities.

Annual meetings of the Joint FAO/WHO Expert Committee on Food Additives have been convened since 1956, while the Joint FAO/WHO Meeting on Pesticide Residues has been functioning regularly since 1961. At the same time, new insecticides for the control of vectors of disease have been evaluated jointly with the FAO and data sheets issued providing basic information on safe use. A classification of pesticides by hazard was adopted by the 28th World Health Assembly in 1975 (resolution WHA28.62). The Joint ILO/WHO Committee on Occupational Health, in its 6th Report (1969), evaluated recommendations and standards for occupational exposure to airborne toxic substances[2]. More recently (in 1977), a programme was initiated on internationally recommended health-based limits in occupational exposure to toxic substances. The International Standards for Drinking Water, first published in 1958, revised in 1963 and 1970[3], are now again being updated. Several expert committees on air pollution have been convened since 1957, while the International Agency for Research on Cancer (IARC) has since 1971 been evaluating the carcinogenic risk of chemicals to man.

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1 Document EB63/20

2 WHO technical Report Series No. 415, 1969

3 World Health Organization. *International Standards for Drinking Water*, 3rd ed., Geneva, 1971

An integrated and expanded programme on the health risks associated with total exposure from various media (air, water, food, the workplace, the home) to specific toxic agents was initiated in 1973 in collaboration with more than 20 WHO Member States and with the support of UNEP. Thus the *Environmental Health Criteria* (the publications resulting from this activity) assess existing data on the relationships between exposure to environmental agents and human health, provide guidelines for setting exposure limits consistent with health protection, identify gaps in knowledge, point out research needs, and attempt to harmonize toxicological and epidemiological methods. Also included in the *Environmental Health Criteria* are preliminary reviews that attempt to identify new or potential hazards from chemicals and other agents likely to be used increasingly in industry, agriculture, and the home.

Levels of chemicals in air, water and food have been measured by WHO since 1975 within the framework of the UNEP programme known as the Global Environmental Monitoring System (GEMS). More recently biological monitoring has been initiated by WHO.

The promotion of appropriate methods for such evaluations has been an essential component of practically all the above-mentioned WHO activities, and this has resulted, in the last 25 years, in a number of technical reports and guidelines on the general principles and methods of testing and evaluating food additives and contaminants, on evaluating teratogenicity, mutagenicity and carcinogenicity and, more recently, on environmental and health monitoring, early detection of health impairment in occupational health, chemical and biochemical methods for assessing the hazard of pesticides to man, and methods used in establishing permissible levels of occupational exposure. In addition, the *Environmental Health Criteria* series includes a monograph on the principles and methods for evaluating the toxicity of chemicals, part 1 of which was published in 1978[1], while a similar monograph on epidemiological methods for investigating the health effects of environmental agents is being prepared in collaboration with the International Epidemiological Association.

Apart from the global activities already mentioned, the WHO Regional Offices, particularly those for Europe and the Americas, are paying increasing attention to the problem of hazardous chemicals. And it should be mentioned, if only briefly, that several other UN agencies have a long tradition in assessing the harmful effects of chemicals, particularly at the workplace, in agriculture and in ecosystems.

The origins of the IPCS go back to resolution WHA30.47 (1977) which reflected the concern of the World Health Assembly about the growing use of chemicals and environmental pollution, and which requested the WHO Director-General to study long-term strategies in this field, *inter alia* with a view to accelerating and making more effective the evaluation of health risks from exposure to chemicals.

In 1978, the World Health Assembly in its resolution WHA31.28 requested the Director-General to implement a programme on this subject through a Central Unit at WHO HQ and a network of national institutions.

In 1979 the WHO Executive Board, by its resolution EB63.R19, endorsed a report of the Director-General that proposed the content and structure of the new programme and the measures for implementing it. Hence, the IPCS, based on existing programmes and activities, operates with the active participation of national institutions under the

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[1] World Health Organization. *Principles and methods for evaluating the* toxicity of chemicals, Part 1, Geneva, 1978 *(Environmental Health Criteria 6)*

guidance and coordination of a Programme Advisory Committee and the WHO Central Unit. Resolution EB63.R19 also called for negotiations with other UN agencies in order to secure their collaboration and to coordinate all activities on chemical safety.

The IPCS became operational in 1980 with the establishment of the organizational bodies designated in the report of the WHO Director-General.

B. Programme objectives

The present and future objectives of the IPCS can be summarized as follows:

1. to carry out and disseminate evaluations of the effects of chemicals on human health and on the quality of the environment;
2. to develop guidelines on exposure limits (such as acceptable daily intakes, and maximum permissible or desirable levels in air, water, food and the working environment), for several types of chemicals including household products, contaminants, cosmetics, food additives industrial chemicals, toxic substances of natural origin, plastics, packaging materials, and pesticides;
3. to develop methods that could produce internationally comparable results, particularly as regards epidemiological and experimental laboratory methods, the effects of exposure to multiple chemicals and the extrapolation of experimental data to effects on human subjects;
4. to coordinate laboratory testing and epidemiological studies, when an international approach is appropriate, and to promote research on dose-response relations and on mechanisms of the biological action of chemicals;
5. to develop know-how for coping with chemical accidents and to promote effective international cooperation in this field;
6. to promote technical cooperation with respect to specific issues concerning control of toxic substances in Member States;
7. to promote training and development of manpower in the field of toxicology.

These are indisputably ambitious objectives, but it must be emphasized that the IPCS is not an entirely *de novo* activity. The 3 Cooperating Organizations (COs), i.e. ILO, UNEP and WHO, have already a distinguished record of results in evaluating the safety of chemicals; the IPCS aims at strengthening the existing activities and initiating new ones.

To achieve these objectives, the necessary resources, financial and human, must be provided by the Member States. The response so far is encouraging, a number of countries having already made substantial voluntary contributions to the Programme.

C. Organizational structure of the Programme

The following elements make up the organizational structure of the IPCS.

1. The *Central Unit* (CU) is responsible for the overall management and cohesion of the Programme. Its main functions are:
   a) to develop plans and programmes of work;
   b) to coordinate the Programme components located at national and other Lead Institutions (LIs) and at Regional Offices, and to ensure liaison with other international organizations;
   c) to provide technical and scientific support for the Programme.
2. The *Inter-Secretariat Coordinating Committee* (ICC) is a managerial body on which the 3 COs are represented and which is chaired by the Manager of the CU.
3. The *Programme Advisory Committee* (PAC) is composed of 20 members appointed by the Director-General of WHO in consultation with the Executive Heads of the

other 2 COs. As its name implies, the PAC advises the Executive Heads of the COs on policy questions and in setting the overall goals and global priorities of the programme.

4. In contrast, the *Technical Committee* (TC) consists of the directors of the LIs and is the operative organ with multidisciplinary scientific and technical capacity. The TC prepares the annual workplans and sets operational priorities with a view to achieving the policy goals set by the PAC.
5. The working mechanism of the IPCS is a network of LIs and Participating Institutions (PIs), designed to achieve an organized distribution of work among the countries actively participating in the IPCS. The LIs are designated by the Executive Heads of the 3 COs after negotiation with the respective governments, to ensure that IPCS commitments are met, and that support (including sufficient national staff) is provided. In designating an LI, internationally recognized competence in a specific field is the criterion of choice. The Programme Manager will delegate to LIs responsibility for specific IPCS activities.
6. Sub-networks, made up of PIs and designed for specific programme areas, are established to work with the LIs and are guided and coordinated by the LIs.

Two international LIs have been designated. The IARC is the LI for chemical carcinogenesis, and part of its work under this heading will be an extension of the established Monographs on the Evaluation of Carcinogenic Risk. In addition, the IARC will participate in selecting further priority chemicals and in IPCS work to improve methods for testing chemicals. The International Register of Toxic Chemicals (IRPTC) of UNEP is operating as LI for the collection, retrieval and dissemination of information. There are now more than 10 LIs, mostly in the OECD countries represented at this meeting.

D. Programme outputs expected in the immediate future

A start has been made to extend international activities on the health and environmental evaluation of chemicals. In the immediate future, it is hoped that the outputs of the IPCS will be as follows.

1. *Evaluations of the effects of chemicals on human health and the environment*
   These may vary in form from comprehensive criteria documents to singlesheet risk assessments of new chemicals. It cannot be overemphasized, however, that every output of an LI (criteria document, toxicological monograph etc.) will, after approval by the Manager CU, be sent for review and comment to national focal points and, as appropriate, to other specialized agencies of the UN system, to intergovernmental organizations and to selected individual experts. A second draft will then be prepared on the basis of the comments received, and the document finally subjected to evaluation by a task group composed of independent international experts, proposed by Manager CU and nominated by the Director-General of WHO, and serving in a personal capacity, before final acceptance and publication. To date, about 14 classes of chemicals or individual chemicals have been evaluated in the *Environmental Health Criteria.* In addition to the publications already issued, some 25 studies are at various stages of preparation. A detailed plan of activity was drawn up following the 2nd session of the IPCS Technical Committee in February 1981[1], in accordance with the recommendations of the Joint IPCS/CEC Task Force on Priority Chemicals, that met at Ispra, Italy, in November 1980[2], and existing

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1 WHO document EHE/81.21
2 WHO document EHE/81.18

programmes. The evaluations of food additives and pesticide residues in food previously mentioned constitute another important IPCS input under this heading.

2. *Guidelines on appropriate methods for exposure measurement and assessment, on toxicity testing, epidemiology studies, and risk assessment and hazard evaluations*
   Close coordination with the several organizations actively working in this field has been established, e.g. the Commission of the European Communities (CEC) and the Organization for Economic Cooperation and Development (OECD), or will be established, e.g. the Council for Mutual Economic Assistance (CMEA), and will be maintained, to ensure a collaborative approach and to avoid costly and unnecessary duplication.
3. *Manpower development*
   Under this heading, the WHO Regional Office for Europe (EURO) is assuming the global role within the framework of the IPCS.

To conclude, it should be stressed that a more stringent evaluation of the chemicals to which we are exposed is needed by all Member States, and there is no doubt that, for countries unable to make such evaluations, an international assessment is more acceptable than one carried out by another national authority. Consistency in testing will facilitate comparability and acceptance of the data obtained in different countries, and will promote both international trade in chemicals and the standardization of control measures.

The increase in the number of accidents involving toxic chemicals makes it imperative to share our expertise and experience, and the IPCS provides an international forum for doing so. The joint efforts of the Member States of the IPCS cooperating organizations, as well as other related international activities, should gradually produce visible results in this respect.

J. Ian Waddington

The Programme on European Co-operation on Environmental Health Aspects of the Control of Chemicals

1. Introduction

Following the resolution adopted at the twenty-ninth session of the Regional Committee in Helsinki in September 1979, the Regional Office launched an intensive programme on Toxic Chemicals Control.

Funds available for this purpose under EURO Regular Budget were considerably amplified by voluntary contributions made by several European governments for this programme. The UNDP approved the project on European Cooperation on the Environmental Health Aspects of the Control of Toxic Chemicals. Funds earmarked by the UNDP for this project are used to facilitate participation in the programme of those countries which are entitled to UNDP support.

In line with the Regional Committee's Resolution, the regional activities related to environmental health aspects of the control of toxic chemicals are centred on:

a) development of trained manpower of all categories, including medical toxicologists;
b) contingency planning for emergencies involving the release of chemicals into the environment;
c) development of health aspects of environmental impact assessment;
d) collaboration and exchange of information concerning the development of methodologies and control procedures.

The basic task of establishing dose-response relationships and health criteria is the function of the Central Unit for the International Programme on Chemical Safety (IPCS) in WHO Headquarters in Geneva. It is expected that the regional programme will utilize the outputs of that activity and may contribute to it, but they should not duplicate it. Therefore, the regional programme is centred on problem-solving rather than on basic investigations of health effects.

Specific activities under each of the above priority headings implemented or launched during 1980 and 1981 are described below.

2. Programme Planning and Priorities

The establishment of priorities for toxic chemicals control in Europe is an important component of the European Programme on Environmental Health Aspects of the Control of Chemicals, being carried out by the WHO Regional Office for Europe in conjunction with the UNDP-supported project on this subject. Fig. 1 shows the flowchart of activities leading to the publication of a document on priority setting.

The Consultation on Priority Problems in Toxic Chemicals Control in Europe was organized by the WHO Regional Office for Europe with the support of the Austrian Government. The meeting was held in Baden, Austria, from 3 to 6 November 1980 and was chaired by Professor M. Haider. Dr. J. Daimer welcomed the participants on behalf of the Austrian Government.

The purpose of the Consultation was to establish priorities for investigations and action by the national institutions and government agencies concerned.

The discussions were based on a comprehensive background study aimed at identifying and defining the toxic chemical problems which arise during the entire economic cycle

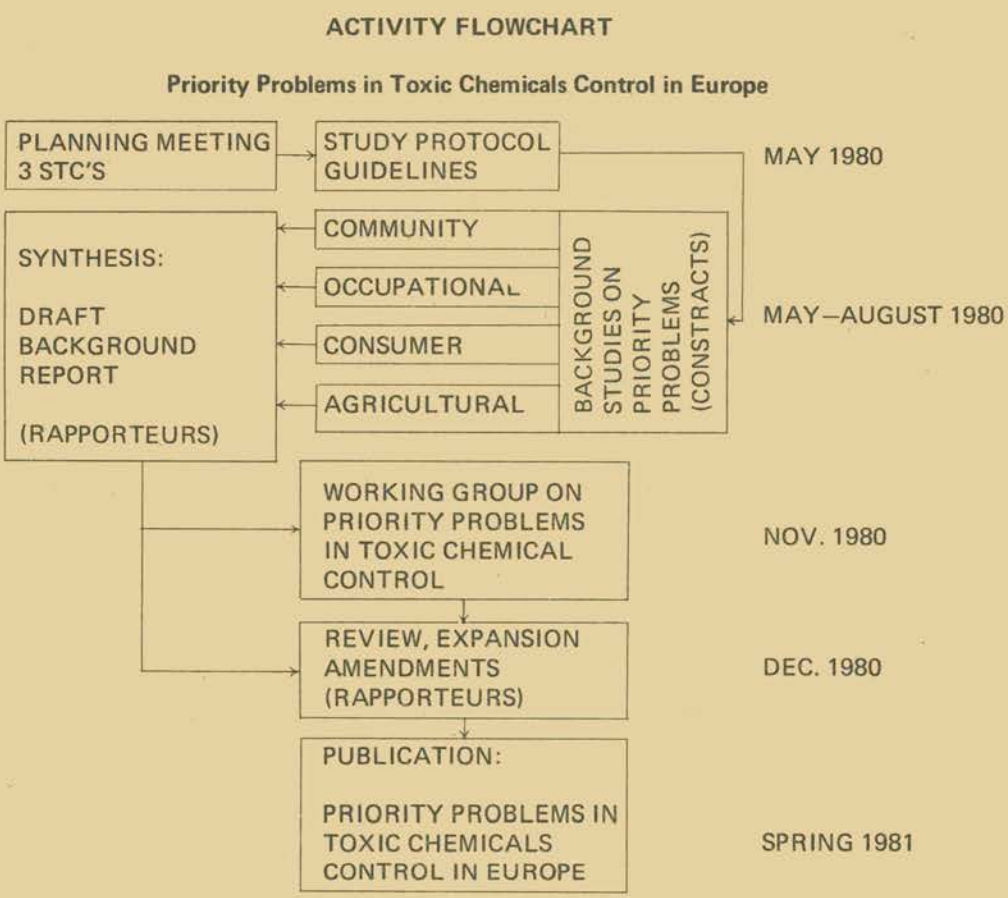

Figure 1

of extraction of raw materials, primary and secondary manufacturing, storage, distribution, consumption or use and, finally wastes disposal. At each stage, various categories of the population, e.g. workers, consumers and/or members of the community, may be exposed to toxic chemicals contained in the raw materials, products, by-products or wastes. These toxic chemicals may affect the various groups by any one or a combination of routes, such as food, contact, water, air or soil, producting a range of known or suspected health effects.

An important element in the study was an attempt to identify major constraints which prevent the solution of the problems, such as lack of precise knowledge of sources, exposure and effects, inadequate technology for prevention of exposure, excessive cost of preventive measures, cost or other disadvantages of substitutes or alternatives, lack of adequate legislation or regulation, and considerations of trade and competition.

The result of this effort was presented in the form of a multidimensional matrix identifying the products and processes which involve exposure to toxic chemicals, the types and routes of exposure, the categories of population affected, the types of effect and the predominant constraints on preventive action. It became clear that the multiplicity of sources, chemicals and their effects is such that any attempt to produce a

complete catelogue at this stage would be self-defeating. Therefore, the background study was not exhaustive but rather meant to develop a rational approach to the problem as a basis for setting priorities.

The discussion at the meeting was structured into three major sections, divided according to the types of population primarily exposed, i.e. workers, consumers and members of the community.

It was stressed that the above classification, useful as it is for the purpose of analysis, is arbitrary because individuals may belong to more than one of the above categories and, thus, be subject to multiple exposure.

An attempt was made to illustrate this by analysing one major human activity, i.e. "agriculture", where occupational, community and user types of exposure are closely interrelated and superimposed. The relationship between exposure and sociocultural aspects was highlighted in discussing problems arising in the use of pesticides in less developed countries.

The Consultation stressed the importance of international cooperation in dealing with priority problems in toxic chemicals control in Europe. The WHO European Regional Programme on Chemical Safety was considered the appropriate vehicle for achieving pan-European collaboration in this field.

The objectives of the regional programme on toxic chemicals control were considered to be highly relevant to the perceived priority problems in Europe, and the foreseen outputs and activities to be appropriate for the creation of a framework of regional cooperation in dealing with these problems.

It was felt that the priority problems identified by the Consultation were relevant to European countries, including the less developed ones, and that full participation of these countries in the regional programme would be essential for its success. The Consultation noted with satisfaction the current support of UNDP for this purpose and welcomed the prospects for continuation and extension of this support.

The Consultation noted with satisfaction the donations made by certain countries for the European component of IPCS and expressed the hope that the number of countries making voluntary contributions would increase in the future.

The Consultation noted with satisfaction the coordination of the European component of the global work of IPCS and the cooperation achieved with a number of intergovernmental organizations, and expressed its hope that the cooperative effort would be further broadened and strengthened.

The Consultation noted with approval the recommendation of the IPCS technical committee that the Regional Office be entrusted with global responsibility for elements of the programme, viz: manpower development and contingency planning for response to accidents and emergencies involving release of toxic chemicals.

The Consultation identified priority problems requiring urgent consideration and attention by the governments and national institutions concerned, IPCS and other organizations, as listed in the recommendations cited in the Summary Report (see Annex 1).

3. Manpower Development and Training

3.1. Background

Safeguarding human health and environment against deleterious effects of potentially toxic chemicals requires extensive testing and evaluation of toxicity of chemicals as

well as adequate control mechanisms. These indispensable activities are presently hampered by lack of personnel adequately trained to perform the multitude of tasks involved in evaluation and control of chemicals.

Since the awareness of the need for evaluation and control emerged very recently, there is little precedent and experience in developing professional and auxiliary personnel needed for the job.

In well established professions such as, for example, medicine, engineering or law, the designation "physician", "engineer" or "lawyer" imply a person possessing certain skills and capabilities acquired by a certain process of education, training and experience and performing a reasonably well defined range of functions and tasks.

The word "toxicologist", on the other hand, is interpreted in various countries and various societies in totally different ways, depending on recent historical developments governed, in many cases, by purely local circumstances or by chance.

At present, toxicologists come from many different backgrounds, such as medicine, biological sciences, chemistry, pharmacy or even nuclear physics. Some become toxicologists after formal academic specialist training; other through more or less structured apprenticeship programmes, while still others acquired the necessary capabilities from the experience of doing the job, supplemented by reading scientific and technical literature.

Similarly, the functions and tasks performed by toxicologists vary widely, ranging from interpretative and advisory functions at the highest levels of decision-making to performance of routine analytical tasks.

It is generally recognized that not all the functions related to testing, evaluation and control of chemicals are, can or should be performed by toxicologists. A wide range of other professions must be involved in this truly interdisciplinary activity.

Therefore, in addition to developing a core of professional toxicologists of various categories, it will be necessary to impart various degrees and types of knowledge of toxicology to a wide range of people who are involved in various degrees with chemicals control in their normal work. These include biologists, chemists, zoologists and technicians in the laboratories, public health and occupational health inspectors, agricultural and environmental inspectors and, last but not least, decision-makers who are faced with a very difficult task of making far-reaching decisions, often on tenuous and always on imperfect evidence.

Figure 2 shows the main components of our manpower development programme, which is described in some detail below.

3.2. Occupational Profiles

The objective of this activity is to define the final product or products of the manpower development programme, viz "the toxicologist" and the various categories thereof.

As mentioned in paragraph 2 above, there is presently no broad consensus on this subject. It is necessary to define the profession in objective, widely applicable terms, namely in terms of tasks to be performed and skills required for the performance of these tasks.

By grouping these tasks according to selected criteria, professional profiles of various categories of toxicologists may be obtained.

MANPOWER DEVELOPMENT

OCCUPATIONAL PROFILES	DEMAND	RESOURCES AND TOOLS
ANALYSIS OF TASKS & SKILLS	ASSESSMENT OF FUTURE DEMAND	POST-GRADUATE PROGRAMME
PROFESSIONAL PROFILES OF:	SURVEY OF EXISTING FACILITIES	PERIPHERAL ACADEMIC PROGRAMMES
– VARIOUS TYPES OF TOXICOLOGISTS	ASSESSMENT OF NEEDS	MEDIUM-TERM CONTINUING EDUCATION COURSES
– MEMBERS OF TOXICOLOGY TEAM	ASSISTANCE IN DEVELOPMENT OF ADDITIONAL CAPACITY	SHORT AD-HOC COURSES
– OTHERS		

NATIONAL AND INTERNATIONAL RECOGNITION OF QUALIFICATIONS

TO ACHIEVE

RATIONALIZATION OF TRAINING PROGRAMMES
EXPANSION OF CAPACITY OF TRAINING INSTITUTIONS
INSTITUTION OF NEW TRAINING PROGRAMMES
IMPROVED CAREER DEVELOPMENT OPPORTUNITIES
ADEQUATE SUPPLY OF PERSONNEL OF VARIOUS CATEGORIES

Figure 2

A Working Group on Occupational Profiles in Toxic Chemicals Control was convened in Brussels in December 1980, in collaboration with the Commission of the European Communities.

The Group agreed on the following approach in development of occupational profiles:

- description of tasks
- description of areas of knowledge
- description of the knowledge required as a function of tasks
- description of occupations requiring toxicological knowledge.

The following categories of tasks were established:

1 experimental animal toxicology
2 experimental phytotoxicology
3 clinical toxicology

4 epidemiology
5 exposure evaluation
6 risk assessment
7 advice and consultation
8 management and training in toxic chemical assessment.

The Group considered each group but paid particular attention to experimental toxicology.

It was concluded that a toxicologist is in effect defined by the tasks he could be expected to perform, in many cases in collaboration with other toxicologists or allied scientists. The concept of the toxicological team was particularly emphasized in the light of the increasing number of scientific disciplines involved in toxicological assessments. The leader of such a team would be a senior toxicologist. The tasks that a toxicologist should be responsible for were established.

The Group strongly endorsed the importance of the role of the senior toxicologist, both in giving advice to governments and in developing toxicological services. Urgent attention should be given to the training and the development of such key scientists.

The group considered several other professions or occupations for which extensive knowledge of toxicology is required (e.g. occupational health physicians and epidemiologists), and their professional profiles in relation to toxicology.

The Group identified a series of other professions where some knowledge of toxicology is desirable and recommended that their profiles in relation to toxicology be developed. It drew up a preliminary list of these professions, recognizing that this could be extended.

The Working Group developed a number of specific recommendations which are quoted in full in the Summary Report (see Annex 2).

A comprehensive publication on "Occupational Profiles in Toxic Chemicals Control" is now in the final stages of preparation and will be available soon.

While it is believed that the basic classification of tasks to be performed and skills needed will be applicable globally, the criteria for grouping these component tasks into professional profiles may vary from region to region and from country to country.

It is, therefore, necessary to organize regional or sub-regional consultations to examine and adapt the model to local circumstances.

3.3. Training Curricula

Based on the activities described in paragraphs 3.1. and 3.2. above, model training curricula would be developed for adaptation and use by training institutions.

A Planning Group on Development of Curricula for Manpower Training for Occupations in Toxic Chemicals Control will be held in Brussels, 15–19 June 1981.

The purpose of this Planning Group is to prepare a strategy for the developmental process. This will require consideration of the design and structure of curricula, an examination of different types of curricula and a decision on the scope of likely curricula as regards both the time and the degree of detail required. A modular approach may give the flexibility needed for adapting curricula to differing educational systems. Once a strategy has been formulated, a plan should be made for its implementation.

An attempt will also be made to produce an outline curriculum for one type of toxicologist (e.g. consultant toxicologist) which could serve as a model.

The Planning Group will also consider a proposal for a model curriculum for a medium term (3–4 months) course designed for people who have important functions in the chemicals control field but who do not have a specific background in toxicology. This course may also be useful for professionals in other disciplines than toxicology who nevertheless need some knowledge of their subject for performance of their normal tasks, e.g. public health inspectors, food control officers, factory inspectors etc.

3.4. Forecast of Demand for Personnel

The objective of this activity is to obtain rough estimates of the future demand of the various categories of personnel, taking into account the foreseen developments in industry and the probable expansion of control activities.

A methodological model for assessment and forecast of demand is being developed. It is intended to test this model by performing surveys of demand in one or two countries.

After testing and adjustment, as needed, the model will be put at the disposal of governments and educational institutions for adaptation, adoption and use in planning for expansion of existing programmes or institution of new ones.

3.5. Survey of Existing Training Programmes

A survey of all European institutions of higher learning is now in progress to determine the numbers, types, contents and scope of training programmes currently offered. The survey focuses on two types of programmes, viz: (a) programmes designed to produce toxicologists, and (b) programmes for professionals in other disciplines but which contain significant elements of training in toxicology.

3.6. Consultation on Manpower Development in Toxic Chemicals Control

The activities enumerated above, viz the occupational profiles, survey of existing training programmes, forecast of demand and model training curricula, would constitute a base for development of rational training programmes.

It is proposed to call, probably early in 1983, a large consultation of toxicological experts and educators to review this material and to map out a strategy for implementation.

3.7. Short Training Courses

The strategy outlined above will take some time to produce the desired objective.

In the meantime, it is proposed to hold a number of short training courses on subjects which are considered as high priority. The courses are to be organized by national institutions with assistance and support from the regional offices.

The first of the series of training courses to be sponsored by the WHO Regional Office for Europe within the framework of the regional programme on chemical safety is the Course on Toxicology of Pesticides to be held in Sofia, Bulgaria, 31 August–11 September 1981. The course is being organized by the Bulgarian Institute of Hygiene and Occupational Health with the participation of ILO, who will cover the aspects of workers' safety, and FAO who will deal with the problems of agricultural product safety and environmental Protection.

4. Contingency Planning for Accidents and Emergencies involving the Release of Toxic Chemicals

As the first step towards development of a European contingency response system for emergencies and accidents involving the release of toxic chemicals, the Regional Office had commissioned two background studies:

a) conceptual model of a countrywide emergency response system for chemical accidents; this model identified system components such as the definition of responsibilities at various levels, communication channels, access to information, equipment and manpower, etc.;
b) survey of existing system components in European countries; this survey, which was conducted by the Monitoring and Assessment Research Centre, UK with the cooperation of UNEP/IRPTC, was designed to provide information on existing emergency response systems related to toxic chemicals in European countries.

These two background documents were submitted to the Working Group on Contingency Planning for, and Response to, Emergencies and Accidents involving Potentially Toxic Chemicals held in Bilthoven, Netherlands, 9–13 February 1981.

The main purpose of this meeting was to help structure a model of a comprehensive contingency plan, at various levels, for effective response to accidents involving the release of toxic chemicals. This model will then be included in a guideline document, which governments can use to set up or complete their emergency response systems.

In addition, two case study reports were presented at the meeting, one dealing with the accidental release of 2, 3, 7, 8-tetrachloro-dibenzo-p-dioxin (TCDD) at Seveso, Italy, from an industrial plant and the other describing a train accident which involved the release of chlorine at Missisauga, Ontario, Canada.

The case studies were used to analyse the adequacy and completeness of the conceptual model of the emergency response system in order to ascertain if the existence of such a system at the time of the accidents would have improved the speed and effectiveness of the response.

The discussion resulted in certain modifications to the model submitted at the meeting.

The Working Group recommended i.a. that the WHO Regional Office should develop and publish a guideline document on model contingency plans for response to accidents and emergencies involving release of toxic chemicals. This guideline document is currently in preparation.

The Working Group adopted a number of recommendations which are summarized in the Summary Report (see Annex 3).

Additional activities on this programme component are shown schematically in Fig. 3.

5. Monitoring and Epidemiological Studies for Chemicals Control

The main aspects of this programme component are shown diagramatically in Fig. 4.

The overall approach was developed on the basis of a paper on "Monitoring and Epidemiological Programmes in the Control of Toxic Chemicals", which was a working paper for the Planning Meeting on Monitoring and Epidemiological Studies for Toxic Chemicals Control, held in Copenhagen, 5–8 May 1981.

The Planning Meeting was convened by the WHO Regional Office for Europe. It was attended by 14 specialists in monitoring and epidemiological studies from 11 coun-

CONTINGENCY PLANNING FOR EMERGENCIES

ALERT SYSTEM	RESPONSE-SYSTEM	RESOURCES
DEFINITION OF EMERGENCY	EXPERTISE	ROSTERS OF EXPERTS
FOCAL POINTS	TESTING & MONITORING	ROSTERS OF INSTITUTIONS
RESPONSIBILITIES	MATERIALS, EQUIPMENT AND MANPOWER	DATA BANKS OR ACCESS
COMMUNICATION CHANNELS	EVACUATION AND CARE	RESERVES OR ACCESS TO EQUIPMENT
	REHABILITATION	MANPOWER & MATERIALS
	PUBLIC INFORMATION	PROCEDURES

FRAMEWORK FOR INTERNATIONAL COLLABORATION

PREVENTION: "EPIDEMIOLOGY" OF ACCIDENTS
REHABILITATION: GUIDELINES FOR REHABILITATION OF AFFECTED AREAS, INCLUDING GROUND WATER, SOIL, ETC.

TO ACHIEVE

MORE RAPID AND EFFECTIVE FUNCTION OF ALERT SYSTEM

MORE EFFECTIVE RESPONSE SYSTEM, INCLUDING:
PRE-ARRANGED PROCEDURES FOR RAPID DELIVERY OF INFORMATION, EXPERTISE, EQUIPMENT AND MATERIALS

ANALYSIS OF CAUSES OF PAST ACCIDENTS TO ASSIST IN PREVENTION

IMPROVED AND MORE RATIONAL REHABILITATION PROCEDURES

IMPROVED PUBLIC INFORMATION PROCESS

Figure 3

MONITORING AND EPIDEMIOLOGY

MONITORING	EPIDEMIOLOGY
PURPOSE, SCOPE, PRIORITIES	PURPOSE, SCOPE, PRIORITIES
PARAMETERS AND MEDIA	PROTOCOLS FOR TRIAL STUDIES
SAMPLING PROCEDURES	AMENDMENTS & ADJUSTMENTS
ANALYTICAL PROCEDURES	FULL SCALE STUDIES
DATA PROCESSING	DATA PROCESSING, EVALUATION
INFORMATION DELIVERY	DISSEMINATION
EVALUATION & ADJUSTMENT	TECHNICAL COOPERATION
TECHNICAL COOPERATION	

COMPARABILITY OF RESULTS AND SYNERGISTIC EFFECTS

TO ACHIEVE

ALLOCATION OF RESOURCES ACCORDING TO PRIORITIES
IMPROVEMENTS IN METHODOLOGY
STRENGTHENING OF TECHNICAL AND INSTITUTIONAL CAPABILITY
DISSEMINATION OF INFORMATION ON SOURCES, LEVELS & EFFECTS

Figure 4

tries. The Meeting considered aspects such as the integration of studies for occupational and general population exposures and health effects; the development of exposure assessment methods; the role of epidemiology in chemicals control and problems of availability of an access to relevant data.

The Meeting made recommendations for the overall development of monitoring and epidemiological studies on toxic chemicals in the European Region. In addition, proposals for nine specific monitoring and epidemiological studies were submitted for consideration by the Regional Office as candidates for internationally coordinated projects. These are:

1. Health effects of cadmium exposure in the general population.
2. Process dependent risks of delayed health effects due to occupational exposure to chromium and nickel.
3. Health risks of exposure to organic chemicals in the water supply.
4. Health effects of man-made mineral fibres.
5. The use of zinc protoporphyrin (ZPP) levels and other diagnostic tests to determine childhood exposure to lead.
6. The role of formaldehyde in the epidemiology of chronic non-specific lung disease (CNSLD).
7. The health effects of chronic exposure to aromatic amines.
8. Cadmium and mercury release from copper amalgam used in fillings in children's milkteeth.
9. Health effects of exposure to organo-phosphates in community and occupational groups.

The Meeting agreed upon the type of information which is required in the preparation of protocols for monitoring and epidemiological studies, and the format for presentation. Proposals for studies 1 and 2 above were written under this agreed format to serve as examples of detailed protocols.

The Meeting made a number of specific recommendations which are included in the Summary Report (see Annex 4).

6. Toxic Wastes Management

Improper or careless disposal of toxic waste during the previous decades has been causing increasing problems in the industrialized countries of Europe and elsewhere.

It has been recognized now for some time that certain formerly acceptable methods for disposal of industrial waste products (for example, land disposal in a way that contaminates groundwater) are serious sources of pollution and constitute hazards to human health, making it imperative that guidelines be prepared that will help Member States to take appropriate action to reduce these hazards.

A more recent concern is the transfrontier transportation of hazardous waste and, in particular, the possibility of exports of such waste to developing countries. The second major objective of the Group was, therefore, to consider pertinent measures to control such transportation.

A Working Group on Guidelines for the Control of Toxic and Other Hazardous Chemical Wastes was organized in Garmisch-Partenkirchen, 17–20 March 1981. The meeting was jointly convened by the WHO Regional Office for Europe and the UNEP International Register of Potentially Toxic Chemicals to discuss a code of practice and guidelines for the management of toxic and other hazardous waste.

The Group addressed both of these topics in their broadest aspects. A draft code of practice was distributed in advance and was reviewed in detail. In addition, the Group was invited to comment on and suggest topics to be included in a more general policy guidelines document, dealing *inter alia* with transfrontier transportation and due to be produced after the meeting.

The Working Group recommended i.a. that the UNEP International Register of Potentially Toxic Chemicals and the WHO Regional Office for Europe should jointly produce documentation, including both executive guidelines and a code of good practice, which will serve as a guide to decision-makers with responsibility for the management of hazardous waste. Many detailed recommendations on the form and content of such documentation were made by the Group. These are included in the Summary Report (see Annex 5).

7. Legal and Administrative Procedures for Control of Chemicals in Europe

A preliminary survey of administrative procedures for toxic chemicals control has been launched. The objective of this study is to provide a picture of the distribution of responsibilities for chemicals control in the various European countries and of the ways and means by which these responsibilities are discharged by the agencies concerned. This study is being implemented by the UNEP International Register of Potentially Toxic Chemicals and the Monitoring and Assessment Research Centre, UK, in cooperation with the Institute of Hygiene and Occupational Health, Sofia, Bulgaria.

Although the survey is not yet completed and information on several countries is missing, draft reports have been prepared and are available.

The reports outline the arrangements and procedures for the control of chemicals in European countries. Such arrangements and procedures are frequently modified, and a report on this subject could never claim to be complete or totally up-to-date.

The present survey provides an overview of major actions, both current and planned. It reviews the principal Acts, as well as non-statutory schemes, in each country together with the basic regulations that have been issued under them, and the procedures that have been established to apply them. The authorities who bear the main responsibility for their implementation are also indicated. It is believed that this may be helpful as a guide both to the questions that must be considered by those concerned with or affected by the control of chemicals, and to where most recent information and detailed advice can be obtained, as necessary.

Legislative procedures, advisory mechanisms, reviews, appeals, enforcement and penalties are briefly mentioned by way of introduction to the section on each country.

Laws and regulations relating to all stages of the lifecycle of a chemical have been included, whether they were introduced with the explicit aim of controlling chemicals, or for a more general purpose. Emergency provisions are not included; they are covered under section 4 of this report: Contingency Planning for Accidents and Emergencies involving the Release of Toxic Chemicals. It is expected that the final report of this study will be issued in summer 1981.

The report on this survey will serve as one of the main background documents to be submitted to the Working Group on Regulatory Schemes on Potentially Toxic Chemicals in Consumer Products (other than food and water) to be held in Varna, Bulgaria, 21–25 September 1981. It is expected that a guideline document on legal and administrative aspects of regulation of this type of products will be developed.

8. Quality Control and Good Laboratory Practice

An Expert Consultation on Quality Control in Toxicological Test Laboratories was held at the Institute of Occupational Health in Helsinki, 22–24 September 1980, with the participation of six experts from five countries of the European Region and two representatives of other International Organizations, viz OECD and CEC.

The purpose of the meeting was to consider a series of documents on the quality of studies upon which risk assessment of chemicals to human health and the environment is based. As a general prelude to the detailed study of a document on guidelines for investigations in occupational medicine, the principles of good laboratory practice were discussed. The Consultation acknowledged that considerable efforts have been made on a document on Good Laboratory Practice by the Organization of Economic Cooperation and Development.

After discussion and detailed consideration, the Expert Consultation endorsed and recommended adoption of the OECD GLP document with suitable editorial amendments to adapt it to a WHO Pan European context. The OECD and CEC representatives welcomed this opportunity to open the GLP document to a wider international audience.

9. Risk Assessment in Toxic Chemicals Control

A Seminar on Evaluation and Risk Assessment of Chemicals organized by the Institute of Occupational Medicine in Lodz, Poland, in collaboration with the Institute of Occupational Health in Helsinki, Finland, and the Institute of Radiological Health in Belgrade, Yugoslavia, was held 1–6 September 1980. As the name implies, the Semi-

RISK ASSESSMENT

1. DATA
   - CHEMICAL
   - TOXICOLOGICAL
   - EPIDEMIOLOGICAL
   - CLINICAL

2. EXTRAPOLATION
   - ANIMAL-MAN
   - OCCUPATIONAL EXPOSURE – COMMUNITY EXPOSURE
   - SHORT-TERM-LONG-TERM

3. RISK ASSESSMENT PROCESS
   - PROBABILITY OF EFFECTS
   - SEVERITY OF EFFECTS
   - EXTENT OF EFFECTS

4. DECISION-MAKING PROCESS
   - EVALUATION OF PUBLIC PROPENSITY FOR RISK ACCEPTANCE
   - EVALUATION OF ALTERNATIVES – PERMIT
     - FORBID
     - RESTRICT
     - SUBSTITUTE
   - EVALUATION OF BENEFITS, DISBENEFITS, COSTS.

Figure 5

nar was centred on the process of risk assessment based on the available toxicological and epidemiological evidence, and taking into account the benefits, dis-benefits, and the implied costs of the possible control actions. The Seminar was attended by senior scientists and decisionmakers who are faced with the difficult task of making important decisions based on imperfect information.

The major elements of risk assessment are shown in Fig. 5, and these were covered in the lectures and discussions held during the Seminar.

Considering the interest aroused by this activity it is planned to organize, jointly with CEC, another seminar on this subject, to be held in Brussels in 1982.

10. Technical Cooperation

The list of subject areas covered under this component of the programme is shown in Fig. 6.

Some of the activities falling within this programme component are described in some detail in the preceding sections of this report. In addition, the following related activities have been implemented in 1980/81:

– Consultation on Methods of Monitoring and Evaluating Airborne Man-Made Mineral Fibres (Copenhagen, May 1980)

TECHNICAL COOPERATION

SUBJECT AREAS

TOXIC CHEMICALS IN:
- DRINKING WATER
- WATER & WASTEWATER TREATMENT PLANTS
- SLUDGE USED AS FERTILIZER
- HAUSEHOLD PRODUCTS
- BUILDING MATERIALS
- FOOD AND PACKAGING
- SOLID & LIQUID WASTES
- AIR (EXTERIOR AND INTERIOR)
- WORKING ENVIRONMENTS
- ALLERGENS

SPECIFIC INDUSTRIES
- ASBESTOS
- MAN-MADE FIBRE
- METALLURGY (NON-FERROUS)
- RUBBER
- ENERGY GENERATION

AGREEMENTS ON:
- GOOD LABORATORY PRACTICE
- QUALITY CONTROL (LAB)
- NOTIFICATION AND LABELLING PROCEDURES
- REGULATORY PROCEDURES

METHODOLOGY
- MULTI-MEDIA MONITORING
- TESTING PROGRAMMES, INCLUDING MUTAGENICITY
- MULTIPLE EXPOSURE ASSESSMENT
- GOOD LABORATORY PRACTICE & QUALITY CONTROL
- RISK ASSESSMENT AND OTHER DECISION AIDS

TO ACHIEVE
- EXPANDED TECHNICAL AND INSTITUTIONAL CAPABILITY
- OPTIMIZATION OF EFFORTS AND RESOURCES
- MORE EFFECTIVE IMPLEMENTATION OF CONTROL MEASURES
- FRAMEWORK FOR REGULAR INFORMATION EXCHANGE
- FRAMEWORK FOR PERMANENT COOPERATION

Figure 6

- Working Group on Health Implications of High-Level Radioactive Waste Disposal (Bruges, Belgium, June 1980)
- Working Group on Health Implications of Accumulation of Micropollutants on River Sediments (Trier, FRG, August 1980)
- Meeting on the Delayed and Chronic Effect of Chemicals in the Workplace (Kiev, USSR, October 1980).

Annexes 6 to 9 contain summary reports of these meetings.

Summary Reports:

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

ANNEX 1

Consultation on Priority Problems in Toxic Chemicals Control in Europe

Baden, 3–6 November 1980

ICP/RCE 903 (5) (S)
1 May 1981
4938B
ORIGINAL: ENGLISH

Summary Report

1. Introduction

The establishment of priorities for toxic chemicals control in Europe is an important component of the European Programme of Environmental Health Aspects of the Control of Chemicals, being carried out by the WHO Regional Office for Europe in conjunction with the UNDP-supported project on this subject.

The Consultation on Priority Problems in Toxic Chemicals Control in Europe was organized by the WHO Regional Office for Europe with the support of the Austrian Government. The meeting was held in Baden, Austria, from 3 to 6 November 1980 and was chaired by Professor M. Haider[a]. Dr. J. Daimer[b] welcomed the participants on behalf of the Austrian Government.

The purpose of the Consultation was to establish priorities for investigations and action by the national institutions and government agencies concerned.

The discussions were based on an extensive background paper prepared by Dr. I. Farkas[c], Dr. M. Conte de Barros[d], Professor F. A. Fairweather[e] and Professor F. Schmidt-Bleek[f].

The discussions were based on a comprehensive background study aimed at identifying and defining the toxic chemical problems which arise during the entire economic cycle of extraction of raw materials, primary and secondary manufacturing, storage, distribution, consumption or use and, finally, wastes disposal. At each stage, various categories of the population, e.g. workers, consumers and/or members of the community, may be exposed to toxic chemicals contained in the raw materials, products, by-products or wastes. These toxic chemicals may affect the various groups by any one or a combination of routes, such as food, contact, water, air or soil, producing a range of known or suspected health effects.

An important element in the study was an attempt to identify major constraints which prevent the solution of the problems, such as lack of precise knowledge of sources, exposure and effects, inadequate technology for prevention of exposure, excessive cost of preventive measures, cost or other disadvantages of substitutes or alternatives, lack of adequate legislation or regulation, and considerations of trade and competition.

The result of this effort was presented in the form of a multidimensional matrix identifying the products and processes which involve exposure to toxic chemicals, the types and routes of exposure, the categories of population affected, the types of effect and the predominant constraints on preventive action. It became clear that the multiplicity of sources, chemicals and their effects is such that any attempt to produce a complete catalogue at this stage would be self-defeating. Therefore, the background study was not exhaustive but rather meant to develop a rational approach to the problem as a basis for setting priorities.

2. Discussion

The discussion at the meeting was structured into three major sections, divided according to the types of population primarily exposed, i.e. workers, consumers and members of the community. Persons exposed to toxic chemicals by virtue of their occupation, including "do-it-yourself" amateurs, were classified as "workers".

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a Director, Institut für Umwelthygiene, Vienna
b Ministerialrat, Ministry of Public Health and Environment, Austria
c Deputy Head, Department of Toxicology, National Institute of Hygiene, Budapest
d Head, Contamination Division, General Directorate for the Protection of Agricultural Products, Oeiras, Portugal
e DHSS Consultant Adviser in Toxicology, St. Bartholomew's Hospital, London
f Federal Environmental Agency, Berlin (West)

The category of "consumers" was defined as that section of the population whose exposure is caused by the act of using a product as food, clothing, shelter, etc., or parts or ingredients thereof. "Community" was considered to include populations outside the plant or workplace, who are exposed to a chemical by virtue of living in an affected area.

It was stressed that the above classification, useful as it is for the purpose of analysis, is arbitrary because individuals may belong to more than one of the above categories and, thus, be subject to multiple exposure.

An attempt was made to illustrate this by analysing one major human activity, i.e. "agriculture", where occupational, community and user types of exposure are closely interrelated and superimposed. The relationship between exposure and sociocultural aspects was highlighted in discussing problems arising in the use of pesticides in less development countries.

3. Conclusions

1. The Consultation stressed the importance of international cooperation in dealing with priority problems in toxic chemicals control in Europe. The European component of IPCS was considered the approppriate vehicle for achieving pan-European collaboration in this field.

2. The objectives of the regional programme on toxic chemicals control were considered to be highly relevant to the perceived priority problems in Europe, and the foreseen outputs and activities to be appropriate for the creation of a framework of regional cooperation in dealing with these problems.

3. It was felt that the priority problems identified by the Consultation were relevant to European countries, including the less developed ones, and that full participation of these countries in the regional programme would be essential for its success. The Consultation noted with satisfaction the current support of UNDP for this purpose and welcomed the prospects for continuation and extension of this support.

4. The Consulation noted with satisfaction the donations made by certain countries for the European component of IPCS and expressed the hope that the number of countries making voluntary contributions would increase in the future.

5. The Consultation identified priority problems requiring urgent consideration and attention by the governments and national institutions concerned, IPCS and other organizations, as listed in the recommendations below.

6. The Consultation noted with satisfaction the coordination of the European component of the global work of IPCS and the cooperation achieved with a number of intergovernmental organizations, and expressed its hope that the cooperative effort would be further broadened and strengthened.

7. The Consultation noted with approval the recommendation of the IPCS technical committee that the Regional Office be entrusted with global responsibility for elements of the programme.

4. Recommendations

4.1. Governments and National Institutions

1. The European governments and national institutions are invited to extend full cooperation and assistance to the regional programme on toxic chemicals control, by making available the outputs of their current and future work on matters related to the programme and by making available, to the extent compatible with national priorities, the services of their experts.

2. In planning relevant national, sectorial and institutional activities, an effort should be made to relate them, to the extent possible, to the objectives and activities of the regional programme in order to maximize the synergistic effect of pooled resources.

4.2. WHO Regional Office for Europe

1. The environmental impact assessment (EIA) component of the regional programme, including development of methodologies for comprehensive assessment of all relevant environmental factors and their interaction, should receive priority. Environmental monitoring and epidemiological studies designed to verify the assessments should be included in the programme. Specifically, EIA studies of aluminium, copper and dyestuffs industries should be undertaken.

2. Promotion of emergency response systems should receive high priority, covering aspects such as focal points, rosters of experts, and adequate training for dealing with emergency situations arising from production, storage, distribution and use of toxic chemicals, including pesticides and their wastes.

3. Toxic wastes management should become an integral part of the regional programme, including attention to low-waste technology, recycling and safe disposal practices.

4. The continued development of guidelines and limits for protection of the outdoor and indoor environment and the production of handbooks on various aspects of environmental management should be encouraged. Specifically, guidelines should be developed for:

a) performance of epidemiological studies related to occupational exposure to toxic chemical substances;
b) reduction of exposure to carcinogenic substances and suspected carcinogenic aromatic amines;
c) development of regulatory schemes and control systems relating to consumer products (building materials, paints and glues, floors and other coverings, cosmetics and toys).

5. Methodologies for studies on persistence and environmental pathways of toxic chemicals should be developed. The methodology for evaluation of delayed and long-term toxic effects of low-dose exposure to chemicals and their mixtures, with reference to different biosystems and epidemiological studies, should also be developed and/or improved.

6. Considering the increasing proportion of populations suffering from allergies, hypersensitivities and intolerances, there is a need to instigate studies in this area as a matter of high-priority.

7. The manual on drinking-water control, at present being developed by the Regional Office, should include a description of adequate methodology to ensure that toxic chemicals are not present at unacceptable levels in water supplies and are not generated through water treatment processes.

8. Specific studies on risk assessment of heavy metals and toxic chemicals arising from combustion processes, such as polyaromatic hydrocarbons, chlorinated dioxins and dibenzofuran, should be undertaken.

9. Specific studies on interaction between heavy metals, e.g. cadmium, lead and zinc, should be undertaken in conjunction with investigations performed in areas where combined effects can be expected, e.g. mining, industrial activities and the deposition of wastes, particularly sludges.

10. Internationally comparable monitoring and epidemiological studies on exposure to asbestos, man-made fibres and aromatic amines, chlorophenols, petrochemicals, solvents and heavy metals (Pb, Cd, Cr, Mn, Hg) should be launched as appropriate. Epidemiological evidence on toxicity of groups of chemicals in specific situations or from specific sources, including pesticides, food and feed additives, should be collected.

11. A multimedia environmental and health monitoring study should be conducted in various types of production plants using vinyl chloride. The objective of the study would be to contribute to the harmonization of exposure limits and to improve medical surveillance.

12. The indoor environment should be given adequate attention, including the development of methodologies for assessment of emissions from building materials, paints and glues, floors and other coverings.

13. The training component should include:

a) training of research workers in the methodology of toxicological evaluation;
b) training in environmental and occupational epidemiology;
c) training of personnel involved in occupational and environmental exposure control;
d) training in pesticide toxicology;
e) training in the analysis of chemical contaminants in the environment and their residues in food.

14. The Programme component dealing with the development of arrangements for information exchange and technical cooperation should include the development of a system for rapid exchange of relevant information on toxic chemicals. A system for the rapid dissemination of new information relevant to reassessment of health risks should also be developed.

15. Programmes of information and education of the public and all persons involved in handling toxic chemicals should be developed.

4.3 International Programme on Chemical Safety

1. There is a need to improve methodologies for risk assessment, including animal study, extrapolation, modelling and risk-benefit analysis. The effect of interactions of various chemicals should be studied.

2. The following groups of chemicals and single chemicals deserve high priority for health effect evaluation.

Anionic surfactants
Aromatic amines (especially β-naphthylamine)
Inorganic fluorides
Nitroso compounds
Polyaromatic hydrocarbons (PAH)

Acrylonitrile	Manganese
Arsenic	Nickel
Benzidine	Nitrobenzene
Beryllium	Styrene
Cadmium	Tetrachloroethylene
Chromium	Tetrachloromethane
Dioxane	Trichlorethylene
Ethylene oxide	
Formaldehyde	

3. Steps should be taken to stimulate research necessary for the generation of data where gaps in knowledge have been identified, especially as regards delayed and long-term effects of toxic chemicals, including pesticides and food additives, in order to enable the development of criteria for food, and occupational and environmental safety limits.

4. There is a need to generate data which would facilitate evaluation of pesticides and food additives by relevant expert committees and bodies, and enable them to develop or update health-based exposure limits, acceptable daily intakes, or other measures as appropriate, for a larger number of compounds. Such evaluation should take into account impurities and by-products arising from changes in technology.

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

ANNEX 2

Working Group on Occupational Profiles in Toxic Chemicals Control

ICP/RCE 903 (8) (S)
10 February 1981

Brussels, 15–19 December 1980

ORIGINAL: ENGLISH

Summary Report

Introduction

The meeting was convened in collaboration with the Commission of the European Communities and was attended by 20 temporary advisers from 18 countries in the European Region, 2 representatives of the Commission of the European Communities, a representative of the Council of Europe, 4 staff members of WHO headquarters and the Regional Office for Europe and 5 observers.

In the WHO European Region, as in other parts of the world, there is a shortage of properly trained personnel for toxic chemicals control, both in the core area of toxicology for evaluating data in terms of their practical significance to man and in the related activities for which toxicological knowledge is required. Before suitable schemes can be instituted to educate the personnel needed, the tasks entrusted to such personnel must be defined and hence the knowledge and skills needed to carry out the tasks determined. The purpose of the meeting was thus to review the tasks in toxic chemicals control in this context and to produce occupational profiles based on those tasks.

Discussion

A review was made of the work of the International Programme on Chemical Safety and the Regional Office for Europe in toxic chemicals control. The importance to the human species of control of toxic chemicals in the environment was emphasized. The question of occupational profiles in toxic chemicals control was discussed in detail. The multidisciplinary nature of the problems faced and the need for toxicological teams to carry out toxicity assessment was emphasized. The interrelationship between laboratory assessment and epidemiological assessment was stressed, taking into account the problems in extrapolating from laboratory studies to observed human illness. The difficulties in allowing for interactions between toxic chemicals, such as synergisms and antagonisms, were considered, as was the importance of ecotoxicology. The relevance of the various scientific disciplines needed for a toxicological team was reviewed.

Conclusions

The Group noted the recommendations made by the Consultation on Manpower Development in Toxicology, Copenhagen, 1978 (EURO Reports and Studies, No. 9).

In particular, the Group strongly endorsed the necessity for governments to recognize that toxicology is a specialist subject in its own right, and to create sound career structures for toxicologists.

The Group noted with approval the increasing cooperation between WHO, other United Nations organizations and international organizations such as CEC, CMEA, OECD and the Council of Europe. In particular, the cooperation of CEC in the present meeting had made available valuable additional expertise.

It was agreed that it is important to consider the future development of toxicology and the type of toxicologist that should be developed, recognizing that the current development of toxicology in an *ad hoc* manner is not satisfactory. Thus, for example, universities should be encouraged to develop degree courses in toxicological sciences, as well as postgraduate training in advanced toxicology.

The Group recognized that, by whatever route the necessary skills and knowledge are acquired, the element of inservice experience is crucial. In all a person would need some three to five years of relevant studies and practice to develop sufficient expertise to be recognized as a toxicologist.

The Group agreed on the following approach:

- description of tasks,
- description of areas of knowledge,

– description of the knowledge required as a function of tasks,
– description of occupations requiring toxicological knowledge.

The following categories of tasks were established:

1. experimental animal toxicology
2. experimental phytotoxicology
3. clinical toxicology
4. epidemiology
5. exposure evaluation
6. risk assessment
7. advice and consultation
8. management and training in toxic chemical assessment.

The Group considered each group but paid particular attention to experimental toxicology.

It was concluded that a toxicologist is in effect defined by the tasks he could be expected to perform, in many cases in collaboration with other toxicologists or allied scientists. The concept of the toxicological team was particularly emphasized in the light of the increasing number of scientific disciplines involved in toxicological assessments. The leader of such a team would be a senior toxicologist. The tasks that a toxicologist should be responsible for were established.

The Group strongly endorsed the importance of the role of the senior toxicologist, both in giving advice to governments and in developing toxicological services. Urgent attention should be given to the training and the development of such key scientists.

The Group considered several other professions or occupations for which extensive knowledge of toxicology is required (e.g. occupational health physicians and epidemiologists), and their professional profiles in relation to toxicology.

The great importance of epidemiology and monitoring programmes for the evaluation and risk assessment of toxic chemicals was recognized.

The Group identified a series of other professions where some knowledge of toxicology is desirable and recommended that their profiles in relation to toxicology be developed. It drew up a preliminary list of these professions, recognizing that this could be extended.

Recommendations

1. WHO and other organizations should bring to the attention of governments the urgent need for toxicological expertise, permanent toxicological services and, for all relevant personnel categories, toxicological training programmes.

2. Governments should support the development of degree courses in toxicological sciences at universities and the development of appropriate career structures. It is also important that in the medical profession toxicology be recognized as a specialty. National and international postgraduate training in advanced toxicology should be encouraged.

3. Governments should support and encourage a multidisciplinary approach to toxicological problems and assessments.

4. In consideration of the importance of ecotoxicology in relation to toxic chemicals control and human welfare, urgent attention should be given to developing a list of tasks and occupational profiles for this discipline. Ecotoxicology should be included as an area of study in the development of curricula for training personnel in toxic chemicals control.

5. WHO should give high priority to furthering the programme on manpower training in toxicology, particularly the development of curricula and a survey of institutes in the Region which can provide training in toxicology.

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

ANNEX 3

Working Group on Contingency Planning for, and Response to, Emergencies and Accidents involving Potentially Toxic Chemicals

ICP/RCE 903 (7) (S)
4579B
31 March 1981

Bilthoven, Netherlands, 9–13 February 1981

ORIGINAL: ENGLISH

Summary Report

The Working Group, convened by the WHO Regional Office for Europe with the collaboration and support of the Government of the Netherlands, was attended by 25 specialists from 17 countries, together with representatives of WHO, ILO and UNEP/IRPTC. It was organized within the framework of the WHO European regional programme on chemical safety, being carried out by the WHO Regional Office for Europe and, more specifically, as part of the project for regional cooperation in environmental health aspects of the control of chemicals.

Dr. L. Ginjaar, Minister of Health and Environmental Protection, addressing the meeting on behalf of the Netherlands Government, stressed the importance of the subject for both developed and developing countries.

Virtually all sectors of the population are exposed to potentially toxic chemicals: they include agricultural and industrial workers, consumers and users of everyday products or simply those members of the community who are exposed to such chemicals in the air or in drinking-water.

Given the tremendous volume of chemicals now being extracted, manufactured, transported, stored, used or disposed of as waste, it is inevitable that accidents will occur with increasing frequency throughout the world. Considering the potential damage, both short-term and long-term, that the accidental release of chemicals may cause to human health and the environment, it is essential that every country should develop adequate mechanisms for dealing with such accidents.

The main purpose of this meeting was to help structure a model of a comprehensive contingency plan, at various levels, for effective response to accidents involving the release of toxic chemicals. This model will then be included in a guideline document, which governments can use to set up or complete their emergency response systems.

In preparation for the meeting, the Regional Office had commissioned two background studies:

a) conceptual model of a countrywide emergency response system for chemical accidents; this model identifies system components such as the definition of responsibilities at various levels, communication channels, access to information, equipment and manpower, etc.;
b) survey of existing system components in European countries; this survey, which was conducted by the Monitoring and Research Centre, London, with the cooperation of UNEP/IRPTC, was designed to provide information on existing emergency response system related to toxic chemicals in European countries.

In addition, two case study reports were presented at the meeting, one dealing with the accidental release of 2, 3, 7, 8-tetrachloro-dibenzo-*p*-dioxin (TCDD) at Seveso, Italy, from an industrial plant and the other describing a train accident which involved the release of chlorine at Missisauga, Ontario, Canada.

The case studies were used to analyse the adequacy and completeness of the conceptual model of the emergency response system in order to ascertain if the existence of such a system at the time of the accidents would have improved the speed and effectiveness of the response.

The discussion resulted in certain modifications to the model submitted at the meeting.

Recommendations

The principal recommendations of the Working Group included the following.

1. Governments should be encouraged to develop nationwide comprehensive contingency plans for effective and rapid response to accidents involving the release of potentially toxic chemicals. The plans should cover response at all levels, including the operational level (industrial plants, transport and storage facilities) and the level of local, regional and national government agencies. They should include such key items as definition of responsibilities, lines of communication, access to information, equipment, manpower, etc. These plans should be compatible with contingency plans for other peacetime emergencies, including natural disasters.

2. To assist governments in this task, the WHO Regional Office for Europe should develop and publish a guideline document on model contingency plans for response to accidents and emergencies involving the release of potentially toxic chemicals. The model submitted to the Working Group, after modification and amplification, could serve as a basis for this guideline document.

3. The Regional Office should initiate an activity aimed at chemical accident prevention. A study of past accidents, their causes and the circumstances in which they occurred should serve as a basis for identifying accident-prone processes and situations, thus facilitating the definition and implementation of preventive measures.

4. Since chemical accidents are likely to occur in the future in spite of all the preventive measures that may be taken, the Regional Office should develop guideline documents on the rehabilitation of affected areas, including contaminated groundwater and soil.

5. The effectiveness of the emergency response depends to a large extent on the availability of trained personnel. Training for emergency and accident prevention and response should be included in the manpower development component of the international programme on chemical safety, for which the WHO Regional Office for Europe has global responsibility.

6. National and international information systems containing data on chemicals and their toxicity should be strengthened, linked and geared to provide the relevant information quickly to those responsible for handling emergencies and accidents.

7. To assist the authorities in making the difficult and often crucial decisions on evacuation, WHO should develop guidelines on "emergency tolerance limits" for various chemicals.

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

ANNEX 4

Planning Meeting on Monitoring and Epidemiological Studies for Toxic Chemicals Control

Copenhagen, 5–8 May 1981

Summary Report

The Planning Meeting was convened by the WHO Regional Office for Europe. It was attended by 14 specialists in monitoring and epidemiological studies from 11 countries. The meeting was organized within the framework of the WHO European Regional Programme on Chemical Safety.

The meeting was opened by Mr I. J. Waddington, Director, Promotion of Environmental Health, on behalf of the Regional Director, who stressed the importance of the meeting in the development of internationally coordinated monitoring and epidemiological studies in toxic chemicals. The meeting should consider both the overall approach to be taken and also propose some specific studies for consideration.

The overall approach was briefly discussed on the basis of a "Monitoring and Epidemiological Programme in the Control of Toxic Chemicals", which was a working paper for the meeting. In particular the paper recommended the development of exposure assessment capabilities in the European Region, and a programme for monitoring of critical pathways of *multi-media pollutants.*

The Meeting was presented with descriptions of problem areas in chemicals selected from the list of priorities which were established during the Consultation on Priority Problems in Toxic Chemicals Control in Europe, which was held in Baden, 3–6 November 1980. The problem areas include water quality; industrial problems; building materials and consumer products; heavy metals and food contamination. The purpose of these presentations was to assist the Meeting in their choice of chemicals/problems to be recommended for internationally coordinated monitoring and epidemiological studies.

In general discussion the Meeting considered aspects such as the integration of studies for occupational and general population exposures and health effects; the development of exposure assessment methods; the role of epidemiology in chemicals control and problems of availability of and access to relevant data.

The Meeting made recommendations for the overall development of monitoring and epidemiological studies on toxic chemicals in the European Region. In addition, proposals for nine specific monitoring and epidemiological studies were submitted for consideration by the Regional Office as candidates for internationally coordinated projects. These are:

1. Health effects of cadmium exposure in the general population.
2. Process dependent risks of delayed health effects due to occupational exposure to chromium and nickel.
3. Health risks of exposure to organic chemicals in the water supply.
4. Health effects of man-made mineral fibres.
5. The use of zinc protoporphyrin (ZPP) levels and other diagnostic tests to determine childhood exposure to lead.
6. The role of formaldehyde in the epidemiology of chronic non-specific lung disease (CNSLD).
7. The health effects of chronic exposure to aromatic amines.
8. Cadmium and mercury release from copper amalgam used in fillings in childrenas milkteeth.
9. Health effects of exposure to organo-phosphates in community and occupational groups.

The Meeting agreed upon the type of information which is required in the preparation of protocols for monitoring and epidemiological studies, and the format for presentation, proposals for Projects 1 and 2 above were written under this agreed format to as examples of detailed protocols.

Conclusions and Recommendations

Conclusions

1. The Consultation stressed the importance of internationally coordinated monitoring and epidemiological studies on potentially toxic chemicals in the European Region.

2. A number of priority problems in toxic chemicals which were identified at an earlier consultation* were discussed, and outline proposals for monitoring and epidemiological studies were submitted for consideration by WHO.

3. Detailed proposals were developed for internationally coordinated pilot monitoring and epidemiological studies on two classes of chemical problems of current concern in the European region. These proposals are by way of illustration of the types of protocol required for design of pilot studies. The problems chosen do no: necessarily represent the most immediate priority for internationally coordinated studies.

Recommendations

A. The link between monitoring and epidemiology

1. There is a need for substantial improvement in the compatibility of monitoring data and data produced or used by health information systems and epidemiological studies. This will be facilitated by:

(i) The preparation of detailed protocols for studies involving both monitoring and epidemiological components;
(ii) the establishment of systems to link health information and environmental monitoring programmes;
(iii) the encouragement of regular contacts, common training activities and cooperative projects for epidemiologists and those involved in monitoring programmes.

B. Exposure assessment

2. Biological monitoring is a very valuable tool for the assessment of exposure to chemicals. National and international efforts in the European Region should be strengthened to obtain compatible data from biological monitoring programmes and to accelerate development of biological monitoring. These efforts should build upon the foundations of the UNEP/WHO Pilot Project on Biological Monitoring, with which close links should be ensured.

3. Particularly in cases where direct measurement of exposure through biological monitoring is impracticable, attempts should be made to relate measurements of ambient levels of chemicals in air, water, food or products to actual individual exposures. Pilot projects to elucidate these relationships should be devised, taking due account of existing relevant international monitoring programmes, in particular the UNEP/WHO Pilot Project on the Assessment of Exposure to Air Pollutants, and the Joint FAO/WHO Food and Animal Feed Contamination Monitoring Programme.

4. A systematic evaluation of alternative methods for estimation or measurement of exposure should be undertaken for each chemical selected for study. The evaluation should summarize relevant available knowledge, identify the population groups likely to be at risk, and specify the usage of methods available.

C. Multiple pathways and exposures

5. In cases where present or likely future exposures to a chemical from diverse sources may be of concern, pilot monitoring projects which link exposures to the contributing sources should be undertaken, so that the main sources can be identified, and the critical pathways can be established.

6. In addition to risk evaluations of individual chemicals, population and source related studies should be undertaken in order to determine the nature of exposure to diverse chemicals and the resulting health risks. Pilot monitoring and epidemiological studies of multiple exposures should be carried out.

D. Development of epidemiological methodology

7. There is a need for developing environmental research based on quantitative, experimental and quasi-experimental epidemiological methods. Such research should cover fields including dose or time-distribution of the dose and effect, extrapolation to low doses, multiple exposure analysis, attributable risk assessment, interactions, multiple effects host susceptibility assessment of efficiency and effectiveness of various environmental protection interventions.

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* Consultation on Priority Problems in Toxic Chemicals Control in Europe, Baden, Austria, 3–6 November.

8. There is a need for a better adaptation of epidemiological tools to the specificities of environmental problems. This should lead to the search for the most relevant health parameters, including pre-recorded health statistics (for long-term environmental effects), short-latency effects (e.g. human reproduction); intermediate steps in morbidity processes (e.g. biological monitoring, paraclinical investigation). Efforts should also be made to match the epidemiological methodology used (e.g. clinical, analytical, ecological epidemiology) to the type of monitoring and/or population available.

E. Sampling, analysis, quality assurance

9. Monitoring and epidemiological procedures for sampling, analysis, data handling and presentation should be standardized, as far as practicable, for those chemicals which have been identified as of priority in the European region.

10. The development of quality assurance procedures resulting from the UNEP/WHO Health Related Pilot Projects should be used as a basis for their more extensive development in the European region, as necessary.

F. Monitoring networks and epidemiological surveillance

11. In some cases the results of internationally coordinated pilot monitoring and epidemiological studies may indicate the need for larger-scale projects or routine national monitoring and epidemiological programmes. Where the chemicals or problems in question are of common interest to a number of countries in the European region, individual national activities should, as far as possible, be designed and coordinated at the international level, and be based on existing capabilities throughout the European region.

G. Links with other international activities and activities in other regions

12. Monitoring and epidemiological programmes carried out in conjunction with WHO Regional Office for Europe should take due account of relevant existing or planned programmes under the auspices of other international organizations, in particular UNEP, CEC, CMEA and OECD. Active cooperation should be established with related programmes of other organizations whenever appropriate.

13. The experience gained and the results of monitoring and epidemiological programmes on chemicals carried out in the European region should be made available to those other regions which are likely to encounter similar problems in the future.

H. Pesticides

14. More countries in the European Region should be encouraged to participate in the GEMS programme of monitoring pesticide residues in breast milk. In countries which are already participating in this programme, the data should be made available for use in risk assessment as soon as practicable. Furthermore due to the importance of this problem in the European Region, internationally coordinated activities in this field should be launched.

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

ANNEX 5

UNITED NATIONS ENVIRONMENT PROGRAMME

International Register of
Potentially Toxic Chemicals IRPTC

Working Group on Guidelines for the Control of Toxic and Other Hazardous Chemical Waste

Garmisch-Partenkirchen, 17–10 March 1981

ICP/RCE 402 (1)
4877B
27 April 1981
ORIGINAL: ENGLISH

Summary Report

Introduction

The Group was jointly convened by the WHO Regional Office for Europe and the UNEP International Register of Potentially Toxic Chemicals to discuss a code of practice and guidelines for the management of toxic and other hazardous waste. The participants included 35 environmental scientists, chemists, chemical engineers, civil engineers, toxicologists, physicians, economists, lawyers and administrators from 20 countries in Europe, North America and Asia.

The establishment of policy guidelines and codes of practice for decision makers and management concerned with the control of toxic and other hazardous waste is an important component of the UNEP study on export and disposal of hazardous chemical wastes, and of the programme on chemical safety and environmental health hazards, which is carried out by the WHO Regional Office for Europe under a UNDP-supported project, in conjunction with the International Programme on Chemical Safety.

It has been recognized now for some time that certain formerly acceptable methods for disposal of industrial waste products (for example, land disposal in a way that contaminates groundwater) are serious sources of pollution and constitute hazards to human health, making it imperative that guidelines be prepared that will help Member States to take appropriate action to reduce these hazards.

A more recent concern is the transfrontier transportation of hazardous waste and, in particular, the possibility of exports of such waste to developing countries. The second major objective of the Group was, therefore, to consider pertinent measures to control such transportation.

Discussion

The Group addressed both of these topics in their broadest aspects. A draft code of practice was distributed in advance and was reviewed in detail. In addition, the Group was invited to comment on and suggest topics to be included in a more general policy guidelines document, dealing *inter alia* with transfrontier transportation and due to be produced after the meeting.

Most of the work was conducted in four subgroups. The first of these considered definitions and aspects of public and workers' health. Various definitions were formulated to clarify the scope of the meeting; these were all of a pragmatic nature, it being noted that more precise legal definitions are seldom valid outside their country of origin. In general, it was felt that a hazardous waste should be defined or described by its effect rather than by its form or composition. The adverse effect on human health from hazardous waste may be either immediate or long term, as for example, when a groundwater supply is slowly polluted by improper land disposal. It was generally agreed that the problems of cleaning up dumps abandoned in the past, such as Love Canal, were not within the scope of the meeting, although consideration would be given as to how existing inadequate dumps should be closed so as to prevent problems arising in the future.

The second subgroup considered the technological aspects of hazardous waste management, including waste minimization, recovery or reuse, treatment, storage and disposal. Particular attention was given to the level of residual risk to public and environmental health posed by a given technology. This was regarded as especially important for landfill disposal, and consideration was given to aspects such as the management philosophy adopted for leachate control (e.g. "concentrate and

contain" versus "dilute and disperse") and post-closure care. The cost of a technology is also important in deciding on the "best practicable means" for hazardous waste management.

The third subgroup considered hazardous waste transportation, including its mangement and control both within and between countries. Particular attention was given to the special problems of transfrontier transportation and of the potential export of hazardous waste from developed to developing countries.

The fourth subgroup tackled the problems of planning and administration in hazardous waste management. Topics considered included general policy, planning, tpyes of legislation, mechanisms of regulation and control, enforcement, financial responsibility, insurance, manpower training and public participation.

Conclusions

1. One of the first requirements for the development of a proper system of hazardous waste management is the availability of good information on the quantities and nature of waste, and on currently used management practices.

2. When considering the problems of managing hazardous waste, attention needs to be given to the impact on health and the environment with respect to both short-term acute and long-term, more insidious, effects such as groundwater pollution.

3. Socioeconomic and political aspects have to be considered within the context of hazardous waste management.

4. Many technologies are currently available for hazardous waste management. A particular technology is usually not appropriate for all wastes. When a waste can be dealt with in several ways, generally the more "powerful" the technology and the lower the residual risk, the higher will be the cost. The appropriate technology in any particular case should be based on the concept of best practicable means. Such methods are not static and may change as technology develops and as society demands. Research and development is required in many domains and should be encouraged.

5. With regard to worker protection, a clear distinction should be made between the "hazardous" waste which poses minimal risk to the workers and that which constitutes a significant risk unless special safety precautions are taken. In general, the precautions should be at least as strong as for the corresponding pure substance unless it can be shown that the risk from the waste is significantly less.

6. Transport of hazardous waste is best controlled in the context of general regulations on the transport of dangerous goods. However, hazardous waste can present additional problems in that it has no possitive value to the generator or transporter, its composition may not be precisely known and mixing of incompatible wastes for convenience in transit may create a hazard.

7. Any national policy for hazardous waste management should be such that hazardous waste will have an acceptable legal treatment or disposal route. If this is not so, then the policy will encourage improper disposal.

8. Hazardous waste management legislation can take many forms, depending on the legal system and other factors in the country. Legislation can be based on environmental discharge standards, environmental quality objectives, and economic incentives and disincentives, or a combination of any of these can be used for the purpose.

9. Hazardous waste management must be based on the premise that the waste generator will be held responsible for selecting licensed controactors capable of safe transport and treatment or disposal of the waste. In some instances, it will be necessary for a waste generator to seek advice outside his own competence in order to discharge this responsibility.

10. Where the legal system of the country permits it, both individuals and corporate bodies employing them shall be accountable for the consequences of any proved malpractice or negligence within their responsibility in the management of hazardous waste at any point in the life cycle of the waste. Laws should be formulated to permit their prosecution.

11. "Sudden and accidental" insurance coverage for hazardous waste management facilities is commonly available and often required under existing control programmes. Environmental damage insurance is an important but highly specialized measure. Adequate (or unlimited) insurance of the latter type may not be available unless a state insurance scheme is instituted.

Recommendations

1. The UNEP International Register of Potentially Toxic Chemicals and the WHO Regional Office for Europe should jointly produce documentation, including both executive guidelines and a code of good practice, which will serve as a guide to decision makers with responsibility for the management of hazardous waste (many detailed recommendations on the form and content of such documentation were made by the Group).

2. On certain (mainly technical) aspects of the overall hazard problem, much more detailed background information and documentation should be produced by WHO following the completion of the current activity.

3. Formal, legalistic definitions of terms such as "hazardous waste" should not be attempted in the context of international guidelines at this time. The best way forward is to adopt pragmatic working definitions which focus more on the hazard characteristics of the waste than on its form or composition.

4. Comprehensive analytical data on the composition of many wastes can be extremely difficult to obtain. Therefore, requirements for analytical information on waste composition should be consistent with the necessity to decide upon appropriate management methods and to evaluate inherent risks. Such analysis should use verified protocols and methods.

5. Transfrontier shipment of hazardous waste should be regulated on the basis of pre-notification to the designated competent authorities of both the exporting and the receiving country. It should be the responsibility of the receiving country to ensure that the waste is transported, treated and disposed of according to its standards, but specific attention needs to be given to the problems of developing countries, whose authorities may not have the expertise to evaluate the technical feasibility or environmental safety of the intended disposal facility in their territory.

6. Much is known about technologies for hazardous waste management as applied in developed countries, but rather less where developing countries are concerned. Considerable attention in the ongoing UNEP/WHO activity should, therefore, be given to identifying the specific problems of developing countries and to providing guidance on solving them. Research and development work should also be encouraged.

7. Uncontrolled dumping is an unsatisfactory method of disposal for hazardous waste and should be phased out. However, specific guidance should be given to developing countries, both on alternatives and on procedures for closing existing dumps, so that they do not pose problems in the future.

8. Post-closure care of land disposal sites (landfills, surface impoundments, etc.), which have been used for hazardous waste, should include appropriate monitoring for potential pollution, and also measures aimed at preventing the inappropriate use of the land in the future. The fact that a site has been used for land disposal of hazardous waste should be recorded in the ownership deeds.

9. It is recommended that in the general environmental protection law, which countries have or are planning to promulgate, appropriate institutional measures should be stipulated for the management of hazardous waste.

10. It should be a government's responsibility to provide an adequate system of laws, controls and administrative procedures for hazardous waste management. Other governmental responsibilities will vary according to the constitution and practices in the individual country. However, the right of appeal against decisions by the competent authorities should be safeguarded.

11. Hazardous waste management should be regulated on the basis of "cradle-to-grave" control. Sources (producers) of hazardous waste should be registered, and all interim storage, transport, treatment and disposal facilities should be licensed. A manifest or trip-ticket system should be used to ensure that the waste arrives at its designated destination.

12. Any licence for a waste treatment or disposal facility must specify the right of legitimate access for the competent authorities and must allow them to carry out necessary works to remedy the effects of malpractice at the licence holder's cost if he cannot or will not take remedial action himself.

13. All personnel involved in hazardous waste management should be properly trained, including those at the policy, management and operational levels. Training programmes need to be developed, particularly in countries where hazardous waste management is still in the early stages.

14. Reports and papers relating to the present discussions and to further work in the same field should be distributed to national ministries concerned with commerce and transportation, in addition to those concerned with the environment and health, which normally receive UNEP and WHO materials.

15. Public involvement in hazardous waste management activities should be encouraged, and education of the public in this subject should therefore be undertaken.

16. UNEP/WHO should develop methodology both for identification and location of abandoned dumping sites containing hazardous waste, and for their reclamation, specifically with a view to the guidance of developing countries.

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

ANNEX 6

Consultation on Methods of Monitoring and Evaluating Airborne Man-Made Mineral Fibres

ICP/WKH 014 (S)
21 July 1980

Copenhagen, 29 April–1 May 1980

ORIGINAL: ENGLISH

Summary Report

Introduction

The meeting, convened by the WHO Regional Office for Europe, in collaboration with the Joint European Medical Research Board (JEMRB) was attended by 12 temporary advisers from eight countries and one representative each from IARC, ILO and JEMRB.

The meeting was called in response to resolution WHA30.47 of the Thirtieth World Health Assembly which requested a study on health problems related to the growing use of chemicals. There has been a marked increase in the use of man-made mineral fibres (MMMF) in the community within recent years and a number of epidemiological studies, both national and international, have been carried out on their biological effects. It has been shown, however, that data from such studies must be comparable and, in particular, that research would be assisted if the methods now in use for monitoring and evaluating airborne MMMF were to be standardized. Accordingly, the aims of the meeting were:

- to review the methods used at present and to recommend reference methods for monitoring and evaluating airborne MMMF to ensure that accurate and consistent data are available for use in epidemiological studies;
- to set up a central reference scheme for counting and size analysis of MMMF;
- to establish a scheme for ensuring that the results of atmospheric monitoring are readily available and relevant to the needs of epidemiological studies.

Discussion

The meeting first discussed the progress of the current programme of research into the biological effects of MMMF, which includes animal, epidemiological and environmental studies. This work, sponsored by JEMRB and carried out independently by several research institutes of repute, will be completed by 1982 when it is intended to report the results at a WHO conference in Copenhagen. The epidemiological studies consist of a retrospective historical cohort analysis at 13 European plants (out of 72 surveyed) which have had suitable employment records over at least a 20-year period and where follow-up of mortality and cancer incidence is feasible. Current levels of airborne concentration and size distribution of MMMF have been determined at the plants on a comparable basis, using standardized optical and scanning electron microscope procedures, so that workers can be grouped and characterized according to the levels. Nevertheless, in common with most studies of this type in occupational epidemiology, several problems occur which limit interpretation of the results, namely: absence of reliable past exposure measurements; lack of detailed information on job histories; lack of data on potential confounding variables (e.g., smoking habits); difficulty in following up medical histories and ascertaining causes of death. Furthermore, a large number of observations are required when attempting to detect the occurrence of rare tumours.

It was agreed that these factors indicate a need for continuing surveillance and regular reporting on an international scale. Proposals for feasibility studies at four plants were discussed.

Interlaboratory comparisons of methods for monitoring fibre numbers and mass concentrations, which were carried out during the environmental studies, showed substantial differences, particularly in the case of fibre number counts. It was agreed that account must be taken of the differences when planning future work.

The participants reviewed the methods presently used for monitoring and evaluating MMMF in the various countries. If prospective epidemiological studies are to be successful on and international basis, comparable environmental data will be required for each of the plants included in the scheme. It was clear that a reference method would be needed for the purpose, and a number of proposals on the subject, which had been submitted by the Institute of Occupational Medicine, Edinburgh, were discussed in detail. It was decided to circulate the amended proposals for com-

ment before inclusion in the final report. In addition, a reference scheme to aid harmonization of counting levels and sizing analysis of MMMF was considered equally important for prospective studies.

Conclusions and recommendations

The meeting recognized the value of the retrospective epidemiological and associated environmental studies, conducted under the auspices of JEMRB, in assessing the health risks of exposure to MMMF. Nevertheless, several limitations and shortcomings of the studies were identified, which will affect interpretation of the final results, particularly as current knowledge suggests that dose-related disease response to MMMF, if any, is likely to be long-term in nature. Within this perspective the participants reached the following conclusions and recommendations on the action needed to extend the work and to improve the reliability and comparability of the results.

1. It is considered desirable to carry out prospective epidemiological studies at a large number of plants, both to increase the number of workers under surveillance and to cover the full range of fibres and manufacturing processes. The feasibility of the procedures should be tested in a pilot study.

2. In addition to assessing the feasibility of collecting and recording data on both previous and ongoing work, the prospective epidemiological studies should follow up the adverse effects of MMMF, for which adequate facilities will be required. The effects studied should include mortality and cancer incidence, and corresponding measurements should be made of total inhalable mass and fibre number exposure on a continuing basis.

3. It would be difficult or impractical to provide follow-up facilities in some countries, and hence access to information in death certificates, subject to safeguards of confidentiality, would be desirable for research purposes. WHO could be asked to actively encourage the linkage of occupational information and causes of death data among Member States.

4. Different methods of monitoring and evaluating mass and fibre number concentrations exist in the various countries, and their harmonization is desirable. While differences persist, it is necessary to use a reference method so that results from different plants and countries may be compared for epidemiological purposes.

5. The montoring method adopted for use in the retrospective studies has provided comparable data on plants over a short time period. For theoretical and practical reasons, certain modifications should be made for the development of a revised reference method, which would be subject to review in about three years. The method has certain limitations, namely, being based on optical microscopy, it is not suitable for sizing fibres – an operation that should be performed by electron microscopy; and it may not be suitable for dealing with new fibre types of a refractive index of < 1.5. These and related technical matters (including the possible effects of electrostatics on sampling) should be investigated by the technical committee referred to under point 6 below.

6. Account must be taken of the substantial differences between laboratories in evaluating airborne concentrations of MMMF, especially fibre number concentrations, which were identified during the retrospective studies. In principle it would be desirable to proceed with the development of a central reference scheme for counting and sizing MMMF, aimed at harmonizing the levels and providing a basis for prospective epidemiology. The details of implementing the scheme would be the responsibility of a technical committee set up with the support of JEMRB. The scheme should include research to resolve the technical problems raised during the meeting. It would be operated through appropriate institutes (normally one per country) within the WHO European Region.

7. There is a lack of data on the long-term variability of exposure to MMMF. To assist the development of an experimental protocol for the prospective epidemiological studies in 1982, it would be desirable to undertake some pilot studies of occupational exposure involving the measurement of variability at some (or all) of the four plants selected for the feasibility studies on surveillance and reporting. The agreed reference method should be used for this purpose. This would enable long-term sampling strategies to be assessed in terms of sampling frequency and cost.

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

ANNEX 7

Working Group on Health Implications of High-Level Radioactive Waste Disposal

ICP/RCE 802 (3) (S)
1 September 1980

Bruges, Belgium, 2–6 June 1980

ORIGINAL: ENGLISH

Summary Report

Introduction

The meeting was convened by the WHO Regional Office for Europe in collaboration with the Government of Belgium. It followed two related meetings on the health implication of nuclear power production (Brussels, 1975) and on health aspects related to actinides and their decay products (Brussels, 1979).

The purpose of the meeting was to respond to the need for national health and environmental authorities in European countries to keep themselves and the general public well informed about the health consequences of new developments in the peaceful uses of nuclear industry, and particularly nuclear power. As European countries derive an increasing proportion of their electricity supply from nuclear power reactors, concern is growing about the exposure of workers and the general public to high-level radioactive waste and the environmental consequences of its treatment, disposal and storage.

High-level radioactive waste

The Working Group noted that there are two types of high-level radioactive waste, namely the irradiated fuel itself if reprocessing is not practised and the fission products if reprocessing is practised. If the irradiated fuel is reprocessed by dissolving fuel and container in acid, the fission product waste solution is rather high in dissolved solids; if the container is first stripped off mechanically, the fission product waste solution is low in dissolved solids and may be concentrated to a smaller volume. Both fission product waste solutions have been successfully stored in tanks and could be stored indefinitely by a programme of transfer to new tanks, but conversion to solid form provides safer and more economic storage.

Incorporation into borosilicate glass, which can accept 25 %–30 % of dissolved solids (as oxides), has proved the most successful method of conversion of fission products to solid form and the process is now being operated commercially in France. There is no reason to suppose that the glass blocks and waste irradiated fuel could not be stored indefinitely and safely, but the time scale involved raises doubts that the appropriate supervision could be assured. It might actually be safer and certainly would be more realistic to provide for disposal by acceptable methods.

Health criteria

The Working Group considered the health criteria which should be adopted for the disposal of high-level radioactive waste. They concluded that the basic principles of the International Commission on Radiological Protection (ICRP), which have been formulated for practices in which the probability of human exposure is high, should be modified and reformulated in terms of the probability of occurrence of the effects of low-levels exposure. The options for disposal could then be objectively compared by calculating the overall probability of harm. The overall probability is a function of the probability of release, the probability of human exposure through environmental pathways, and the probability of health effects from the exposure. Finally, the selected option could be optimised in accordance with the ICRP principles by evaluating the cost of reducing the probability.

The Working Group drew attention to the need for the international organizations concerned to continue and expand their work in establishing health criteria relevant to the disposal options, to develop appropriate guidelines and research and to make expert advice available. International exchange of information, including records and inventories of disposal sites, is important, There is a need for international agreement and supervision.

Detailed conclusions and recommendations will be presented in the final report of the Working Group.

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

ANNEX 8

Working Group on Health Implications of Accumulation of Micropollutants on River Sediments

ICP/RCE 101 (9) (S)
1 September 1980

Trier, Federal Republic of Germany, 5–8 August 1980

ORIGINAL: ENGLISH

Summary Report

Introduction

In collaboration with the Government of the Federal Republic of Germany, the WHO Regional Office for Europe convened a Working Group to review current knowledge regarding micropollutants in river sediments and their pathways to man. The participants included 32 chemists, biologists, geologists, engineers, physicians and toxicologists from 12 countries.

Pollution of major river systems, as indicated by the analysis of their sediments for metals and organic substances, has been documented in recent years for rivers such as the Danube, Ottawa, Po and Rhine. The Working Group was, however, asked to give detailed consideration to mercury, cadmium, lead and polycyclic aromatic hydrocarbons (PAH). These materials produce serious health effects and information is available on their behaviour in sediments. At the same time, the significance of other inorganic and organic materials was not ruled out.

Discussion

The continued discharge of treated and untreated municipal and industrial effluents into rivers has resulted in the accumulation of micropollutants on their sediments. For more metals, PAH, and many other organic materials, adsorption onto suspended particulate matter results in removal of the major portion of the micropollutant from solution. Furthermore, it is to be emphasized that the deposition of such particulate matter on river beds increases with the reduction of river velocity, due to the flow reaching a wide section of the river, impoundment, or discharge to a lake or estuary.

Bottom sediments provide a record of the pollution input, and monitoring of sediments is therefore important in evaluating the pollution status of waterways. Studies of dated samples from the River Rhine indicate that mercury in recent sediments has decreased in response to changes in the technology used in the chlor-alkali industry. Lead concentrations have stabilized as a result of the element's decreased concentration in gasoline. However, the concentration of cadmium in sediments has continued to increase. Monitoring of river sediments has also been useful in identifying specific sources of pollution. Because trace metals and PAH are concentrated in fine-grained material, it is necessary to separate this portion of the sediment before analysis, or to correct for its dilution by coarser material, in order to compare the analytical results. It is also important to determine the background level and to subtract its value from existing values to determine anthropogenic enrichment.

There is only a partial understanding of the accumulation and remobilization processes for trace metals. It is not yet possible to predict the extent of partitioning between sediment and water based on knowledge of their characteristics. Both solution and sediment characteristics, as well as biological processes, affect the partitioning and the physico-chemical form or species of the metal. Most important is the effect of pH, which is inversely related to the concentration of metal in solution. After sedimentation occurs, the environment is usually changed from oxidizing to reducing, which often results in remobilization of metals, but which can also result in the formation of insoluble metal sulfides as a consequence of the action of bacteria on sulfate. Organisms can also methylate metals, leading to transformation to more toxic forms, such as methylmercury. The presence of organic and inorganic ligands tends to enhance mobilization. Least understood is the chemistry of the phases which bind the metals and the way the distribution of metals among these phases affects bioavailability.

Metals and organics in aquatic sediments can pose a serious health hazard to man. Both mercury and cadmium pollution incidents in Japan were directly attributable to contaminated sediments.

The settling of highly contaminated sediments in estuaries enhances micropollution levels in bivalves and others aquatic food resources. Irrigation or flooding of land with river water containing suspended particulates introduces the pollutants to terrestrial food-chains, and the use of rivers as a drinking-water source may also contribute to man's exposure to pollutants. Dredged materials are likely to contain high levels of micropollutants and that portion which is disposed of on land can significantly increase the level of micropollutants in the soil.

Conclusions

Potential risks to man arise from the mobilization of heavy metals from river sediments. Of particular importance is cadmium in the terrestrial environment, as agricultural land may be contaminated through irrigation and the application of river sediments through natural processes of man's activities. Cadmium is readily accumulated by plants, whereas lead is not and mercury is volatilized by aerobic bacteria. In view of the mobility of cadmium in soil and its long "half-life" in man, there should be a strict control on the agricultural use of dredged sediments, restriction on the non-essential use of cadmium and stringent limitations regarding its emissions.

Serious problems arise from contamination of the aquatic environment. Fish accumulate such micropollutants as arsenic and mercury, while in the estaurine environment it is well known that filter-feeders have an outstanding ability to accumulate heavy metals.

It is desirable to minimize exposure to PAH since some of them exhibit carcinogenic activity. However, exposure of man to PAH from other sources is far greater than that from river sediments.

Measurement of metals and PAH in sediments is an important monitoring tool to assess the pollution status of the aquatic environment, and the temporal and spatial trends. Care must be taken that data are comparable with respect to the effect of grain size. Although analytical methods are available for measurement of total metals and PAH compounds, there are severe deficiencies with respect to the knowledge of speciation in solution and on sediments. Speciation measurements are needed to relate monitoring data to data on biological availability and partitioning.

Recommendations

1. The discharge of hazardous substances which accumulate in river sediments, such as those discussed, should be restricted, as far as possible, by the best technical means available.

2. Future water quality objectives and standards should take into account the accumulation of hazardous substances in river sediments with respect to safe disposal of dredged materials on land, pollution resulting from flooding, and irrigation of agricultural lands. In particular, limits for cadmium should be established.

3. Investigations on the correlation between metal content in flood polluted sites and in areas used for dumping of dredged materials with metal content in crops and livestock are urgently needed to determine the maximum permissible metal content in rivers.

4. Because of the greater public health significance of methylmercury compared with inorganic mercury, fish should be analysed for methylmercury content. Because of the ability of filter-feeding organisms to accumulate micropollutants, multi-elemental analyses of shellfish should be performed.

5. Determination of natural kinetics and mechanisms for the uptake of cadmium, lead, mercury and PAH by aquatic and terrestrial biota should be undertaken.

6. Concentrations of micropollutants in sediments are strongly influenced by grain size effects and appropriate corrections should therefore be made. It is proposed that this be done by separating the fraction $< 63\ \mu m$.

7. Interlaboratory comparison studies should be carried out for PAH in river sediments. The sediments should also be analysed for heavy metals.

8. A reference sediment for PAH analysis should be established and be made available for a multi-year period.

9. For more accurate prediction and description of pollutant behaviour in river lacustrine and estuarine systems, additional research on bioavailability, speciation and dynamic behavior of the pollutants is urgently needed and should be encouraged. For example, the forms of cadmium, lead and mercury, as well as PAH and their association with particulates are still poorly known.

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

ANNEX 9

Meeting on the Delayed and Chronic Effects of Chemicals in the Workplace

ICP/WKH 011 (S)
31 December 1980

Kiev, 21–24 October 1980

ORIGINAL: ENGLISH

Summary Report

Introduction

The meeting was convened by the Regional Office in collaboration with the Government of the USSR and was attended by 17 temporary advisers from 15 countries, representatives of ILO and IARC, and 5 observers from the USSR.

The objectives of the meeting were to:

a) review the present situation with regard to the prevention of delayed effects of occupational hazards in Member States;
b) define the delayed effects in relation to resulting health impairment and type of occupational exposure;
c) stimulate the application of existing knowledge of delayed effects of occupational hazards in the practice of occupational health services, and identify measures for strengthening such services;
d) consider the training of the specialists involved in relation to service requirements;
e) identify gaps in the knowledge and define priorities for further research and development in this field.

Discussion

The principal topics of discussion were as follows:

- the varied approaches taken by Member States to the control of chemicals causing delayed or chronic occupational hazards;
- the requirements for establishment of competent national authorities responsible for regulation of the chemicals;
- methods for determining those chemicals causing delayed and chronic hazards and methods for assuring an awareness of their occurrence;
- the limitations and difficulties in obtaining epidemiological data on delayed and chronic hazards from chemical exposure in occupational settings;
- differences in the availability of data as a result of varied national data collection systems;
- problems arising from prior lack of recognition of delayed and chronic effects of chemicals in occupational settings;
- the use of submammalian experimental systems for determining genotoxic effects of chemicals and interpretation of findings;
- the use of mammalian systems for determining genotoxic effects of chemicals;
- the use of biological methods, including cytogenetic studies, for monitoring the exposure of workers to chemicals having delayed or chronic effects;
- the definition of health impairment resulting from exposure to chemicals having delayed toxic effects;
- methods used for the determination of embryotoxicity of chemicals;
- the relevance of indirect tests for the establishment of carcinogenicity;
- the requirements for establishing carcinogenicity of chemicals;
- the evaluation of the teratogenic effects of chemicals;
- training for programmes to prevent the delayed and chronic effects of chemicals in the workplace.

Conclusions

1. There is a need for competent national authorities to authorize the use of chemicals that can have delayed and chronic effects in workers.

2. Chemicals causing delayed and chronic hazards should be determined. The use of such chemicals should be subjected to authorization and control.

3. The chemicals should be identified on a continuing basis, taking into account the availability of new information and new technological methods for making such identifications. The basic information might be used to establish a system of registration, possibly incorporating provisions for certification on the use of chemicals having delayed toxic effects.

4. The requirements for the safe handling of new chemicals introduced into industry should be detailed. Existing industrial processes should be properly supervised and efforts made to identify existing hazards.

5. Tests for embryotoxicity and genotoxicity at the submammalian level can form an important part of evaluation of the potential delayed toxic effects of chemicals to which workers are exposed.

6. Biological monitoring, including cytogenetic studies, may prove to be a feasible method for following exposure of workers to genotoxic chemicals.

7. The general principles for evaluating the carcinogenic risk of chemicals, as set out in the IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, are considered a satisfactory basis for the definition of carcinogenic chemicals. These principles provide guidelines enabling the competent authorities to establish proper protection of workers from chemicals that have only been found carcinogenic in experimental animal systems.

Recommendations

1. Individual Member States should determine health hazards and make relevant regulations for control of the production and individual use of chemicals that may have delayed health effects in workers.

2. Individual Member States should set up the required research and monitoring services and occupational health infrastructures to assure identification and control of the chemicals.

3. Additional personal information and clearer definition of groups at risk are needed.

4. Scrupulous attention should be paid to the safety precautions specified for the use of chemicals causing delayed effects.

5. The adoption of a worker's "passport" recording details of all employment should be encouraged. Details of environmental conditions should be included.

6. Research should be undertaken on biological monitoring of exposure of workers to genotoxic chemicals.

7. To enable the organization of effective programmes of prevention and control of chemicals having delayed toxic effects, Member States must provide appropriate laboratory facilities and expert monitoring services. The facilities should be capable of determining mutagenic, teratogenic, embryotoxic and carcinogenic effects.

8. All workers employed in undertakings producing or using chemicals that might have delayed toxic effects should be subjected to regular medical examinations and epidemiological supervision.

9. The complexity of the subject requires that a multidisciplinary team of experts be available. It should include physicians, biochemists, biologists, engineers, biometricians and epidemiologists.

10. Information interchange and dissemination is a primary requirement for any effective programme in this field. The competent authorities should be able to require that manufacturers involved in the use of chemicals having delayed toxic effects provide essential information required to deal with health problems.

11. Information exchange between the health authorities and basic research institutions should be maintained.

12. The authorities should provide industry with information on the safe handling of toxic chemicals continuously.

13. The authorities should make sure that workers engaged in the handling of chemicals with delayed toxicity are provided with information on procedures and safeguards to be applied.

14. Chemicals having delayed toxic effects should be appropriately labelled, and the labelling regulations should be legally enforceable.

15. Special regulations should be established to protect any specially susceptible groups of workers such as pregnant women and others.

16. All Member States should ensure that appropriate resources, including funds, personnel, material and facilities, are made available for prevention and control of the delayed and chronic effects of chemicals.

17. The preventive measures needed for the protection of workers may include restrictions on use, with particular reference to:

- use under license and under prescribed rigid control;
- substitution by less harmful chemicals;
- use in enclosed processes;
- limitation of exposure to small numbers of workers for limited periods of time;
- monitoring combined with application of corrective measures at appropriate times;
- application of appropriate measures to limit environmental exposure, e.g. by means of filters, wet processes and effective local and general ventilation;
- provision of protective clothing and equipment.

18. More research is required to evaluate the use of submammalian tests for the determination of the genotoxicity and embryotoxicity of chemicals to which workers are exposed.

19. Training programmes dealing with all aspects of the control and prevention of hazards from chemicals with delayed toxic effects should be provided for all personnel responsible and, for this purpose:

1. there is room for further development of specialized and general schemes, which should form the basis of international courses, symposia and other training activities;
2. further preparation and publication of basic books and manuals on important aspects of this field should be undertaken;
3. there is a need for interdisciplinary courses for those who are to administer the relevant occupational health services;
4. more specialized courses are needed for those in areas such as laboratory work and analytical epidemiology;
5. WHO should prepare a general-purpose guide on epidemiological methods in occupational health;
6. more financial resources need to be made available for training;
7. national authorities should promote industrial funding, exchange fellowship schemes and specialized training courses, which could be developed for international use in specialized centres in cooperation with WHO.

20. Member States should be encouraged to establish registers to record occupational diseases resulting from exposure to chemicals with delayed effects.

21. IARC should be encouraged to add supplementary bulletins to its monograph programme so as to provide public health authorities with up-to-date information on occupational carcinogens.

22. International organizations, including WHO and ILO, should continue and further develop their activities to support countries in controlling hazards due to chemical substances.

Jan Smeets, read by G. Mosselmans

The Control of Existing Chemicals in the European Economic Community

1. Introduction

The last decade, Governments are increasingly faced with problems caused by the use of chemicals of which the negative impact on man and the environment had not previously been recognized or established. Therefore different countries have adopted appropriate legislation, in order to protect man and the environment. Also, Member States of the European Community have taken protective measures against the risks posed by chemicals. However, in the framework of the Common Market, these measures can in principle not be left to the sole initiative of one or more Member States. It has to be avoided that different measures are carried out in each Member State and so eventually create barriers to trade and distortion of competition. Therefore harmonization at Community level is necessary.

The first Programme of Action of the EEC on the Environment, adopted by the Council on 22 November 1973, stresses the necessity to harmonize the measures to be taken at Community level with respect to chemical compounds. Particular attention should be given to those chemicals which could give rise to a risk of injury to different targets (man and environment). This policy statement was reconfirmed in the second Programme of Action on the Environment of 1977. In line with this policy the Commission of the European Communities has forewarded for approval to the Council of Ministers proposals for legislative measures, i. e. Council directives. In doing so, the Commission acts under the dual mandate of the implementation of the General Programme for the Elimination of Technical Barriers to Trade of 22 May 1969 completed by the Council Resolution of 21 May 1973 and the Action Programmes of the European Communities on the Environment.

There are many aspects which could be discussed, such as the protection of workers against chemicals, the measures to be taken against environmental pollution in general and by the chemical industry in particular, the marketing of dangerous chemical substances, disposal of toxic waste.

However, the scope of the present review will be restricted to one major aspect of chemicals control: Community action with respect to existing and commercially available chemicals.

The following three subjects will be presented and discussed:

- labelling of chemicals
- priority chemicals
- specific actions.

2. Labelling of Chemicals

The first major action undertaken by the EEC in the field of existing chemicals relates to the classification, packaging and labelling of hazardous chemical products.

This comprehensive action is considered of great importance, since it harmonizes ten legislative measures in this field and dates with its first directive from 1967.

Since then the Council has issued a number of directives requiring each Member State to develop harmonious laws, regulations and administrative procedures regarding trade in these products. As already stated, these measures should avoid unnecessary technical barriers to trade between the Member States of the EEC. One of these directives

relates to chemical substances, the three others to preparations. The four directives are the following:

- the 1967 directive on hazardous substances (67/548/EEC), which has now been modified six times, the latter being the socalled "6th Amendment" (dealing also with the notification of new chemicals);
- the "solvents directive" of 1973 concerned with dangerous preparations and certain substances solely intended for use as solvents (73/173/EEC), which has been modified for the first time on 22 July 1980;
- the "paints directive" of 1977 concerning paints, varnishes, printing inks, adhesives and similar products (77/728/EEC);
- the "pesticides directive" of 1978 (78/631/EEC).

The provisions of these legislative measures are to be applied when substances or preparations, classified as hazardous within the terms of these directives, are put on the market. They are intended to be a primary means by which the general public and persons at work are given essential information about dangerous substances and preparations.

The 6th Amendment, well known, amongst other measures, for its premarketing notification requirement of new chemicals, contains also provisions applying to both new and existing substances. For new substances, classification and labelling is mandatory and will be based on the data submitted to the competent authority in the notification dossier. For existing substances, classification and labelling should take place in so far as the manufacturer may reasonably be aware of their dangerous properties. The data required for classification and labelling of this category may have to be derived from different sources – for example: previous test data, information required in relation to international rules on the transport of dangerous goods, information obtained from the literature, or information derived from practical experience.

The EEC label aims at drawing the attention of persons handling or using substances and preparations to the inherent danger of certain such materials. The means used are a combination of symbols, risk phrases (R) and safety phrases (S). The symbols highlight the most severe hazards; the R-phrases give a more specific picture of the hazards presented by a substance and the S-phrases give advice on necessary precautions and/or of mishandling to be avoided. In order to obtain a clear and intellegible label, the EEC made an effort not to overload it. The EEC considered that detailed information should be the object of a safety data sheet. Member States make the placing on the market subject to the use of their official language or languages on the labels. It is of interest to remind that there are seven official languages in the European Community. It is clear, that the manufacturer will choose to put on the label the language(s) of the countries where he intends to market his products.

The EEC label is intended to give information on two types of hazards:

- health hazards
- physical hazards

14 definitions of hazards are given in article 2, § 2 of directive 79/831/EEC. Of these 14 hazards, 9 are covered by symbols specified in article 16, § 2:

- very toxic
- toxic
- harmful
- irritant
- corrosive

} health hazards

- extremely flammable
- highly flammable
- oxidizing
- explosive

} physical hazards

It must however be noted that there is only one symbol for "very toxic" and "toxic", and one symbol for "extremely flammable" and "highly flammable".

Precedence rules for the choice of symbols are laid down in article 16 § 4, as no more than two symbols may appear on the label.

The procedure for drawing up a label is the following:

A provisional label is proposed to the national competent authority by the manufacturer; very soon, the manufacturer will dispose of a guide for classification and labelling of dangerous substances/preparations and criteria for the choice of the phrases indicating the special risk and the safety advice, prepared by the Commission. The label remains provisional until it has been submitted by the Member State to the European Community and reviewed by the Committee for the adaptation to technical progress. Thereafter, the substance concerned is listed in annex I of the 1967 Directive.

Annex I of the 1967 Directive lists now about 1000 chemical substances classified with respect to the information appearing on the label. This information includes, in 7 languages, the nomenclature for the identification of the substance, hazard symbols and standard hazard and safety advice statements. It must be stressed that all new chemicals will all end up in annex I. The way by which existing chemicals will appear in annex I needs further discussion with the authorities of Member States and also industry.

Finally, the four directives cited above also establish procedures for amending the requirements or specifications contained within the directives. This technical adaptation is foreseen to keep pace with technical progress and an improved understanding of hazardous substances and preparations.

3. Priority Chemicals

After the implementation (18 September 1981) of the 6th Amendment of the 1967 directive on dangerous substances by the member countries, all new substances will be tested and sufficient information to evaluate the risk to human health and the environment will be available.

It is estimated however, that about 60,000 chemical substances are already on the market. In order to give everybody engaged in environmental management and research an instrument to obtain rapidly reliable information on chemical products of environmental importance, the Council of Ministers decided in 1973 to include into Environmental Research Programme of the European Communities a data bank project on environmental chemicals*: ECDIN (Environmental Chemicals Data and Information Network).

ECDIN is conceived both as an information management tool for the services of the Commission to assist them in their task of implementing and executing existing directives. It serves also as an information service for a wider clientele. The basic principle

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* An environmental chemical may be defined as a substance which actually or potentially occurs in the environment in significant quantities as a result of human activity, capable of harming man, other living beings, or the environment.

of ECDIN is to store relevant information on a chemical produced in sizeable quantities regardless of the form in which it is used, its function or its presumed degree of "harmlessness". Moreover, all chemicals having a high toxicity although produced in lower quantities, and selected toxic natural products should be included. Also included will be degradation products, metabolites, and by-products in the manufacture of the above chemicals.

There is general agreement that in the near future a substantial effort will have to be made to assess the potential risk chemicals present to man and the environment. Case by case, these substances will have to be examined on the basis of sound scientific knowledge, permitting, if indicated, regulatory action. If insufficient data or no data at all are available – most likely in the majority of cases – an effort for testing and subsequent evaluation of data has to be launched.

Given the available resources and the limited laboratory capacities for testing, it is obvious that for this exercise, priorities have to be set up, based on selection criteria, ideally allowing an objective rank-ordering of chemicals.

The second Community Action Programme for the Environment of 1977 (17 May 1977) prescribes the development of a systematic evaluation of existing chemicals with the help of a Committee of Experts. For this purpose, the Scientific Advisory Committee of the European Commission to examine the Toxicity and Ecotoxicity of Chemical compounds was created in 1979. This Committee is composed of national experts highly qualified in this field. At the request of the Commission the Committee gives its advice on all problems related to the toxicity and ecotoxicity of chemical compounds, the use of which may have harmful consequences for human health and for the different media of the environment. The Commission has recently asked the Committee to include in its agenda the problem of priority chemicals.

4. Specific Actions

It was recognized that regulations governing the classification, packaging and labelling of dangerous substances and preparations were not necessarily sufficient in all cases, but that it might also be necessary to prohibit or restrict marketing and use under certain conditions. Therefore the Commission proposed to the Council of Ministers a regulation on the approximation of the laws of the Member States restricting the marketing and use of certain dangerous substances and preparations.

In this context, a Directive was adopted July 27, 1976. It applies to the restriction of marketing and use of polychlorinated bi-phenyls (PCB's) and polychlorinated terphenyls (PCT's), the use of which might endanger human health and pollute the environment. It is specified that PCB's, PCT's and preparations with a PCB and PCT content higher than 0.1 % by weight may not be used except for a limited number of specific use categories, such as closed systems.

The Directive also applies to chloro-1-ethylene (monomer vinyl chloride) and specifies that this substance may not be used as an aerosol propellant for any use whatsoever.

On 24 July 1979, two modifications of the annex of the directive were adopted by the Council (79/663/EEC).

- The first one applies to all liquid substances, as such or as part of a preparation, which are listed in annex I of the 1967 Directive on dangerous substances and classified as very toxic, toxic, harmful, corrosive, explosive, extremely and highly flammable. These substances may not be used in ornamental objects intended to produce light or color effects by means of different phases.

– The second modification refers to TRIS (Chemical name Tris (2,3-dibromopropyl) phosphate; CAS Registry nr. 126–727). This substance may not be used in textile articles intended to come into contact with the skin such as garments, undergarments and linen.

An amendment concerning the restricted marketing and use directive is now proposed with respect to the marketing and use of certain asbestos fibres and certain products containing those fibres. The use of crocidolite fibres, currently considered the most dangerous, is prohibited except in those cases where there is not any risk to the public health. Certain uses of other asbestos fibres, such as chrysotile, amesite, actinolite and tremolite, are also prohibited, for the same reason, but less restrictively.

In conclusion, this "Limitation Directive" has to be regarded as an instrument which the Commission can use to regulate, to limit or to ban chemicals presenting danger to man or the environment or both.

This Directive is not the only tool that the Commission uses. Other restrictive provisions exist also in other specific regulations, such as:

– the Council Directive which prohibits the placing on the market and the use of detergents when the average level of biodegradability of the active surfactants is below 90%;
– the Council Directives which regulate the maximum lead content of petrol, and also the maximum sulphur content of gasoils and fuels.

On the other hand, the problems of safety in the work place are covered by a specific Directive presently under discussion in the Council.

As for chlorofluorocarbons, the Community has taken important actions. The Community's concern about the possible effects of CFCs on the environment resulted initially in the Council Resolution of 30 May 1978. This resolution dealt not only with the limitation of the chlorofluorocarbons F11 (CCl_3F) and F12 (CCl_2F_2) production capacity, but encouraged also research on alternative products and on the elimination of discharge in all sectors. On 26 March 1980, a Council decision required each Member State of the Community to freeze the CFC 11 and 12 production capacity. It also required the reduction by at least 30% of the use of these CFCs in aerosols by 31 December 1981, as compared to the level of 1976.

5. Conclusions

In concluding, one might emphasize the importance of the work already performed at international level in the European Community with particular reference to the classification and labelling of existing substances. Much progress has been made in this field. However, one has also to emphasize the enormous task for the competent authorities to deal retrospectively with all existing chemical substances to protect man and the environment and to achieve this goal.

This workshop has been convened at the appropriate time in order to consider with all those interested on international level the possible ways and means to tackle in a harmonized approach the problems under review, avoiding duplication or multiplication of preparatory work for legislative measures. The preparatory work is so complex and demanding in manpower, time and budgeting, that the best ways of sharing the input need to be considered. There is a lack of sufficient expertise. We have to put together all our means in order to optimize the cost/benefit ratio.

Combating the possible negative effects of chemicals is sometimes hampered by a lack of scientific and technical information. Depending on the state of scientific know-

ledge, sufficient reliable and unchallengeable data on the properties of chemicals and their effects on man and the environment is not always available. Unanimous agreement is therefore sometimes difficult, since there often remains considerable scope for interpretation.

The Commission will continue its endeavours aimed at:

- developing preventive measures which reflect the aims of a consistent policy to protect man and his environment and fit in with economic developments;
- assessing, by all means, the impact of existing chemical substances on man and his environment. It is evident that priorities must be set;
- proposing control measures for the most dangerous substances;
- setting up activities likely to produce international agreements on toxic substances.

Peter J. Crawford

International Harmonization of Chemicals Control in OECD Countries

Introduction

It is my great pleasure to talk today about international harmonization of chemicals control in the OECD countries and how this relates to the issue of existing chemicals. In so doing, I want to demonstrate that harmonization is critical to management of existing chemicals, as was so clearly stated by Dr. Hartkopf this morning. I would also like early in my talk to join others in paying tribute to the German Authorities for their timely and generous offer to host this workshop.

As Mr. Lemerle indicated in his opening remarks, chemicals play a prominent role in our modern world and in contemporary life, and in so doing confer many major benefits. At the same time it has come to be recognized that chemicals can cause unintended deleterious effects on human health and the environment.

This sets the challenge which faces us: developing management strategies which on the one hand reduce the risk of such unintended effects on health and the environment from occurring, but which at the same time assure protection of the vigour of the chemical industry. An essential element in the development of such policies has been international co-operation. Co-operation in the development of common policies to protect one global environment and one human population as well as co-operation to ensure that these benefits are achieved with minimum economic and trade impacts. In a sense what our Chairman described as a world action plan this morning.

When one considers the complex way in which scientific and socio-political factors interact with major economic and trade considerations, it is not surprising that OECD has been involved in the area of chemicals control for more than a decade. After all, OECD countries produce two thirds of the chemicals of the world, and roughly 10% of the huge trade of OECD countries is in chemical products.

One of the major roles of the OECD has always been the harmonization of policies between countries to minimise the effects of national policies on trade, and in this respect the objectives of our work on chemicals have been similar to other work of OECD work on chemicals, namely to protect man and the environment from the hazards associated with their use in such a way as to avoid non-tariff barriers to trade and to manage available resources effectively.

International harmonization

So, I want to deal with the question of harmonization of chemicals control within OECD countries and the extent to which this process has already and will in the future influence the management of existing chemicals.

But firstly, I need to define what I mean by "harmonization". For me, the term suggests an active effort by countries to develop or re-order national policies in order to achieve internationally agreed goals. Thus, I would say that harmonization is something less than standardization – since there is generally a variety of acceptable ways to attain defined goals – but something more than co-ordination, which lacks the connotation of shared objectives. Let me also say that harmonization does not mean to me adoption of the lowest common denominator of national policies.

At the beginning of harmonization efforts in OECD on chemicals control, the accent was on a case-by-case approach, and on reaction to situations where the chemical was believed to be already causing damage to human health or the environment. This

necessarily meant that existing, rather than new, chemicals were the object of study. Thus, major studies were undertaken on pesticides, polychlorinated biphenyls (PCBs), mercury, cadmium, hexachlorobenzene, and chlorofluorocarbons. 1973 saw two Council Actions: the Decision to restrict certain uses of PCBs, and the Recommendation to reduce all man-made emissions of mercury to the Environment.

However, it soon became apparent, both at the national and at the international level, that while such an approach has its merits, it is not broad enough to lead by itself to an adequate general control of chemicals. A more systematic approach was necessary, because prevention of environmental damage rather than reaction to damage after the event was needed.

So, a number of OECD Member countries began, from 1973 onwards, to enact national legislation to provide the necessary instruments for the general, preventive, control of chemicals. Over the same period, the OECD Council passed two Recommendations, in 1974 and 1977, namely The Assessment of the Potential Environmental Effects of Chemicals, and Guidelines for Anticipating the Effects of Chemicals on Man and the Environment. This parallel development had beneficial mutually supporting effects, leading to enactment by Member countries of statutes with similar objectives and similar approaches to implementation. In fact, these chemical laws quite characteristically:

- focus initially on new chemicals;
- incorporate some provisions for the control of existing chemicals;
- indicate the type of information to be generated by industry, including the testing of physical and chemical properties and biological and health effects, production volume use patterns, and so on;
- require industry to notify technical and commercial information and testing results to government authorities.

These approaches represent an important facet of the harmonization process, and have laid the foundation for harmonization efforts in the area we are discussing today, namely existing chemicals.

Harmonization as it relates to the control of existing chemicals

1. The relevance of present work

Some work on the management of existing chemicals on a case-by-case basis has continued (here I am referring to the Information Exchange Activities for PCBs and Mercury, and the latest report on chlorofluorocarbons). But in recent years, this work has increasingly been complemented and overtaken by work in the Chemicals Programme which has been largely directed at assisting Member countries to harmonize those parts of their laws dealing with the management of new chemicals.

Nonetheless, and this is a point I wish to stress, Mr. Chairman, most of the projects presently being conducted in OECD form a good basis for a further effort in harmonization of the control of existing chemicals; of course, this is not fortuitous. Indeed, the distinction between new and existing chemicals is sometimes rather artificial, because there are aspects of management strategies where it is of little importance whether the chemical is new or existing. Examples of OECD work where there is a broad base applicable to existing chemicals include:

- The Council Decision on Mutual Acceptance of Data in Chemicals Assessment, incorporating the Recommendation on application of the OECD Test Guidelines and the OECD Principles of Good Laboratory Practice;
- Work on Decision-Making;

– The Information Exchange Activities;
– The Hazard Assessment Project;
– The Economic and Trade Effects Programme.

Mr. Chairman, I would like briefly to explain how this work does in fact affect the management of existing chemicals.

1.a. Mutual acceptance of data

Let me start by describing one of the most important projects, the Mutual Acceptance of Data, which has been approved by Council Decision. I do not think I exaggerate when I echo Mr. Lemerle's words and hail this decision as one of the most significant actions taken to date in the field of chemicals control at the international level.

The decision indicates:

"that data generated in the testing of chemicals in an OECD Member country in accordance with OECD Test Guidelines and OECD Principles of Good Laboratory Practice shall be accepted in other Member countries for purposes of assessment and other uses related to the protection of man and the environment".

A number of general advantages are associated with such action. It will:

– lead towards more consistent international protection of health and the environment;
– provide guidance in the testing of chemicals in terms of appropriate methods and good laboratory practices;
– promote mutual trust in the quality of test data between countries, based on a clear understanding by scientists and administrators of how to generate high quality test data;
– help to stabilise the regulatory environment for, and reduce the burdens on, the chemical industry, by eliminating the need for duplicative testing and improving the ability of industry to forward plan;
– reduce the possibility of trade distortions resulting from variations between nations in approaches to chemical control;
– reduce strains on government administrations, laboratories, test animals and expert resources – in these areas resource constraints are already developing.

But this decision is of great relevance to the control of existing chemicals, since whenever existing chemicals are tested in the future, the Decision will be the appropriate guide to harmonize the testing requirements and it will set the stage for consistent hazard assessment. It will also provide the basis in OECD for the establishment of situations in which data can be mutually accepted, where those data have already been developed in Member countries on chemicals which already exist on the market.

1.b. Information exchange

Information exchange is one of the most critical elements for policy harmonization among countries, not only to manage new chemicals but also to manage existing chemicals. In OECD, we have established several mechanisms:

– A Notification and Consultation Procedure on Measures for the Control of Substances Affecting Man and His Environment;
– The Complementary Information Exchange Procedure;
– A group charged with the Development of Information Exchange Guidelines for the export of Chemicals.

The former two procedures are confined to exchange of information on regulatory actions, while the latter procedure will, we hope, pave the way for the exchange of substance related information aimed at the identification of potential problems associated with the export of chemicals. All of these activities are directly relevant to existing chemicals.

Closely related to Information Exchange is the question of confidentiality of data. The present Expert Group has considered this aspect against the background of recent legislation dealing predominantly with new chemicals. However, there are some issues of particular relevance to existing chemicals. For example, Governments in meeting their obligations to control existing chemicals will need to establish mechanisms for exchange of data, and will also need to create mechanisms which will allow communities to gain access to data on which decisions are taken which affect their well-being.

As Dr. Hartkopf mentioned in his opening remarks, we will need to consider the relevance of our work on information exchange to any international activity aimed at sharing the burden of management of existing chemicals. We may need different approaches and principles to the sharing of data in this field.

Also closely related to Information Exchange is the work of the Expert Group on Key Terms. In this area, the Expert Group has been working towards a common understanding of important legal terms in chemicals control and the development of harmonized definitions where practicable.

1.c. Decision-Making

Decision-making in the case of existing chemicals can be divided into two major aspects:

- Assessment of scientific hazard; and
- Integration of other factors – political, social and economic – into the final decision-making process.

The OECD Hazard Assessment Project is, as you know, using the OECD Minimum Premarket Set of Data as the basis for its work. This project recognises that: "the hazard of a chemical is a function of two broad considerations, the potential of the chemical to harm biological systems and its potential for exposure."

This work is proceeding well, but there is the other major aspect of the decision-making process, namely the integration of political, social and economic factors. Here, it is quite legitimate to ask the extent to which it is either possible or desirable to move towards harmonization in these non-technical areas, because decisions on specific existing chemicals will vary between countries.

Nevertheless, there are certain elements common to all decisions. This has led some authorities to develop what they describe as a lexicon of factors to be taken into account in decision-making. The lexicon does not represent a rigid approach, but rather it is a framework for analysing and evaluating the various elements which need to be taken into account, as well as a way of presenting options, trade-offs and uncertainties. Here is a critical area of future work, with major relevance to the assessment of data on existing chemicals. OECD is embarked on work in this area.

Of course, one of the challenges for government decision makers is to create a more consistent and transparent decision-making process where industry and community groups and government officials all understand their respective roles. Another challenge – indeed a necessity – is to establish effective links between international policy formulation and national decision making.

Final considerations

An important stimulus to international chemical control was the realisation that the hazards associated with certain chemicals were not confined to national boundaries. In the context of this workshop, it is now widely accepted that the control of existing chemicals can only be successfully achieved by concerted, international action.

The control of existing chemicals is on the international agenda now. The major policy bodies of OECD have already determined that OECD should make a contribution – in particular to the development of harmonized strategies to control existing chemicals. We will need to utilise the results achieved thus far in OECD to build a framework for our work methodically and carefully, with due sensitivity not only to the potential problems posed by existing chemicals, but also to the major social and economic importance of these chemicals.

We must recognize that the screening of some 70,000 chemicals (and here the various figures quoted reflect the need for hard data) already on the market will need to be mutually understood, involving as it does the development of agreed criteria for selection of chemicals for further information-gathering, testing and assessment (clearly, such criteria could span economic, health and environmental considerations). The Management Committee in OECD has initiated consideration of criteria. A significant question yet to be answered is where does the economic importance of a given chemical fit in? For example, should social utility and replaceability be considered versus adverse health effects in some localised occupational exposure situation, even at the stage of establishing criteria for selection?

Secondly because of the burden on national resources, this screening process will require consideration of an equitable allocation of effort between countries, as mentioned by Dr. Hartkopf. Thirdly, as I mentioned earlier, there is an urgent need to consider current data on existing chemicals against the criteria developed by OECD for mutual acceptance of data in order to save valuable resources. Here I am talking about trying to avoid a process in which parallel activity and research is established in many countries following recognition of a problem in one country.

The challenge posed by existing chemicals needs to be met in an efficient and cost-effective way. International "harmonization" is not an end in itself. It is a process guided by perceived needs in any given field of concern. In OECD countries this process has built mutual confidence as a result of shared costs and shared progress. It has, as well, built up a momentum with government decision-makers, the chemical industry, trade unions and academia – who, I see, are all assembled at this workshop today.

We also see present today representatives of other international organisations with responsibilities for various international aspects of management of existing chemicals. OECD is not the only international player in this game, and of course for good management, there must be an international association of players. I think that the various bodies involved should come together at the Secretariat level, and the OECD Secretariat would be pleased to convene such discussions. Even then, with the excellent coordination which already exists it is important to realise that we will only be able to proceed slowly and step-wise in this complex field.

So, colleagues, the need exists, all the players are present, the field is prepared, and we in the OECD Secretariat look forward to a most interesting workshop and feel confident that its conclusions will assist the OECD Chemicals Programme as well as governments, international organisations, industry, the trade unions, academia and interested members of the public to formulate a rational approach to the management of existing chemicals.

CHAPTER II

Analysis of the Legal and Administrative Powers to Control Existing Chemicals in OECD Member Countries

Stanley P. Johnson

Survey of Legal and Administrative Powers to Control Existing Chemicals

I. Introduction

In recent years, much national and international attention has been focussed on the problems of new chemical substances. Within the countries of the European Community, for example, the elaboration of the so-called Sixth Amendment to the 1967 Directive on the Classification, Packaging and Labelling of Dangerous Substances, which established an EEC-wide system for the testing of new chemicals before they are put on the market, was – at least as far as chemicals were concerned – the major activity during the period of several years. In the United States, the salient feature of the Toxic Substances Control Act (TSCA) as it finally emerged in 1976 was the notification requirement for new chemicals. Much of the work carried out in recent years within the framework of the OECD Chemicals Programme has been inspired by the need to flesh out the somewhat rudimentary systems which have been put in place for the testing of new chemicals and to achieve results that are both valid in themselves and internationally comparable. It is obviously a matter of concern that one country's notification system, or one economic grouping's notification system, should be as near as possible to that of other countries, or groupings, particularly where the longrun intention is to move towards mutual recognition of notification (as has already been achieved between the EEC countries in the context of the Sixth Amendment).

The fact that attention in recent years has been focussed on new chemicals does not, and cannot, mean that it is safe to ignore the question of existing chemicals. Indeed, given the limited nature of the available intellectual and administrative resources, it is possible to argue that our environmental priorities are in danger of being skewed. By concentrating as much as we have been doing in recent years on the evaluation of new chemicals, we may in fact be failing to recognize the need for more coherent international approaches to the problems of existing chemicals or what the Germans would call "Alte Stoffe". That is why this meeting is both timely and important. It gives us a chance to take stock of where we stand, as far as existing chemicals are concerned, and to outline certain directions which it may be fruitful to explore in the near future.

II. Review of Existing Legislation

Any survey of legislation relating to the control of existing chemicals has to deal with the life of a chemical at all points, from production to final disposal. It must, as it were, follow the chemical both upstream and downstream. It must be concerned with the impact of the chemical on human health, both directly and indirectly; it must also be concerned with the impact of the chemical on the environment in a larger sense – fauna and flora and the interrelationship between them and man. We have to deal therefore with, amongst other things, planning regulations as these may affect the siting and design of installations; operational procedures and practices, as these may affect the health and safety of workers; standards governing the production processes themselves, which may affect discharges to air, soil and water; standards and practices relating to the disposal of waste, whether in solid, liquid or gaseous form; product specifications, having to do with the safety and acceptability of a product from the point of view of health and the environment, etc. Such a survey, encompassing so many objectives, clearly cannot be undertaken within the space of a forty minute pres-

entation particularly where the intention is to move beyond description towards positive proposals. Fortunately work now in hand within the World Health Organisation, and elsewhere, will shortly give us – so we understand – the basis of a comprehensive inventory of existing chemical legislation in many countries. It is possible therefore, in this talk, to pick out some salient points without necessarily being totally comprehensive.

The first thing to be said is that, on the whole, legislation, or the lack of it, is not the main problem. Certainly there are gaps to be filled here and there. Not all countries within the OECD have a totally comprehensive legislation covering all aspects of the problem, upstream, middle-stream and downstream. Nevertheless, reading the replies to the OECD Questionnaire which was mailed out, a summary of which is available, it is quite clear that the major legislative blocks for an adequate system are already in place; or – at the very least – are now being moved into place. Within the EEC, for example, a draft directive on environmental impact assessment is now being discussed by the Council of Ministers. This, of course, is an instrument of general application which should be of great importance for the "upstream" regulation of chemicals. Annex I of the draft directive contains a list of development projects which must be the subject of environmental impact assessment. The list includes most major industries, including of course the chemical industry. The directive further lays down that the environmental impact assessment to be made is to include a description of the environment likely to be significantly affected by the proposed project, including, in particular, water, air, soil, climate, flora and fauna, the built-up environment and the landscape, taking into account the existing use of these resources; the assessment of the likely significant affects of the proposed project on the environment (direct and indirect, cumulative, short- medium- and longterm, permanent and temporary, positive/negative) resulting from

- the physical presence of the main and associated projects
- the use of the resources of the environment
- the emission of pollution, nuisances and waste, as well as the secondary effects linked to their elimination
- risk of accidents;

and a description of the measures to eliminate, reduce or compensate adverse affects on the environment.

A second Annex specifies a further list of projects where member states of the EEC are themselves to work out criteria and thresholds for environmental impact assessment so that the Commission, duly informed, may have the material to work out a consistent policy.

In itself, the principle of environmental impact assessment is not new. It has been practiced in the United States for many years, following the passage of the National Environmental Policy Act of 1971. And in other countries, such as the United Kingdom, and France, it is argued that environmental impact assessment has been applied through planning procedure even if that particular term of art has been aschewed. What is new about the EEC proposal is that for the first time there is an attempt by ten member nations of the Community to undertake EIA in a common and coherent fashion. The urgent need is for the Council to adopt the directive as soon as possible.

Moving beyond planning, it can be said that in a general way most OECD states have the legislative possibilities of controlling chemicals both from the point of view of protection of workers' health and the environment. Some countries have attempted to separate out occupational exposure from environmental exposure; others have tended

to put the two together. (Whether we are dealing with a single framework, or a split framework, is less important than the actual substance within the framework.) However, it is hard to resist the general conclusion that, though most states have now taken power, in one way or another, to control chemicals in the workplace or the environment, the question of what chemicals are to be controlled and in what way remains very much open both nationally and, a fortiori, internationally.

Some examples make the point.

The United Kingdom

In the United Kingdom, there exists an informal system to review selected existing substances underpinned by Section 6 of the Health & Safety at Work Act 1974 and an assortment of other legislation and administrative practices. In general, the choice of substances for review is pragmatic. In the field of Health & Safety, the review programme is largely controlled by the Advisory Committee on Toxic Substances, which includes representatives of all interested parties and, in particular, of both sides of industry. In the environmental field, the programme is less formalised; reviews tend to be undertaken when a need is identified. It is not clear that this "informal system" has as yet resulted in a priority list of chemicals for review and/or regulation except insofar as this is laid down by already agreed "black lists" (this point will be returned to later).

Some sixty manufacturing processes which emit to air are scheduled under the Alkali and Works Regulation Act 1906, as well as some 2200 works and 3700 operations. Registered industries may be grouped as:

a) chemical and allied industries, for example chlorine, bromine, di-isocyanate and other works.
b) metal industries, for example lead smelting
c) fuel industries, such as electricity and gas generation
d) other industries, such as cement and lime.

Emission limits are specified for only four processes; for other processes the control of emissions is determined by the inspectorate by the "best practical means".

It is intended that the Health and Safety at Work Act, when fully implemented, will subsume the Alkali and Works Regulation Act.

The Control of Pollution Act 1974 will, when fully implemented, extend and strengthen current statutory measures to almost all inland, underground and coastal waters. The Act sets out what must be included in applications for discharge consents; also for the publication of details and the entering of details in registers open to the public.

The Control of Pollution Act also deals with all controlled waste i.e. industrial and trade waste. Section 17 provides for the issue of regulations concerning special waste.

Other UK measures relating to specific chemicals include the Poisons Act 1972, the Pesticides Safety Precautions Scheme, the Food and Drugs Act 1955 and legislation relating, inter alia, to cosmetics, detergents, etc.

France

In France, the Chemicals Control Act which was passed on 12th July, 1977, not only deals with the notification of new chemicals but provides (in Section 7) that "chemicals which are marketed before the entry into force of this Act and are dangerous to man or his environment. . . may be examined or re-examined on the initiative of the

administrative authority. The latter may require producers or importers to supply the necessary technical files for the examination or re-examination of such substances, which may be entered on the list specified in Section 4 and made subject to the measures specified in Section 5." Section 5 of the French Law provides that the "commercial manufacture or importation of chemicals may be prohibited or made subject to a provisional or partial ban on their manufacture, transport or marketing; or restrictions on, or regulation of, the manufacture, composition, storage, transport, packaging, labelling, specific uses, marketing, trade description, advertising and disposal of the substance or any preparations thereof, and any other condition required for maintaining public health standards or protecting the environment."

In practice, it is not clear that the legal provisions existing in France have as yet led to the selection of candidates, among existing chemicals, for review and/or regulation.

Germany

Article 4 of the Act on Protection against Dangerous Substances (known as the Chemicals Act) of 16 September 1980, states that "The Federal Government shall specify, by means of a statutory ordinance requiring the consent of the Bundesrat, the substances as such or as constituents of preparations which were borought into circulation prior to 18 September 1981 in a country which is a member of the European Community. Polymerizates, polycondensates and polyadducts, as well as substances which have been brought into circulation for research or development purposes only or only for use in laboratories, shall not be included."

Article 4 (6) lays down that "In the case of a substance specified in the statutory ordinance provided in paragraph 5 and for which there are real grounds for suspecting that it is dangerous within the meaning of Article 3, No. 3, letter a, b, k, l, m (very toxic, toxic, carcinogenic, teratogenic, mutagenic) or (~) (which possess other extremely harmful properties or which in themselves, or their impurities or decomposition products, are capable of altering the natural state of water, soil or air, of plants, animals or micro-organisms, as well as the balance of nature in general, to such an extent that people are considerably endangered or put at a considerable disadvantage) either on its own or in conjunction with other substances, the Federal Government shall be authorised, after a hearing of experts and by means of a statutory ordinance requiring the consent of the Bundesrat, to prescribe insofar as is necessary to protect human life or health or to protect the environment that the manufacturer or introducer of the substance concerned must notify it in accordance with para. 1 or 2 (which deal with compulsory notification), subject to the proviso that the test documents provided for in Article 7, para. 1 and Article 9, para 1 only cover those properties which offer grounds for suspicion."

This provision regarding compulsory notification of existing substances which is to be found in Article 4 (5) of the Federal German Chemicals Act is of the utmost importance insofar as it applies the whole system [1] of notification which has been worked out for new chemicals in the context of the Sixth Amendment, and which is to be found faithfully reproduced in the Chemicals Act, to existing chemicals. Thus Article 6 of the Chemicals Act deals with the contents of the notification, laying down that the party required to notify shall submit in writing to the Notification Authority his name and address as well as

i) the identifying features
ii) details on the utilisation
iii) harmful effects during the utilisation

iv) the quantities of the substance which he proposes to put into circulation or introduce each year, and
v) the methods which must be used to properly dispose of it to recycle it if possible and to neutralize it, as well as the test documents provided for in Article 7.

Article 7 prescribes the elements of the "base set" as laid down in the EEC Sixth Amendment, including results of acute toxicity tests, tests for carcinogenic or mutagenic properties, test for corrosive, irritative or sensitisation properties, sub-acute toxicity tests, and a test for indications of whether properties of the substance, either alone or in conjunction with other properties of the substance, are a danger to the environment.

Article 9 lays down the additional tests, or "Stufenplan" tests which are required when the quantity of the notified substance reaches a certain level. For example, if the quantity of the notified substance put into circulation within the Member States of the European Communities by the party required to notify reaches 100 tonnes per annum or 500 tonnes (cumulative) since the substance was first manufactured or introduced into these countries, tests documents have to be submitted for

i) sub-chronic toxicity
ii) impairment of fertility
iii) properties which alone or in conjunction with other properties of the substance are a danger to the environment, and
iv) carcinogenic, mutagenic and teratogenic properties.

If the quantity notified reaches 1000 tonnes per annum or 5000 tonnes (cumulative), test documents must be submitted for

i) biotransformation and toxicokinetic properties
ii) chronic toxicity
iii) carcinogenic properties
iv) acute and sub acute toxicity, insofar as the necessity arises from previous test results
v) behaviour-altering properties
vi) properties affecting fertility and teratogenic properties, insofar as the necessity arises from previous test results, and
vii) additional properties which alone or in conjunction with other properties of the substance are a danger to the environment.

As far as the sharing of the burden of testing is concerned, Article 4 (7) applies equally to the notification of new chemicals under the Act or to the notification of existing chemicals, as called for in Article 4 (6). Article 4 (7) specifies that "If a substance which must be notified in accordance with Article 6 is to be put into circulation by

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[1] *Harald Lindemann (D): Comment to S. P. Johnson's Survey of Legal and Administrative Powers to Control Existing Chemicals*

The wording ". . . applies the whole system . . ." is not in correspondance with the German Law, § 4 (6) – not § 4 (5) – and should be avoided for not giving a wrong impression.

The oral information "provides for the possibility" and "to certain designated existing chemicals" is better but not sufficient.

I would propose to formulate ". . . is of importance in so far as it entitles the Government under special limited conditions to apply part of the notification system . . .". Condition is, for instance, that the substance is listed in the final list of existing substances of the EC, the so-called inventory, which is hoped to be available at 1985.

The last point was disputed on legal ground by F. Schmidt-Bleek, Umweltbundesamt.

several manufacturers of introducers, the notification authority can allow just one manufacturer or introducer to carry out the appropriate tests and the other manufacturers or introducers to refer to these tests with his written consent."

Article 17 deals with the authorisation to impose bans and restrictions. Article 17 (1) lays down that the Federal Government shall be authorised, by means of a statutory ordinance with the consent of the Bundesrat, insofar as it is necessary to protect human life or health or the environment against risks which cannot be fully eliminated by classification, packaging and labelling

a) to prescribe that certain dangerous substances, certain dangerous preparations or certain products which contain such substances or preparations may not be manufactured, put into circulation or used either on a commercial basis, within the framework of any other business undertaken or anywhere where employees are involved, or only in a certain condition or for certain purposes, and
b) to prohibit manufacturing or utilisation methods which can produce certain dangerous substances.

Denmark

Has an Act on chemical substances and products. There are also statutory orders on classification, packaging, labelling of chemical substances and products. Measures have been taken in implementation of EEC Directives, e.g. detergents, lead and cadmium in glazes, etc. Suspicious chemicals are given as mercury, cadmium, CFC's, hydrazine, chromates, formaldehyde, pentachlorophenols.

Chemicals are not chosen from any particular list, but rather taken up for evaluation as they are encountered by authorities, e.g. during enforcement, guidance sessions, etc., or as they are brought up by e.g. consumers, industry, science or authorities in other countries.

For several years to come, there will probably be sufficient work to do on chemicals which are already thought to present dangers to man or the environment. Consequently, the starting point might well be a list, brought about as a combination of lists of suspected chemicals known to authorities in the Member Countries.

Belgium

Belgium refers to lists made by the IARC, EEC and WHO as the basis for selecting "existing chemicals" which pose a danger to man and/or the environment. Belgium indicates that the list of "suspicious existing chemicals" needing closer attention, i.e. testing and control is "confidential".

Belgium lists pesticides, drugs and food additives as chemicals which have been controlled in the past. Others, such as PCB's, have been voluntarily withdrawn from the market.

European Economic Commission, EEC

Taking the EEC as a whole, we find that the basic legislative framework is now established or in the process of being established. The Sixth Amendment, as noted above, deals with the notification of new substances. There is another framework directive, which was adopted by the Council on 27th July, 1976, on the approximation of the laws of the Member States restricting the marketing and use of certain dangerous substances and preparations. This directive contains general restrictive provisions applying to the fields which are not covered by other directives, and is a vehicle for Community

measures. So far PCB's and VCM's have been regulated within the context of this directive.

There is also the so-called SEVESO Directive, still being discussed in the Council, which deals with the general problems of siting and operating industrial plants. Annexes to the SEVESO Directive list various processes deemed to be hazardous.

As far as the work place is concerned, there is a proposal from the Commission dated 2nd March, 1979, for a Council Directive on the protection of workers from harmful exposure to chemical, physical and biological agents at work. This again provides a general framework for regulating exposure. In addition, the directive contains an Annex in which a list of chemicals is given, known as a list of "agents", where there is an undertaking that limit values will be worked out at EEC level. The framework directive on occupational exposure differs, therefore, from the framework directive on marketing in that already a priority list or "black list" is built in to the directive. The list includes acrylonitrile, arsenic and its compounds, asbestos, benzene, cadmium and compounds, chlorinated solvents specified as carbon tetrachloride, chloroform, paradichlorobenzene; lead and compounds, mercury and compounds and nickel and compounds.

The EEC directive on occupational exposure is not the first time the notion of a "black list" appears in a Community instrument. The first EEC environment programme, adopted by the Council in November, 1973, lays down a list of substances where the Commission is asked to cover lead and compounds, sulphur compounds, nitrogen oxides, carbon monoxides and various inorganic micropollutants such as mercury, cadmium, zinc, arsenic and cyanide. And as far as discharges to water are concerned, the Community adopted its own black list of priority candidates for control in a famous directive known as ENV 131 (4 May 1976). This black list is described as containing certain individual substances which belong to families and groups of substances, selected mainly on the basis of their toxicity, persistence and bio-accumulation, with the exception of those which are biologically harmless or which are rapidly converted into substances which are biologically harmless. The list includes organohalogen compounds, organophosphorus compounds, organotin compounds, mercury and its compounds, cadmium and its compounds, persistent mineral oils and hydrocarbons of petroleum origin, and certain persistent synthetic substances. The Commission is to prepare individual directives, proposing both emission standards and environmental quality objectives, for the substances on the black list. Already the first draft directives, relating to mercury and the "drins" (aldrin, dieldrin) are being discussed by the Council.

ENV 131 also contained a "grey list" of substances where Member States undertake to lay down individual emission standards whenever they give "consent" to or authorize, a discharge. The list includes some twenty metalloids and metals and their compounds, biocides and their derivatives not included on the black list, toxic or persistent organic compounds of silicon, inorganic compounds of phosphorus and elemental phosphorus, non persistent mineral oils and hydrocarbons of petroleum origin, cyanides and fluorides and substances which have an adverse effect on the oxygen balance, particularly: ammonia and nitrates.

As far as the EEC is concerned then, we have a situation where some of the basic legislation (not all of it) already contains a priority list of chemicals for review and/or control. An effort is now under way through the Commission's Scientific Advisory Committee on Toxicology and Eco-toxicology to establish a priority list of existing chemicals on the basis of certain selection criteria. Whether this exercise produces results

which are consistent with the basic black/grey list approach already adopted in EEC legislation, remains to be seen.

Sweden

Moving beyond the EEC, but still staying within Europe, we find that the central legislation in Sweden for regulation of chemicals is the "Act on Products Hazardous to Health and to the Environment" (1973) and the connected ordinance. Under this legislation any chemical can be regulated if it is liable to cause harm to man or the environment. Regulations may take the form of the imposition of precautionary measures, labelling instructions, permits, notification or reporting requirements and prohibition. There is also the "Work Environment Act" dealing with the protection of workers.

Few chemicals have so far been regulated. For PCB-compounds, there are regulations concerning importation and use which reflect those taken by OECD. Other regulations have been made relating to fluorochlorocarbons.

Norway

According to the Products Control Act of 1976, manufacturers and importers are required to provide for, and make available, such knowledge of the product as may be necessary in order to assess whether it may cause damage to health or disturbance to the environment. Thus, manufacturers and importers are responsible for deriving information from available sources and for undertaking laboratory investigations as may be considered necessary for an evaluation of the products. Other specific Acts regulate air and water pollution, pesticides, food additives, cosmetics, transportation of hazardous goods, and occupational health. The authorities responsible for administering the Product Control Act have a responsibility for ensuring comprehensive approaches and coordination.

Pursuant to the Product Control Act of 1976, there has been proposed a set of rules pertaining to importation, production and distribution of chemical products. The proposed regulations imply, inter alia, a classification and labelling of toxic, harmful, corrosive, irritant, allergenic and carcinogenic substances and products. Furthermore, manufacturers and importers of toxic and carcinogenic products are required to notify to the authorities. The new regulations are expected to become effective during 1981. The official Norwegian list of toxic substances is to be replaced by new lists according to the proposed new set of rules.

There is at present no official definition in Norway of the term "existing chemicals". The Norwegian Government, however, is giving serious consideration to the question of premarketing notification of new substances. In that connection, discussions are taking place concerning the need for establishing an initial inventory of those substances which are considered to be "existing" as opposed to "new". Development of such an inventory is tied in with the work now being planned to build a data base, or register, containing complete information on the composition of all toxic products on the Norwegian market.

Switzerland

In Switzerland, the Federal Act on Trade in Toxic Chemicals does not distinguish between new and existing chemicals, but provides for the registration of a product or substance in a list of toxic chemicals. Article 13 of the Implementing Order (1971)

provides that the classification be determined according to the overall hazard. Some 10,000 basic substances have been classified and more than 40,000 products have been declared. A committee of experts acts as an advisory body on the technical and scientific aspects of the assessment of toxic chemicals. Though these priorities are not laid down in legislation, specific efforts (testing or preparation of criteria documents) have been made or are intended concerning the following chemicals or groups of chemicals:

Heavy metals such as mercury, cadmium, lead, zinc.

Organohalogen compounds such as polychlorinated biphenyls and related substances, hexachlorobenzene, pentachlorophenol, p-dichlorobenzene, and fluorocarbons.

Additives to plastics.

Substances introduced into the environment by their use such as pesticides, detergents and road salts.

Austria

Austria refers to a Drugs Act and to a Plant Protection Act. Austria also refers to the European Community's list as a basis for the selection of chemicals. Beyond that, Austria indicates that there are no detailed criteria available for the selection of chemicals.

The United States of America

In the United States, the Administrator of the Environmental Protection Agency (EPA) must, under Section 4 of TSCA, require testing of a chemical substance if he finds that it may present an unreasonable risk of injury to health or the environment, that there is insufficient information to assess the affects of use of the chemical, and that testing is required to develop such data. He must also require testing if a substance is to be produced in substantial quantities and it may reasonably be anticipated that there will be extensive environmental or human exposures. Mixtures are subject to the testing requirements only if the effects of the mixture may not be more efficiently determined from testing of the constituents of the mixture.

The risk of injury from the substance may result from its manufacture, distribution in commerce, processing, use or disposal. The scope of EPA's authority is thus extended for the first time to the total human or environmental exposure of a chemical substance and does not depend on its particular use or the route of exposure.

A testing requirement must be promulgated by a rule which must be issued by EPA, and the manufacturer or processor must perform any testing required by a testing rule. The testing rule must identify the substance to be tested. In addition to an individual substance or mixture, the EPA Administrator may list groups of substances or mixtures that require testing. The testing rule must also provide standards for conducting the tests. In issuing rules for testing, the Administrator is required by the Act to take into account costs of the tests prescribed and the availability of test facilities to perform the tests. And at least once a year the Administrator must review the adequacy of test standards and revise them if necessary.

The Act establishes an intra-governmental committee to advise the EPA Administrator on the choice of testing priorities. In making recommendations for testing, the committee must consider all relevant factors, including the quantities in which a substance will be produced, the quantities in which it enters the environment, the number of persons occupationally exposed, total human exposure, the similarity to known chemical hazards, the existence of data on health and environmental affects, the likelihood that data can be developed, and the availability of test facilities.

The committee must list substances in the order in which it thinks the Administrator should issue testing rules. It may designate no more than 50 substances as requiring the highest priority for testing. For substances so designated the Administrator must within twelve months either initiate rule making for testing or publish in the Federal Register his reasons for not undertaking rule making. The priority list of chemical substances recommended for testing, as it as present stands, is given as Annex 1 to this paper.

The basic authority of EPA to regulate chemical substances and mixtures is included in Section 6 of TSCA relating to protection against unreasonable risks. If the EPA Administrator "finds that there is a reasonable basis to conclude that the manufacture, processing, distribution in commerce, use, or disposal of a chemical substance or mixture . . . presents or will present an unreasonable risk of injury to health or the environment", he must regulate the substance or mixture to the extent necessary. The regulation of the substance or mixture must be promulgated as a rule in the rule making procedure. The rule regulating the substance must include the "least burdensome requirement" necessary to adequately protect against the unreasonable risk. The rule regulating the substance or mixture must include one or more of the following requirements, any of which may be limited to specified geographical areas:

A requirement prohibiting the manufacture, processing, or distribution in commerce of the substance or mixture.

A requirement limiting the amount of the substance or mixture that may be manufactured, processed, or distributed in commerce.

A requirement prohibiting the manufacture, processing, or distribution in commerce of the substance or mixture for a particular use.

A requirement prohibiting the manufacture, processing, or distribution in commerce of the substance or mixture for a particular use in a concentration in excess of a specified level.

A requirement limiting the amount of a substance or mixture that may be manufactured, processed, or distributed in commerce for a particular use.

A requirement limiting the amount of the substance or mixture that may be manufactured, processed, or distributed in commerce for a particular use in a concentration in excess of a specified level.

A requirement that manufacturers and processors of the substance or mixture make and retain records of the manufacturing process and monitor or conduct tests which are reasonable and necessary to assure compliance with any rule issued by the EPA Administrator.

A requirement prohibiting or regulating the manner or method of commercial use of the substance or mixture.

A requirement prohibiting or regulating the manner or method of disposal of the substance or mixture or any article containing the substance or mixture.

A requirement directing the manufacturers or processors of the substances or mixture to give notice of the unreasonable risk of injury to distributors, to give public notice of the risk from the substance or mixture, and to replace the substance or mixture.

The Act imposed specific restrictions on PCB's.

Under Section 8 of TSCA, EPA may by promulgation of rules require reports on all chemicals produced in the United States, not only on production but also on use, health and environmental effects, and exposures. The reporting provisions of the Act

do not apply to small manufacturers, except that small manufacturers may be required to submit data for use in compiling the initial inventory list. In addition to the reporting requirements, the Act specifies record-keeping requirements, which apply to all manufacturers regardless of size. The Act requires a manufacturer to inform the Administrator immediately if he obtains information that a chemical product presents a substantial risk of injury to health or the environment.

Other laws administered by EPA that provide authority for regulating health or environmental risks from chemical substances or mixtures include:

The Clean Air Act which provides authority for regulating air pollutants.

The Federal Water Pollution Control Act, which provides authority for regulating water pollutants.

The Marine Protection, Research and Sanctuaries Act, which provides authority for regulating ocean dumping.

The Safe Drinking Water Act, which provides authority to regulate substances in drinking water.

Other laws such as the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA) are not administered by EPA but cannot be ignored in any survey of legislation dealing with existing chemicals.

In May 1977, the EPA, the FDA (Food and Drug Administration) and the CSPC (Consumer Products Safety Commission) jointly issued proposed regulations prohibiting the manufacture, processing, and import of fluorocarbons for use in most aerosol products. These regulations were issued in final form on 17th March 1978. Most of these regulations were promulgated pursuant to TSCA. Separate regulations prohibiting the use of fluorocarbons as propellants in food, drugs, and cosmetic products were promulgated under the Food, Drug and Cosmetic Act. Although these rules were issued under separate legal authority, their practical effect is the same.

The Inter-agency Testing Committee (ITC) scoring system was published by EPA on 1st October, 1977. It is used as a screening tool to identify chemicals in need of testing. It is based on selection criteria which include biological toxicity, production and release data, human exposure and environmental fate.

Canada

On December 1, 1979, the annual review of the List of Priority Chemicals and Schedule of the Environmental Contaminants Act was published in the Canada Gazette, Part 1. The list included those substances for which regulations were being developed under the Environmental Contaminants Act or about which further information was required to determine whether regulation or other action was necessary. The Environmental Contaminants Act is capable of regulating the importation, manufacture and processing of any chemical substance that poses a threat to human health or the environment. Chemicals that are used solely as drugs, food additives or pesticides are arbitrarily excluded from consideration because they are already scrutinised or controlled under other Federal legislation. On November 29, 1980, a revised List of Priority Chemicals was published in the Canada Gazette, Part 1.

Category 1 is defined as "those substances which the government is satisfied pose a significant danger to human health or the environment and for which regulation or specific control strategies are being developed."

The use of PCB's is already subject to certain restrictions. Other regulations are being developed.

Restrictions on the use of fluorocarbons as aerosol propellants in hair sprays, deodorants and anti-perspirants came into effect on May 1, 1980.

Category 2 comprises "those substances which are being investigated to determine the nature and the extent of the danger to human health or the environment and the appropriate means to alleviate that danger."

The list at the moment comprises: cadmium and chlorophenols.

Category 3 comprises "those substances which may pose a significant danger to human health or the environment and about which further detailed information (for example toxicology and amounts used) is required."

The list covers: chlorobenzenes, hexachlorobutadiene (HCBD), hexachlorocyclopentatiene and adducts, mercury, organotins, phthalica acid esters triaryl phosphates and related substances.

In 1979 a second list of chemicals entitled Candidate Chemicals was drawn up for the purpose of specifically evaluating potential environmental contamination problems. The data for substances on this list were generally weak. In order to obtain more detailed information on commercial use patterns of these substances, notices under the Environmental Contaminants Act have been issued. Following review of the available data and of the results of the information gathering exercise that are expected by early 1981, some of the substances may warrant detailed investigation and may be placed on the List of Priority Chemicals or may not warrant further investigation and be deleted from the list.

The Candidate Chemicals List comprises: aromatic amines, chlorinated naphthalenes, chlorinated parafins, chlorinated styrenes, halogenated diphenyl ethers, haloginated ethanes and ethylenes, halogenated methanes, halogenated tomenes, bromobenzenes and fluorobenzenes.

Canada does not have an "Official list of existing chemicals" comparable to the inventory developed under the Toxic Substances Control Act in the United States.

Under the Environmental Contaminants Act, there are provisions for collecting information under Section 3 (1), 4 (1), and 4 (6).

Under the Clean Air Act, there are provisions for collecting information on the amounts of specific pollutants being discharged to the environment.

Paragraph 14 of the Hazardous Products Act contains provisions for collection of information on regulated products.

In 1978 a total ban on the use of mirex was applied under the Environmental Contaminants Act.

Japan

Under the Chemical Substances Control Law 1973 a List of Existing Chemicals has been drawn up. The list consists of chemicals which were actually being manufactured in Japan or imported at the time of promulgation of the law (16th October 1973), excluding those which were being manufactured or imported for testing and research and those which were being manufactured or imported as reagents. According to the provisions of Section 2 of the Law chemical substances other than in the List of Existing Chemicals are treated as *new* chemicals. This list has approximately 24,000 entries (1980).

The Toxic Substances List has been prepared by screening the List of Existing Chemicals using mainly LD50 acute toxicity.

The Priority List has been prepared by screening the Toxic Substances List to select candidate substances for the environmental survey. The following selection criteria have been applied:

i) production or import greater than 100 tons/year;
ii) chemical in behaviour similar to PCB in chemical structure and use;
iii) structure – reactivity correlation useful, in order to rationalise testing and assessment;
iv) chemicals, which have been known or considered hazardous to man and the environment by references and other information.

The Priority List * contains 2140 chemicals in nine sublists:

List No.	Compound	Entries
1	CH Halogene	254
2	CH other	64
3	Organophosphorous	68
4	CH Halogene	283
5	Organo-sulphur	178
6	Organo-nitrogene	574
7	Organo-oxygene	508
8	Hydrocarbons	140
9 (1)	Inorganic (metal)	33
9 (2)	Inorganic (non-metal)	38

Tests to check the ecotoxicological effects are to be done for the chemicals on the Priority List. The Environment Agency conducts an Environmental Survey. A few substances which are found to be problematic as a result of this Survey may be the candidates for control by various national regulations. However, the results of the Environmental Survey do not necessarily mean the exercise of any specified national law. Under Article 27 of the Chemical Substances Control Law, the Director General of the Environment Agency, when he deems it necessary for attaining the purpose of this Law, may request the competent Minister to take the measures provided for under Article 22 and 23.

Article 2 of the Law introduces the notion of a "specified chemical substance" which is defined as: a) a substance which does not lend itself easily to chemical changes caused by natural effects, and is also easily accumulated in biological organisms; b) when ingested continuously, there is a fear that it may be harmful to human health.

A chemical substance may also be a "specified chemical substance" in the sense of the Law where it lends itself easily to chemical changes caused by natural effects, and where the chemical substances (including elements) produced by the chemical changes are of the same nature as those noted above.

Article 22 of the Law states that "when a chemical substance has been designated (this is to be by Cabinet order) as a specified chemical substance, the competent Minister may, when he deems it to be particularly necessary in order to prevent the progress of environmental pollution by the said chemical substance, and within the range in which this is necessary, order a person or persons engaged in the business of manufacturing or

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* Ref: Chemicals in the Environment, Environmental Agency Japan, Office of Health Studies, Report No. 5, September 1979.

importing the said chemical substance, or products in which the said chemical substances used, to arrange for the recovery of the said chemical substance or the said products which have been manufactured or imported, or to take other measures necessary to prevent the progress of environmental pollution by the said chemical substance."

Article 23 specifies that "when the competent Minister deems that there is sufficient reason to suspect that a chemical substance other than a specified chemical substance may correspond to one of the items in Article 2, Paragraph 2, (see above) he may, within the range where this is necessary in order to prevent the progress of environmental pollution by the said chemical substance, make the necessary recommendations concerning restrictions on the manufacture, import, or use of the said chemical substance to persons engaged in the business of manufacturing, importing or using the said chemical substance."

Australia

There is no single comprehensive law in the mould of TSCA or European equivalents. Existing relevant Commonwealth Laws included the Therapeutic Goods Act and the Customs (Prohibited Imports) Regulations. The latter is not confined to any particular class of chemicals in its application. States' laws typically include laws to schedule and control poisons, register and regulate use of pesticides and veterinary drugs, therapeutic substances, food additives, etc. State environmental and other authorities often administer air quality and water quality laws, or administer discharge standards on many chemical substances.

There is currently no comprehensive system of selecting existing chemicals for further study, although there are comprehensive Commonwealth and State notification, assessment and registration procedures for pharmaceuticals, food additives, veterinary drugs, pesticides, agricultural chemicals and poisons. A voluntary interim notification scheme for new chemicals is soon to be introduced for all chemicals not controlled by existing procedures. This scheme will also be used for the assessment of existing chemicals. The existing chemicals will be those which are listed on an existing Chemicals Inventory, prepared by cooperation between industry and government.

Available resources do not permit comprehensive assessment of more than a handful of chemicals each year, and the number of less comprehensive assessments would number only several tens per annum.

New Zealand

Legislation to regulate chemicals includes the Poisons Act 1960, Poisons Regulations 1964, and Noxious Substances Regulations, 1954. The Toxic Substances Act 1979 has yet to come into force.

In the reply to the questionnaire, New Zealand indicates that, being a small chemical importing country and, therefore, having very limited toxicological resources and expertise, it does not "select" existing chemicals for study. "Such concerns tend to be 'imposed' upon us, after they have originated in other, larger countries."

III. Conclusions

What conclusions can be drawn from this survey of legislation affecting existing chemicals? What further action needs to be taken? And by whom? Legislating for chemicals is legislating for pollution as a whole. Take the gamut of any country's legislation, or

any group of countries like the European Community, and you find that most anti-pollution measures are in some sense anti-chemcial measures. Air quality objectives or standards, water quality objectives or standards, point source emission standards, whether these are dealing with discharges to water or to air, regulations concerning product specifications (eg maximum permitted content of lead in petrol or mercury in paint), waste disposal regulations, including (and particularly) regulations dealing with the disposal of toxic and hazardous waste, regulations dealing with the transportation of dangerous goods and substances, etc. – all this is in a very real sense dealing with chemical pollution. Even planning legislation, and the requirement – for example – for environmental impact assessment – is dealing with chemical pollution insofar as it deals with the siting and operation of major industrial installations which give rise to this form of pollution.

The question of chemical pollution can be handled in matrix form. Running horizontally, left to right, can be placed the various stages of a chemical's life from the original planning decision, through construction and operation of a plant, through the discharge of waste phase (whether to water, air or soil), through the disposal of residual waste phase, through reclamation and so on.

On the vertical axis can be listed the legal and administrative measures which are called for, or which should be called for, at any particular phase including, for example, the setting of quality objectives, the setting of emission standards, rules on disposal of waste and so on. In each square of the matrix can be listed the countries which have enacted legislation, or other measures, of a particular sort to cover the phase of the chemical's life in question. No such comprehensive effort is attempted here because that is not the purpose of the Seminar. However, as an illustration of what is meant, a matrix drawn up for the United States is attached as Annex 2 to this paper.

What an exercise of this kind reveals, or should reveal, is that while there are some gaps in the basic legislation – in the EEC for example the principle of environmental impact assessment is still not yet accepted – the essential legislative framework is in many, or even most, countries in place. What has not yet been worked out, either at the national or the international level, is a strategy for establishing targets for legislation. A good deal of fire-power has been built up, or is in the process of being built up, but we are not yet sure in what direction that fire-power should be used. The essential problem is the definition of priorities. If we insert cadmium, for example, into the matrix, we have to approach it in a coherent way and include it not just in one or two phases (for example, in discharges to water) but at all points. Often we are dealing with pollutants which reach the environment through a multitude of pathways. To close off just one pathway, without closing off others at the same time, is often to guarantee a diversion, rather than a suppression, of pollution.

The first priority, in the attempt to set priorities, has to be the assembly of information. What are the chemicals in circulation? What do we know about them?

As far as the first question is concerned, in the United States we have the Inventory of Existing Chemicals. In Europe, there is the list published by the Swiss authorities of basic substances ("substances de base"); we have the German Temporary Inventory and under the EEC Sixth Amendment there is provision for an EEC Inventory which is now being prepared. In Norway, there is a list of toxic substances, now being revised; in Japan, there is the MITI Inventory.

Both in the United States and in Europe, the existence of an Inventory owes much to the legal need to distinguish "new" chemicals from "existing" chemicals. If the legal definition of a "new" chemical is something which is not on the inventory, then clearly

it is necessary to have an inventory. (There is, of course, an important conceptual distinction between the U.S. approach and the EEC approach. In the United States a "new" chemical can, after notification and evaluation, become an "old" or "existing" chemical on being transferred to the Inventory. In the EEC, a "new" chemical remains a new chemical throughout its life, subject to the renotification procedures which are laid down in the directive. It is also worth noting that the Sixth Amendment will enter into force in the EEC on the 18 September 1981 before the Inventory has been prepared.)

There is a case for the compilation of an international Inventory, on the basis of Inventories already in existence or being prepared, if only to avoid duplication of effort and to facilitate the elaboration of internationally compatible and mutually acceptable notification schemes for new chemicals. It seems likely, however, that the material contained in one or several Inventories cannot by itself be a sufficient basis for the "information-review" exercise which should be a fist step in the effort to select priorities. There is both too much information in an Inventory, and too little. (It is also possible that an Inventory could leave out of account altogether some important chemicals simply because in the process of production or disposal, they are transformed and released in a form (or chemical structure) which is not the same as their Inventory entry. Does dioxin appear as such on the U.S. Inventory?)

A first step therefore is the exchange of information on chemicals which are "candidates" for review. What is known about the impact of these chemicals, on health and environment, and on the pathways by which they reach their target? This exchange of information exercise can properly be conducted within an international framework, such as OECD. (Within the ten countries of the EEC, of course, a preliminary review and information exchange can, or should, take place within the Commission's Scientific Advisory Committee on Toxicology and Exotoxicology which itself will draw on the information and analysis provided by individual Member States.) In this preliminary phase, the collaboration of industry is obviously of critical importance. Almost all the legislation examined provides for the provision of information by industry to competent authorities. But it is obviously desirable that this should be achieved without undue pressure having to be exerted. The next step in the operation, and it is again one which can properly be conducted within a framework such as OECD, is the establishment of priorities for testing. There are, of course, numerous national or international lists already in existence. The London and Oslo Conventions on the dumping of waste at sea have their "black lists" and their "grey lists". The Paris Convention, which deals with the pollution of the sea from land-based sources, also has a black and grey list. As mentioned, EEC Directives dealing both with occupational health and discharges to water, contain black lists of pollutants; Canada has its list of priority chemicals; priorities abound in US anti-pollution legislation of every kind; the Interagency Toxic Substances Testing Committee in the United States has – as mentioned – produced its list of priority substances; WHO's International Programme on Chemical Safety is engaged on the exercise of evaluating the health and environmental effects of new and existing chemicals, etc.; the International Agency for Research on Cancer has evaluated over 450 chemicals for carcinogenic risk to humans; Japan has, as noted, its Priority List of Chemical Substances.

Of course, all these lists can be put together and their similarities and discrepancies can be studied and ultimately a "list of lists" can be produced. More important should be the attempt to identify the criteria under which the selection of priority chemicals should be made. In this connection mention has been made of the ITC scoring system;

the EEC Scientific Advisory Committee is also now in the process of considering selection criteria and an appropriate scoring system. Other countries are doing the same. There is a clear case for working out at an international level the criteria for assessing existing chemicals and then for applying these criteria, again on an international basis to the "candidate" list. Again, the cooperation of industry will be essential. Exposure data, for example, is bound to be one important criterion for the selection of priority chemicals and in real life production is often a surrogate for exposure. Equally, the burden of testing must ultimately devolve on industry itself. We can envisage that in certain cases industrial consortia will be formed to carry out appropriate testing and they will work out amongst themselves appropriate means of sharing the cost (as is provided for, e.g., in the German Chemical Act).

It is not the purpose of this paper to suggest what the criteria for the selection of chemicals should be. The criteria at present chosen to assess hazards usually include most of the following: acute toxicity, carcinogencity, mutagenicity, teratogenicity, neurotoxicity, other toxic affects, physico-chemical properties, persistence, accumulation, degradation, nature of transformation products, impurities, routes of entry into the environment, dispersion and distribution within the environment, amounts manufactured or imported, population affected, toxicity to terrestrial and aquatic organisms, damage to property and impact on climate and weather.

What matters now is to achieve an international consensus as to how these criteria are to be weighed, both relative to each other and in absolute terms. Are we to use a "scoring" system or hazard index system, as appears to be the case with the Interagency Toxic Substances Testing Committee in the United States? Or are we to attempt to develop lists of priority chemicals by obtaining committee consensus on a more qualitative basis, as appears to be the case with the International Programme on Chemical Safety (see Report of the Joint IPCS/CEC Task Force on Priority Industrial Chemicals, Ispra, Italy, November 17–19, 1980). The list of priority chemicals as developed by the IPCS Task Force is attached as Annex 3.

When it comes to action, there is again a need for international coordination. One extremely significant feature of the German Chemicals Act, as noted above, is that it will apply the whole information and legislation procedure of the Act (and of the Sixth Amendment) to the manufacturer or importer of an existing chemical substance, that is to say all the information required by the base set and the further tests which are required under the Stufenplan if he crosses the appropriate thresholds. The advantages of extending this kind of provision to the other countries of the EEC, and beyond, would be obvious insofar as notification (and the provision of information) is a necessary first step in any strategy designed to reduce the adverse affects on health and the environment of selected priority chemicals.

After that point, we enter what was described earlier as the "broad gamut of pollution control possibilities". Priority pollutants will not always manifest themselves in the same way in the various parts of the world. The pathways will be various. In one country, dealing with mercury may be a matter of dealing with discharge from the chlor-alkali industry; in another country it may be a matter of dealing with mining waste. It will not always be possible, or desirable, to agree on internationally harmonized systems of control, though as far as industrial emissions are concerned (at least from new plant) there is a clear case for the application of best available technology. There is also an unanswerable case for international action to be agreed where the pollutant is present in, or manifests itself through, products that are widely traded. The action taken in the last few years on PCB's and CFC's (fluorocarbons) was valid

for trade, as well environmental reasons. To say this, is not to say that all measures to control pollution, or regulate the impact chemicals on health and the environment, should be agreed at international (or OECD's) level before they are put into effect. Countries, or groups of countries (like the EEC), will have their own sensitivities and their own reactions as to the urgency of *doing something*, even where the toxicological and ecotoxicological data are agreed. What matters ultimately is to reduce the overall impact of a "priority" pollutant and to do so in a manner which is as cost-effective as possible.

Much of the work now being carried out under the OECD Chemicals Programme will be of relevance to the problem of "existing" chemicals.Testing guidelines, for example, or good laboratory practices or procedures to protect confidentiality which are now being prepared to help put into effect the systems for notifying "new" chemicals, will also be of importance as the concept of notification is applied – as is suggested here – to old chemicals identified as being dangerous to health or the environment. So too will any arrangements that are made as far as sharing the cost of testing is concerned. The need now is for OECD to build on what it has already achieved under the Chemicals Programme and to prepare, for existing chemicals, a "step-wise" approach along the lines suggested above, i.e.:

Step 1 Selection of candidates for review
Step 2 Selection of priority chemicals for testing
Step 3 Definition on those elements of a control strategy that are appropriate for international agreement and action.

ANNEX 1

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The TSCA Section 4(e) Priority List

Entry	Date of Designation
1. Acetonitrile	April 1979
2. Acrylamide	April 1978(b)(d)
3. Alkylepoxides	October 1977(a)
4. Alkylphthalates	October 1977(a)
5. Alkyltin compounds	October 1980
6. Aniline and bromo, chloro and/or nitro anilines	April 1979
7. Antimony (metal)	April 1979
8. Antimony sulfide	April 1979
9. Antimony trioxide	April 1979
10. Aryl phosphates	April 1978(b)
11. Benzidine-based dyes	November 1979
12. Benzyl butyl phthalate	October 1980
13. Butyl glycolyl butyl phthalate	October 1980
14. Chlorinated benzenes, mono- and di-	October 1977(a),(c)
15. Chlorinated benzenes, tri-, tetra- and penta-	October 1978(c)
16. Chlorinated naphthalenes	April 1978(b)
17. Chlorinated paraffins	October 1977(a)
18. Cresols	October 1977(a)
19. Cyclohexanone	April 1979
20. o-Dianisidine-based dyes	November 1979
21. Dichloromethane	April 1978(b)
22. 1.2-Dichloropropane	October 1978
23. Fluoroalkenes	October 1980
24. Glycidol and its derivatives	October 1978
25. Halogenated alkyl epoxides	April 1978(b)
26. Hexachloro-1.3-butadiene	October 1977(a)
27. Hexachlorocyclopentadiene	April 1977
28. Hydroquinone	November 1979
29. Isophorone	April 1979
30. Mesityl oxide	April 1979
31. 4.4-Methylenedianiline	April 1979
32. Methyl ehtyl ketone	April 1979
33. Methyl isobutyl ketone	April 1979
34. Nitrobenzene	October 1977(a)
35. Phenylenediamines	April 1980
36. Polychlorinated terphenyls	April 1978(b)
37. Pyridine	April 1978(b)
38. Quinone	November 1979
39. o-Tolidine-based dyes	November 1979
40. Toluene	October 1977(a)
41. 1.1.1-Trichloroethane	April 1978(b)
42. Xylene	October 1977(a)

(a) Responded to by EPA Administrator 43 FR 50134–50138
(b) Responded to by EPA Administrator 44 FR 28095–28097
(c) Responded to by EPA Administrator 45 FR 48524–48564
(d) Responded to by EPA Administrator 45 FR 48510–48512

ANNEX 2

Chart 1	Manufacturing/ Processing	Commercial Distribution	Emissions, Effluents	Transportation	Imports	End Use (Products)	Storage/ Disposal	Workplace Exposure
Prohibitions Bans	TSCA 5(e), (f);[1] 6(a) CAA 211(c) CPSA 19(a) (1),(2)	TSCA 6(a)(1); 6(a)(2) CAA 211(c) CPSA 8; 19(a) (1),(2) FIFRA 6; 12(a); 13(a) FFDCA 301(a), (d) FHSA 4(a),(f)	CWA 307(a)(2) 306 311(b)(1) (B) SDWA 1424(a)	TSCA 6(a) (1);[4] 6(a)(2) CPSA 8; 19(a)[5] HMTA 105(a)	TSCA 13(a) (b) FIFRA 6; 12(a); 13(a) CPSA 17(a) FHSA 14(a) FFDCA 801 (a)	CPSA 8 TSCA 6(a) (2)(A); 6(a)(5) FIFRA 6; 12(a); 13(a) FHSA 2(q)(1) (A)(B)	TSCA 6(a) (6) RCRA 3004, 3005	OSHA 13(a)[8]
Quantity Limitations	TSCA 5(f); 6(a)(2) CPSA 9(d)(2) CWA 301; 302; 304; 306	TSCA 6(a)(1); 6(a)(2)	CAA 110(a) (2)(B)[3] CWA 301 307(a)(2)	TSCA 6(a)(1); 6(a)(2) HMTA 105 (a)[6]	TSCA 6(a)(5) CPSA 9(d)(2)	TSCA 6(a)(5)		
Guidelines Standards, Quality Criteria	TSCA 6(b)(2) CAA 111(b) (e) RCRA 3002 (2),(3)		CWA 311(b)(1); 307(a)(2); 303;304; 306 CAA 108;109; 111(a); 112(b)(1); 160,169; 202 SDWA 1421;1412	FIFRA 19(b)[7] RCRA 3003 HMTA 106(a) CWA 311	TSCA 6(b)(2) CPSA 17(a) (1) FFDCA 801 (a)	CAA 202(a) (1) CPSA 7(a)(1); 7(c) FIFRA 3(d) FFDCA 401; 406; 408 TSCA 6(a)(5)	CWA 307(a) (5) FIFRA 19 RCRA 3004, 3005, 4004, 1008 TSCA 6(a)(6)	OSHA 5(a);6(a); 6(b)(5); 6(c)(1); 20(a)(2), (3);22
Required Labeling/ Packaging Provisions	TSCA 6(a) (3)[2]	TSCA 6(a)(3)		TSCA 6(a) (3) RCRA 3003 (a)(2) HMTA 105(a)	TSCA 13(a) FIFRA 17(c) CPSA 17(a) (2) FHSA 14(a) FFDCA 801 (a)	TSCA 6(a)(3) FIFRA 3(c) (5)(B) CPSA 7;14(c) 27(c) FHSA 2(p);3(b) PPPA 3 FFDCA 505(d) 502;403;602; 512(d)(1)	TSCA 6(a)(3) RCRA 3002 (2),(3) 3004	OSHA 6(b)(7)

Chart 1	Manufacturing/ Processing	Commercial Distribution	Emissions, Effluents	Transportation	Imports	End Use (Products)	Storage/ Disposal	Workplace Exposure
						512 (d)(1)		
Registration Certification or Permits	CSPA 14(a) CAA 165(a); 172(b) FIFRA 7(a) FFDCA 510	CAA 211(a), (b); 203(a)(1) FIFRA 3(a); 6 FFDCA 505; 512	CWA 301(b)(2);401; 402 SDWA 1421; 1424(b)	HMTA 106(b); 106(c) RCRA 3003	FIFRA 17(c) CPSA 17(a)(2)	FIFRA 3(a); 4(a); 5;6; 18 CPSA 14(a) FFDCA 505 512 706 CAA 204; 211(b)	CWA 405 RCRA 3005	
Recall, Replace, Repurchase, Seizure	TSCA 6(a)(7) CPSA 15(d) FHSA 15(a)(1)	CPSA 15(d), (c) FHSA 15(a)(2) FIFRA			FIFRA 13	TSCA 6(a)(7) FIFRA 12;13 CPSA 15(d), (c) FHSA 6;15(a) FFDCA 304		
To Require Notice of Hazards to those Exposed	TSCA 6(a)		CWA 311(b)(2)			CPSA 15		OSHA 6(b)(7); 8(c)(3); 13(c); 20(a)(b)
Imminent Hazards	TSCA 7	CPSA 12 TSCA 7 FIFRA 6(c)	CWA 504 CAA 303;311 RCRA 7003 SDWA 1431	TSCA 7 RCRA 7003 HMTA 11(b) CWA 311	TSCA 13(a) CPSA 17(a)(3) FHSA 14(a) FIFRA 6(c)	TSCA 7(a)(1) FIFRA 6(c) SDWA 1431(a) CPSA 12 FHSA 2(q)(2); 3(e)(2) FFDCA 505(e); 512(e)(1)	TSCA 7(a) RCRA 7003	OSHA 13

ANNEX 3

IPCS

Chemicals in the secretariat list recommended for action

No.	Chemical	Working Env. (Man)	General Env. (Man)	General Env. (Non-Human)	Type of Document	Reasons	Remarks
1.	Acrylamide		*		Criteria Document	High exposure; possible water contaminant; delayed neuro-toxicity	-
2.	Alkyl epoxides		*		Preliminary class study	Possible wide community exposure; possible mutagen; carcinogen; teratogen	-
3.	Halogenated alkyl epoxides	*	*		Comprehensive review	Extensive exposure; possible carcinogen	-
4.	Aniline and derivatives		*		Preliminary class study	Exposure; toxicity	-
5.	Asbestos		*		Alert/warning	Carcinogen	Information on hazard and problem available but needs to be disseminated
6.	Benzene	*	*		Criteria document	High exposure carcinogen	1. Urgent need for document. 2. Important to evaluate long-term exposure to low levels
7.	Benzidine and benzidine based dyes	*	*		Criteria document	High exposure; widely used; well-known carcinogen	Consider short document too
8.	Dimethyl sulphate	*			Criteria document	High exposure; widely used; cancer risk; neurotoxicity	-

No.	Chemical	Working Env. (Man)	General Env. (Man)	General Env. (Non-Human)	Type of Document	Reasons	Remarks
9.	Chlorofluoro carbons		*	*	Criteria document	Widely recognized problem; increased UV flux; skin cancer; some mutagenicity data	Data available
10.	Formaldehyde	*	*		Criteria document	Wide exposure; suspected carcinogen; local irritant; sensitizing effect	-
11.	Organochlorine solvents	*	*		Criteria document	Wide exposure; suspected carcinogen; neurotoxicity	1. Consider short document too 2. Include chloromethanes, ethanes, propanes, ethylenes etc.
12.	Pentachlorophenol and its salts	*	*		Criteria document	Wide exposure; possible carcinogen; (chlorance)	Commercial grades to be noted
13.	Phenols		*		Preliminary class study	-	Determine extent of problem and decide on chemicals to be included
14.	Phenylene diamines	*	*		Criteria document	High exposure; carcinogens and suspected carcinogens; suspected mutagens; sensitizers (dermatological effects)	-
15.	Phtalic acid and esters	*	*	*	Criteria document	Widespread use; local irritant and sensitizing agent in respiratory organs; possible environmental effects	-

Additional Chemicals Recommended for Action

No.	Chemical	Working Env. (Man)	General Env. (Man)	General Env. (Non-Human)	Type of Document	Reasons	Remarks
1.	Dioxanes		*		Preliminary study of a single substance	Presence in a wide Range of consumer products and cosmetics	-
2.	Epichlorohydrin		*		Alert/warning	Suspected carcinogen	Information on hazard and problem available but needs to be disseminated
3.	Ethylene and propylene oxides		*		Criteria document	Possible Carcinogens	-
4.	Man made fibres		*		Preliminary study of a single substance	Determine possible adverse effects	-

STATEMENTS BY DELEGATES ON CHAPTER II

Edward W. Langley (United Kingdom)

The Health and Safety at Work Act 1974 requires the testing of all substances supplied for use at work and provides Government with the powers for choosing any existing substance for priority examination. Similar powers exist for protecting the environment also under the Control of Pollution Act.

The Health and Safety Commission, with the tripartite involvement of industry, trade unions and Government, has the power to require examination of existing test data and, if necessary, to initiate further testing. The Executive has access to all firms' information.

When a substance has been identified for priority examination, the Health and Safety Executive in collaboration with industry carries out a critical review of available information in order to evaluate the hazard. They also examine data on exposure to the substance to evaluate the probable risk. It is hoped to publish such critical reviews in the autumn of 1981.

The results of these studies are submitted to the Advisory Committee of the Health and Safety Commission. The committees are made up of experts from industry, trade unions, local authorities and independent experts who assess the risk and agree levels of exposure.

The identification of substances for priority examination involves a consideration of observations on the health of workers, new information and political pressures. Both government and industry have been opposed to the development of priority lists of an arbitrary nature. Political pressures and circumstances vary from country to country and it is difficult to see yet how arbitrary lists could be drawn up on an OECD basis.

The limited resources available will for some time be fully occupied with essential work for new chemicals and those identified as long-term hazards to human health.

The Department of the Environment also examines existing chemicals on a similar priority basis and published the results of reviews.

Each country also has differing mechanisms for reaching agreement with all the interests concerned on the level of risk which is thought to be acceptable. No attempt should be made to harmonize regulatory action although there may well be instance where general agreement on action can be reached.

Vittorio Silano (Italy)

Mister Chairman, we would like to thank you for the opportunity we have been given to briefly present some aspects concerning the Italian approach to the control of existing chemicals.

An area that is considered of highest priority in Italy with respect to the control of existing chemicals is the prevention of hazards deriving from genotoxic chemicals and, particularly, from carcinogenic or potentially carcinogenic chemicals. A typical example of this interest is the "circolare" 46/1979 on aromatic amines. To deal better with this problem, several years ago the Minister of Health appointed a National

Advisory Committee on "Carcinogenesis, Mutagenesis and Teratogenesis". This Committee has evaluated, at the request of different administrative bodies or on its choice, a number of different chemicals including (just to mention some examples) aromatic amines, some aromatic and/or halogenated solvents, some dyes, some human and animal drugs, nitrite, nitrate and nitrosamines, trinitrofluorenone, formaldehyde and synthetic sweeteners. The recommendations given by this Advisory Committee have been or are being implemented either by means of the specific relevant standards existing for chemicals submitted to registration (or to some other form of authorization) such as pesticides, drugs and food additives or by means of basic or specific standards for protecting workers at work and consumers and communities in their living environment. Therefore, great attention is being paid in Italy to the work of specialized Agencies and Organisations, e.g. WHO, ILO, IARC in Lyon and the NCI in the USA, or laboratories involved in testing chemicals for their carcinogenic potential such as Prof. Maltoni's laboratory in Bologna (Italy) and others inside and outside Italy.

Another point I should like to mention is that Italy has participated at the EEC level in the elaboration of several Directives that have been mentioned already by Mr. Mosselmans and Mr. Johnson. Therefore, I will not go any deeper into this topic.

All the control activities I have just described concern chemicals already identified as problems. A more global approach to the protection of man and environment has been adopted in December 1978 with the approval by the Italian Parliament of the Health Reform Bill. According to this Bill (art. 9) the Istituto Superiore di Sanità in Rome has the duty of establishing and periodically updating a *National Inventory of Chemical Substances* containing the chemico-physical and toxicological data relevant to assess the health and environmental risk associated with their presence in the environment. Since then, better ways of performing such a task have been extensively investigated and we are now considering as (a good) solution having two different types of inventory systems. The first one (type A) is comprehensive, including all the available data and on evaluation of the data performed by a national expert group. It should be applied in next years to a few hundred of chemicals. The second type of inventory (type B) is more limited and only includes data from a relatively small selected number of sources. The type B inventory is intended to include, in particular, the data of use in case of accidents or emergencies involving a release into the environment of potentially dangerous chemicals. In the next few years, inventory system type B is expected to be applied to a few thousand of chemicals. At present we are establishing priorities for the chemicals to be dealt with type A or type B inventory systems. In this respect, we welcome the organization of this meeting and the OECD program on existing chemicals as well as the program on existing chemicals carried out by other International Organizations and particularly by WHO.

In Italy, the work on establishing the above mentioned National Inventory started several months ago and we have now in the computer a large number of chemico-physical and toxicological data on about 1.200 chemicals. These data have been collected and stored according to a previously established scheme that allows easy addition and retrieval of data.

Pascal Deschamps (France)

Many thanks to S. Johnson for his excellent presentation of the legislative situation in different OECD countries. It was not possible to present in a short time the specifics

of each country's laws; that is why I asked to have the floor to elaborate on the French situation.

1. First of all, there are chemicals and chemicals.
Some are produced for special purposes, e.g. drugs, agricultural chemicals and food additives. These have to be licensed and there is for these chemicals no distinction between old an new chemicals.

2. In addition to the chemicals control act of 1977, which deals with effects due to use of chemicals, there are quite a number of other laws in this matter:

- Nature protection (1975)
- Worker protecion (1976)
- "Classified installation" (1975) (control of air, water and noise emissions from effluents of plants, noise . . .)
- Waste control (1976)
- Consumer protection (1978)
- Transport of dangerous substances (1945)

There are different acts, because different people are involved. Some producers are centralised, the others are decentralised. But all stages of the life of a substance may be controlled. Therefore, it is more important to know what the French authorities intend to do.

3. Dr. Johnson's paper is a good presentation of the French Chemicals Control Act. There is no selection of candidates at a national basis and the preparation of a priority list is not mandatory. Why should it be mandatory to make such a list? It is not clear that it would add anything of benefit if it were.

France was first in the European Communities to adopt a chemicals control system. So we paid much more attention to new chemicals. For old chemicals, we wish to be pragmatic. Let us take an example: We are now studying antifouling paints chemicals, in the form of a first evaluation of the responsibility of these compounds in provoking oysters damages; of course, each review or use restriction must be scientifically and technically well-founded, because industry has to pay for testing and it is industry that bears the economic consequences.

If this first evaluation of these paint chemicals demonstrates possible responsibility for damage to oysters, an order of the French Minister of Environment will oblige producers or importers to provide results of a testing programme, which may allow risk assessment for man and environment; this risk assessment will be conducted by an expert commission of 52 members, in fact in sub-commissions. This commission will, if necessary, propose use limitation of antifouling paint chemicals.

4. We would like the draft of "questionnaire answers" be amended; you may read, on p. 3 of the document, that France did not answer the questionnaire. In fact, we answered that the questionnaire does not fit the needs of the French authorities, but there was no deliberate intention not to respond to an OECD exercise. There are no criteria for selecting a priority list; so, practically, for the questionnaire, many of our answers would be: "not applicable".

Jacques Exsteyl (Belgium)

From a general strategic point of view priority should be given to the problems of existing chemicals in the area of occupational safety and public health.

Whatever the considerations are, work under this perspective deals with criteria of identification, classification, evaluation of hazards in occupational health, bans, and restrictions, i.e. controlled authorised use of most dangerous substances and preparations.

In addtition, all other problems of industrial hygiene are related to this work: the occupational environment and the so-called industrial environment, and also control of toxic waste and disposal.

Thus, under the scope of industrial hygiene an effort is made not only to protect the worker in his work place, but also is of value to the protection of the public at large.

A global strategy in health and environmental protection will be needed to deal with difficult questions taking into account scientific and social approaches in each political decision.

Hanno Schulze (Federal Republic of Germany)

In addition to the statements on the legal situation in the United Kingdom, Italy and France, I want to stress the point, that in the Federal Republic of Germany, too, there are several laws and regulations dealing with existing chemicals: This includes provisions on prevention of air and water pollution, waste disposal, fertilizers, pesticides, feedstuffs, drugs, food and commodities and occupational health. The experience from the implementation of these laws has increased our knowledge on hazardous effects of chemicals on man and the environment.

There is an essential principle of the German constitutional law, that all the mentioned Federal Law is implemented and enforced by the States (Länder) to a great extent. Therefore, we have a close co-operation between Federal and States administration. There are permanent conferences and committees of the Ministers of the Federal Government and the States Governments (Conference of the Ministers of Environmental Protection, of Health, of Labour, of Agriculture etc.) and of the experts of the Federal and State Ministries on all aspects which are covered by laws mentioned above. The newest one of these expert committees is the Committee on Environmental Chemicals, dealing with the environmental aspects of chemical substances. Scientific assistance to Federal and States authorities is given by the "Deutsche Forschungsgemeinschaft". In the field of environmental chemicals, the Senate Committee on Environmental Research of the Deutsche Forschungsgemeinschaft has established the working group "Environmental Effects of Chemicals".

In the paper of S.P. Johnson, special attention is drawn to the importance of planning legislation for the prevention of hazards of chemicals to man and the environment. The State of Bavaria of the Federal Republic of Germany has combined planning and environmental protection in one ministry: the Bavarian State Ministry for Regional Development and Environmental Protection. This Bavarian model was introduced to the international public during the UN Conference on the Environment in Stockholm 1972.

CHAPTER III

Identification and Quantification of Criteria for Selecting Existing Chemicals for Gathering Information, Testing and Assessment on a Case by Case Basis

Michael Gilbertson and Jim E. Brydon

Selecting Priority Existing Chemicals for Review and Testing – Based, in Part, upon the Results of the Questionnaire

As in many other countries, we in Canada have been trying to come to grips with existing chemicals for several years. Like many countries we have a variety of Acts of Parliament to deal with specific products, uses and discharges. Because of the vast number of existing chemicals in commerce, we have to decide as in other countries which chemicals to investigate or to control first. Most of us have now had several years experience in selecting candidates and lists in a variety of contexts.

We were asked by the FRG Organizing Committee to base our discussion on the results and responses to their questionnaire. In what follows, we will be dealing in turn with lists of chemicals, then selection criteria and their application in a system for selection of chemicals substances.

In this afternoon's presentations you will hear details of the important experience in Japan and the U.S. of selecting existing chemicals. We will, therefore, make no attempt to describe their schemes in detail in this presentation, but will, of course, refer to their work.

Purpose of Selection

This brings me to the first point we want to make which concerns the purpose of selecting chemicals and why OECD should be involved in existing chemicals at all. It deserves some discussion which I hope will clarify some of the points I wish to make.

Given the myriad of substances in commercial use and the limited resources to deal with them in any country, many people have pointed out that the purpose of selecting existing chemicals is to reduce the large number of substances to a manageable number to reach some goal or to respond to some need. In most cases the common ground is an investigation of potential or existing hazard.

From the common ground, we find further goals, e.g. a determination of the hazard in the work place, the hazard in drinking water, the hazard posed by accumulated intake in our food. The FRG Organizing Committee has suggested for example that the term "A chemical" denote existing chemicals posing a health hazard and "B chemical" an environmental hazard. Furthermore, there are various stages in our concern or level of investigation which have an important bearing on our selection of chemicals. In the early stage we may have limited hard information on which to base our selection. Again, the FRG Organizing Committee has suggested that we use the term "Class II" chemical for those for which insufficient data are available for the purpose of assessment. At this most basic level, where subjective judgement predominates, OECD might compile a fairly extensive list of chemicals for which information such as the OECD "Minimum Premarketing Set of Data" might be developed. Depending on the results, compounds could be selected for further investigations to include occupational health surveys, long-term toxicity testing or measurement of actual environmental levels to assess the danger posed by the chemical to human health or the environment. In the later stages, we may find that there is sufficient information to permit a sound decision about the real or potential hazard and to point the way to effective control decisions. Such chemicals are described by the FRG Organizing Committee as "Class I" Chemicals.

Many of the most troublesome compounds have already been regulated by OECD countries and there are several examples of OECD activity in developing an harmonized international approach. PCBs, mercury and CFCs were not, however, selected by OECD; they happened and the issues were raised in the Chemicals Group. There are, however, several unregulated compounds that have some, but not all, of the particular characteristics that have lead to toxicological problems. There are others about which little or nothing is known. In our view it is these Class II chemicals that particularly need to be addressed by OECD. I will return to that point later.

Priority Lists – FRG Survey

The first problem that OECD needs to address is the compilation of a list. The following question was posed in the FRG questionnaire for this meeting: – "Which of the chemicals lists known to you should form the basis for the selection of chemicals which are to be tested for their potential danger to man or the environment"? There was a very wide variety of lists of substances that were referred to in the responses and our hosts, the FRG Committee have compiled these into a chart on pages 26 and 27 of their draft document "Summary of Answers to the Questionnaire". As you can see, there are no obvious favorites.

How can we use these lists to serve our needs? It seems that the most satisfactory answer to this question is to ask the purpose for compiling an OECD list. If the purpose is to get an understanding of the universe of chemicals in commerce, Class II chemicals, then clearly the U.S. inventory compiled under the authority of the Toxic Substances Control Act is a valuable starting point. Similarly the Japanese have prepared an extensive inventory of chemicals in Japanese commerce. If the purpose is to control known carcinogenic substances that have been well researched and for which there are extensive reviews of the toxicology, environmental levels and pathways and of the amounts in commerce then the list of compounds reviewed by the International Agency for Research on Cancer, Class I chemicals, is the kind of list we would be looking for. In fact, we really should look at something between these two extremes.

It is interesting to note that the consultants that prepared the priority list of chemicals for the Interagency Testing Committee in the U.S. did not screen the entire universe of commercial chemicals. Instead they took twenty four pre-existing priority lists of chemicals and used nineteen as the basis for the initial compilation. After the lists had been merged this gave a preliminary list of 8846 compounds that were submitted to various screening processes to yield the first series of chemicals for testing under the Toxic Substances Control Act. The screening process will be discussed in some detail this afternoon by Marilyn Bracken.

The Japanese have taken a somewhat different approach. They selected 800 chemicals for biodegradation tests. Those that are not biodegradable are tested for bioaccumulation. Those that are not degradable and also can bioaccumulate are subjected to chronic toxicity testing. The following criteria are used in their flow scheme:

i) the compound is a PCB alternative or has similar structure;
ii) the compound is used in great quantity;
iii) the compound is used in great quantity but has a structure that is significant from the standpoint of the environment or health. Compounds that were not degraded and that were bioaccumulated and had properties of chronic toxicity were designated as specified chemical substances.

The lists that were suggested by the respondents to the questionnaire might form the basis for the selection of chemicals which are to be tested through OECD. They were, however, extremely diverse and were developed for a variety of purposes but can be categorized into various classes. First, there are the three lists developed by the US, Japan and the EEC, that describe the universe of compounds. Second there are a wide variety of lists that have been compiled pursuant to various acts or programs in particular countries or groups of countries. Third there are lists developed internationally such as the Great Lakes list and the Rhine list. Fourth there are the lists of substances that are being worked on by international non-governmental organizations including IARC, WHO and IPCS.

This seems quite a useful classification because it shows the two extreme approach to the problem and the middle ground. Members of OECD will need to decide early in their deliberations whether they are going to select compounds using the "universe approach", the "acts and programs approach" or "international organizations approach". The particular approach that is chosen will depend upon the purpose for which an OECD list is developed and we will discuss the purpose below.

We could develop several lists to specifically reflect these purposes. One fairly extensive list could be for compounds for which the OECD list of "MPD" could be developed as a preliminary screen. A second list could be for a second level of testing including environmental surveys of levels and effects as well as further toxicology. Other lists for more detailed investigation could be developed for a group of substances of greatest concern. In this regard the US ITC model for selecting compounds for testing under the Toxic Substances Control Act may prove particularly useful because at each level of selection further testing could be required. Not only are these lists developed for different purpose in different contexts but are based on different criteria in their selection.

Selection Criteria – FRG Survey

I would like to turn now to the process of selection of chemicals. A publication of the US Environmental Protection Agency has compiled abstracts on 32 schemes that have been used for various purposes by various regulatory agencies. We have our own Canadian scheme which forms the basis for the priority list of chemicals under the Environmental Contaminants Act. Japan has published a detailed rationale for selection of existing chemical substances which will be explained in detail this afternoon. There is no dearth of selection procedures nor of criteria for selection of chemicals. We were not surprised by the variety of national approaches revealed by the FRG questionnaire for the development of criteria for selection. If you take a moment to turn to pages 30 to 37 of the summary compiled by FRG, you will see what I mean.

A Proposed Matrix

To help us in our thinking, we thought that it would be useful to reduce the criteria to two simple ideas that come from Paracelsus and classical toxicology; exposure (dose) and effects (toxicity). The evidence on the exposure and effects of chemicals can come from three distinct kinds of investigation; a) controlled experimental studies usually undertaken in the laboratory (which is the only way for new chemicals) b) field surveys and observations and c) commercial surveys of quantities manufactured used or released to the environment. These ideas can be more easily visualised with reference to the following matrix (Figure 1).

	Exposure	Effects
Controlled Laboratory Experiments		
Field Surveys and Observations		
Commercial Surveys		

Fig. 1

It seems worthwile to spend a bit of time filling in this matrix because the criteria from all countries for selection of chemicals for all regulatory purposes can be included in this common format. We think that the use of this matrix will help to ensure that no important pieces of evidence are omitted from consideration in selecting chemicals for investigation, testing or control.

Of course, you are undoubtedly all familar with the work on new chemicals under the Chemicals Testing Program. The objective of that work was to establish a system of

controlled laboratory experiments or tests that were required by all member countries in the reporting of new chemicals prior to marketing. Transformation of the physico-chemical data from these tests can be used to predict the likely fate and distribution of a new chemical not only in the environment but also in organisms. This leads to an estimate of potential exposure and is represented by the box at the top left corner. I understand that Mr. Theodore Mill's presentation this afternoon will be partly concerned with explaining these methods of transformation. There are others, of course. Obviously for an existing chemical for which there is an established environmental concern, the MPD set required for "new" chemicals will represent only a bare minimum and further elaboration beyond the MPD may be required.

Interpretation of controlled toxicity studies and deductions from structure/activity relationships can be used to predict the likely effects of the compounds on human health and on other organisms in the environment. This type of information appears in the top right box. I believe that Mr. Mill's and Mr. Kobayashi's presentation will also describe these interpretations.

As far as field surveys and observations are concerned OECD has been only marginally involved through the Wildlife Sampling and Analysis Program. There is, however, an enormous amount of information, published and unpublished, in this category from analytical results of determinations of levels of chemicals in organisms and in the environment. This is vital information for ascertaining whether a compound is a concern. It warrants detailed examination because if a chemical is found in environmental samples distant from known point sources it is likely to be persistent and if it is found in biological samples it is likely to be bioaccumulated. This evidence fits in the second box on the left side.

In addition, field observations of organisms can establish the existence of disease (effects) within a population both human and environmental that may be related to a chemical. For instance the observation of an abnormal incidence of a rare cancer-haemangiosarcoma-led to the prediction and finding of the carcinogenic properties of vinyl chloride. This kind of evidence fits in the second box on the right side.

Finally, the occurrence of chemicals in the environment may also be estimated through surveys of the quantities in commerce and the prediction of likely sources and losses of a chemical to the environment.

Now let us analyze the criteria that were included in the questionnaire to see where they fit into the matrix (Figure 2).

Matrix-Application to FRG Survey

The following overlay rearranges the criteria in the questionnaire into the effects/exposure format. Most criteria fit easily into this format; however, two criteria are difficult to assign. The first is abiotic accumulation potential and the second is structure/activity relationships. Abiotic accumulation potential seems to relate to sorption phenomena and hence this has been put into the table under exposure. Structure/activity relationships are used for prediction of the likely toxicity of a compound. Structure/property relationships are used for the prediction of the environmental fate (particularly bio-accumulation potential) of the compound.

This rearrangement of the criteria shows that while controlled laboratory experimental studies are well represented in the questionnaire responses in both exposure and effects criteria, less emphasis has been given to the field surveys and observations by member OECD countries.

	Exposure	Effects
Controlled Laboratory Experiments	Persistence Compartmentalization into Air/Water/Soil Bioaccumulation Biodegradation Abiotic degradability Sorption Structure/Activity Relationships	Acute Toxicity Chronic Toxicity Mutagenicity Teratogenicity Carcinogenicity Ecotoxicity Structure/Activity Relationships
Field Surveys and Observations		Carcinogenicity in humans
Commercial Surveys	Amount produced Method of production Use patterns Amount marketed	

Fig. 2

In the questionnaire, provision was made for "other" criteria that member countries have used in selecting chemicals. These have been included in the next overlay (Figure 3). Actual exposure in the field is determined by sampling and measuring levels of substances in specimens (including humans). The determination of actual effects occurring in the environment requires surveys of the incidence of various diseases and their relationship to exposure to chemicals.

Selection Evidence	Exposure	Effects
Controlled Laboratory Experiments	Persistence Compartmentalization into Air/Water/Soil Bioaccumulation Biodegradation Abiotic Degradability Sorption Structure/Activity Relationships Human Uptake & Excretion Metabolism Water Solubility	Acute Toxicity Chronic Toxicity Mutagenicity Teratogenicity Carcinogenicity Ecotoxicity Structure/Activity Relationships Skin sensitization Corrositivity Reproductive Toxicology
Field Surveys and Observations	Measuring levels in human tissues Measuring levels in environmental samples	Carcinogenicity in humans Toxicosis (Morbidity & Mortality) Mutations Reproductive failure Neurotoxicology
Commercial Surveys	Amount produced Method of production Use patterns Amount marketed Amounts in dump sites Amounts released to environment	
Political	Social judgement Public perception Pressure groups Political pressure	

Fig. 3

Under the commercial data, consideration of the amounts in dump sites and amounts calculated and/or measured as being released to the environment can also be used as criteria for selection. This work may also include actual identification of the chemical in waste streams and evaluation of chemical processes and technology to determine the likely losses to the environment.

In addition, we have included a new category called "Social judgement" which includes such factors as public perception, political pressure and pressure groups. Many

Selection Evidence	Exposure	Effects
Controlled Laboratory Experiments	Human Environmental	Human Environmental
Field Surveys and Observations	Human Environmental	Human Environmental
Commercial Surveys		
Socio/ Political		

Fig. 4

of you will agree that these have a considerable bearing on selection of chemicals for a variety of purposes.

Next, it seemed to us that this series of criteria could usefully be reorganised under a series of new headings. The first new division should be into human and environmental aspects of exposure and effects, using the evidence from the laboratory and the field (Figure 4).

Selection Evidence	Exposure	Effects
Controlled Laboratory Experiments	Human Pharmacodynamics Environmental Pharmacodynamics Chemodynamics	Human Toxicity Environmental Ecotoxicity
Field Surveys and Observations	Human Measuring Levels Environmental Measuring Levels	Human Monitoring Effects (Epidemiology) Environmental Monitoring Effects (Epizootiology Epiphytology)
Commercial Surveys	Commercial Surveys	
Socio/ Political		

Fig. 5

Controlled laboratory experiments on human, fish and wildlife uptake, excretion and metabolism of chemicals are generally known as pharmacodynamics. The developing science of calculating the movement and compartmentalisation of chemicals from physico-chemical properties and key environmental measurements has come to be known as chemodynamics (Figure 5). Controlled experiments on the effects of chemicals on humans and other organisms are known as toxicity and ecotoxicity testing respectively. Field surveys to analyse human and environmental samples are designed

for measuring levels of the substances in these materials. The analysis of the incidence of effects is known as epidemiology, in humans. Studies of the incidence and etiology of diseases in animals and plants are known as epizootiology and epiphytology respectively. We can now use this classification system to reorder the selection criteria. (See handout Figure 6). We believe that it is reasonably complete and the simple hierarchy seems to us to permit more orderly thinking when we examine what we are doing or what we are about to do.

As far as we are aware, the criteria used in all of the selection schemes fit into these categories although special emphasis has been given to certain criteria for a particular program. A good example of special emphasis is the Japanese scheme where they have used biodegradation as the first step in a sequential scheme. We may not be able to improve on the matrix but we can elaborate the criteria within each category and improve the ways in which we transform and interpret the information. For example the EPA laboratory in Athens, Georgia, has made a significant contribution to the methods of transforming physical-chemical data into information on the fate and distribution of a substance. To give another example, the U.S. National Cancer Institute has developed a computer methodology for the prediction of carcinogenic activity of a compound based on its structural relationship to known carcinogens. Among others, Japan, Canada and Sweden have made significant efforts to identify previously undetected compounds in the environment. Other countries have attempted to relate actual effects that have occurred in the environment to particular compounds. Any of these studies or their interpretations can lead to the selection of a compound.

Class A and B Chemicals

While we believe that our proposed matrix will promote logical thinking in the selection process, an additional statement is needed about the particular goal for selection. For example, are we interested only in Class A or in B or in both types of chemicals? Is selection for the purpose of developing priorities for assessment of air pollutants or pollutants of the total environment? And, in addressing these questions at this meeting or in the OECD system, can we develop some way of attaching priorities to the various answers? Japan, among others, seems to attach a high priority to environmental chemicals which have an indirect impact on human health (Class A + B). The pervasiveness and irretrievability of HCB and PCB are important factors in pointing us to environmental chemicals. On the other hand, the UK, among others, seems to attach a high priority to occupational health (Class A). The criteria devoted to determining direct exposure become important factors in identifying priority chemicals in the occupational health field. If we are going to attempt such priority setting on the international scene, we need to take into account many of the other specific goals which have special needs and, therefore, adopt a special way of selecting criteria. For example, Mr. Kobayashi, in describing the Japanese system will very clearly show the differences in the criteria used to select chemicals for testing as compared to selecting chemicals for environmental monitoring.

We conclude from this, therefore, that deciding the priority of Class A or B chemicals is not sufficient. There are subsets and refinements of these two classes which must be reviewed and some even approximate ranking must be allocated before we can attempt to address the criteria for selection of individual chemicals.

Class I and II Chemicals

A second factor affecting selection criteria is the state of knowledge. The FRG Organizing Committee has split chemicals into two groups i.e. Class I where the infor-

mation is sufficient to do a hazard assessment and Class II where it is not. How does this affect selection criteria? It may sound ridiculous to say that we need a lot of information in order to have sound criteria for selection and, at the same time, we need to select priority chemicals in order to gather the information necessary for a sound selection. It is not ridiculous, it is a reality.

One approach to this problem, which we tend to favor, is the Japanese scheme or perhaps some variation of it. In reviewing the potential candidates among the 10–50-thousand existing chemicals, we have few criteria available to use and must use the subjective judgement of experts. One of the criteria is the significant use pattern where the possibility of loss to the environment can be estimated. Even that must be used with caution because, as the Japanese have found with their new chemical notifications, many chemicals of concern to them are used in small amounts i.e. less than 1 tonne. In any case, the exercise of reducing the number of existing chemicals to a manageable size for testing, review and investigation should be done internationally and could be led by the OECD Chemicals Programme.

The second phase in the Japanese scheme is a logical analysis of the potential problems posed by that reduced list of chemicals from the first phase. Some observers seem to be suggesting that MPD-type testing be undertaken on this reduced list of chemicals. It would be expensive and we seriously doubt its value. We tend to favour the Japanese approach perhaps combined with some selected elements of the MPD list added to their scheme. We suggest that some of the models for determining environmental fate or environmental exposure could be used to select specific elements, e.g. solubility or vapor pressure to be related to classes of chemicals or their use patterns.

The third phase in the Japanese scheme is detailed work on those chemicals which are screened out during the second phase. The testing or environmental monitoring required can be determined with the aid of the matrix which we have developed in this paper. This, in fact, is the U.S. approach in naming 50 chemicals for testing. This work could be expensive if the numbers are great. It can be done, in part, through international cooperation and could be led by the OECD Chemicals Program.

The fourth phase, detailed assessment of hazard, is implicit in the Japanese scheme and in the assigned title of this paper. The criteria in our matrix can be used in a very systematic way to select chemicals for detailed review and assessment. Many countries and many international organizations are engaged in the preparation of lengthy, detailed and expensive assessment documents. WHO has published many. The IPCS program has embarked on more. Canada and other countries have published documents on e.g. PCBs and As and are now doing others which unfortunately will be found to duplicate the work of others. There is a clear indication of a need for international cooperation dealing with these Class I chemicals, even though the numbers are likely to be fewer than the Class II chemicals.

However, in the application of the selection criteria some countries may have vastly different priorities and needs. They also insist on making their own decisions about potential hazards. International cooperation will have to be very carefully managed if we are to be able to remove duplication of work in a satisfactory way. Is there a role for the OECD Chemicals Program? We think that OECD should take a low profile in the area of Class I chemicals and that IPCS take a low profile in the area of Class I chemicals and that IPCS should be encouraged to do what it can to continue serve member countries needs in providing detailed assessments of Class I compounds.

We believe, therefore, that a continuous screening system, possibly patterned after the Japanese or U.S. approach, offers the best possibilities: Specific selection criteria can

SELECTION EVIDENCE	EXPOSURE	EFFECTS
	HUMAN	**HUMAN**
	Pharmacodynamics	**Toxicity**
	Uptake, Distribution Excretion, Metabolism Structure/Activity Relationships Etc.	Acute Toxicity Chronic Toxicity Mutagenicity Teratogenicity Carcinogenicity Skin Sensitization Corrosivity Reproductive Toxicology Structure/Activity Relationships, Etc.
CONTROLLED LABORATORY EXPERIMENTS	**ENVIRONMENTAL**	**ENVIRONMENTAL**
	Pharmacodynamics	**Ecotoxicity**
	Uptake, Distribution Excretion, Metabolism Bioaccumulation Structure/Activity Relationships, Etc.	Acute Txocity Chronic Toxicity Structure/Activity Relationships Etc.
	CHEMODYNAMICS	
	Persistence Compartmentalisation into Air/Water/Soil Biodegradation Abiotic Degradability Sorption Water Solubility Structure/Activity Relationships, Etc.	
	HUMAN	**HUMAN**
	Measuring Levels	**Monitoring Effects (Epidemiology)**
	Tissues Food Work Place Air and Dust Drinking water Etc.	Toxicosis Cancer Deformities Mutations Reproductive Failure Neurological Damage, Etc.

SELECTION EVIDENCE	EXPOSURE	EFFECTS
FIELD SURVEYS AND OBSERVATIONS	**ENVIRONMENTAL** **Measuring Levels** Wildlife & Fish Tissues Sediments/Soil Air Water Etc.	**ENVIRONMENTAL** **Monitoring Effects (Epizootiology, Epiphytology)** Wildlife & Fish Toxicosis Cancer Deformities Mutations Failure Reproductive Neurological Damage, Etc.
COMMERCIAL SURVEYS	Amount Produced Method of Production Use Patterns Amount Marketed Amounts in Dump Sites Amounts Released to Environment	
SOCIO/ POLITICAL		Social Judgement Public Perception Political Pressure Pressure Groups

Fig. 6: Matrix of selection criteria for developing a list of existing chemicals for review and testing

be used in the screen at different phases of the system. Throughout much of the exercise, the aim is to eliminate chemical compounds. In the rest of the exercise, the aim is to rank those compounds for further consideration.

An OECD Role

This brings me again to the central question of this paper – why are we selecting chemicals? It seems that there are really only two general purposes for selection of chemicals; one is to establish (and rank?) the need to investigate them further, the other is to control them. Because control of existing chemicals is likely to result in substantial economic disruption, the scientific case that has to be prepared to defend a government regulatory action must be meticulous. We cannot prepare meticulous scientific cases on all chemicals, thus we have to select for further study those compounds that seem to pose the greatest danger. Many OECD countries have already prepared their scientific rationale for regulatory controls on the most noxious compounds.

What could OECD contribute by selecting chemicals? Here I return to the matrix (Figure 1) because there are different sources of the information for making the defensible scientific case. Much of the controlled laboratory experimental work, both for

assessing the likely exposure and the effects, need be done only once. Providing that this kind of testing is undertaken using internationally-acceptable procedures it is unnecessary for another country to repeat this work. Much of the physico-chemical work is already published in chemical handbooks, but most is probably available only through the scientific literature.

In contrast the field surveys and observations on levels (exposure) and incidence of effects and commercial information on production and release tend to be specific to a particular country or region. These data are useful to other nations for the purpose of warning them that they may have a particular problem. They cannot however readily be transferred to make the case for regulatory controls in another country without at least preliminary surveys to show that the problem also exists or will exist in that second country. Much of this kind of information is published in the scientific literature or in government reports. In this third phase of the investigation process, it is essential to consider the country-specific aspects derived from field surveys and observations and from commercial surveys.

OECD can make the greatest contribution concerning existing chemicals by concentrating on 1. the selection of chemicals in the various phase of the investigation process and 2. on international mechanisms to obtain information from controlled laboratory experiments.

Katsutoshi Kobayashi

Safety Examination of Existing Chemicals – Selection, Testing, Evaluation and Regulation in Japan

1. Introduction

1. In 1973, the "Law Concerning the Examination and Regulation of manufacture, etc., of Chemical Substances" (Chemical Substances Control Law) was established in Japan. This legislation not only requires an examination of chemical safety prior to its production or import, but also regulates the production, import, usage, etc. of chemicals which seem to cause adverse effects on environment and human health. This law is the forerunner of the assessment system for new chemicals in the world. It calls for the testing and evaluation of new chemicals based on three viewpoints – namely "chemical changes occurring under natural environment," "accumulation in the organism", and "effects on human health when taken continuously".

2. The law requires a notification and adequate testing of new chemicals and their evaluation. However, approximately 20,000 chemicals, which had been commercially manufactured or imported at the time of the promulgation of this legislation, are not legally required to be tested nor examined but to be merely registered on the list of existing chemicals of the Ministry of International Trade and Industry (MITI).

However, at the time of establishment of this legislation, the Diet concluded the necessity or prompt safety examination of existing chemicals and thus, such safety examination has been continued for seven years, since the law came into force.

3. As a result of this Government evaluation, chemicals which proved to be resistant to degradation, having high bioaccumulation potential, and chronically toxic are designated as "specified chemicals" and regulated by the law. The examination, moreover, not only helps control these specified chemicals, but also offers significant knowledge on the fate and effects of chemicals in the environment.

4. Thus, this report is intended to serve as a reference for future projects of existing chemicals in OECD by introducing our experiences in examining the hazard of existing chemicals against human health and the environmental mainly from the viewpoint of the chemical fate and the environmental natural effect.

2. Concept of Safety Examination

1. The basic concept of chemical safety in this report is the protection of environment and human health from the persistent chemicals in the environment. The system of examination of chemical safety which complies with such a basic concept requires an entirely new approach. We have, thus, carefully studied a most rational yet effective scheme of examination by arranging safety tests such as biodegradability, etc. The basic concept underlying this scheme may be illustrated as follows.

2. The chemicals which are released into the environment, never cause effects on human health and the environment without having some form of contact with them. The route to exposure in the environment is quite complex. These exposure routes may be categorized into two major processes:

a) The first possibility is general environmental exposure. In this case chemicals or chemical products are discharged into the environment such as rivers, lakes, swamps, etc. and come into contact with man or the ecosystem through the intake of water or air.

b) The second possible process is known as indirect human exposure via the food chain. This process is somewhat similar to the former to the extent of pollution of environmental water, soil, etc. through chemicals discharged into rivers, lakes, ocean, etc. However, the effects on human health in this process originate from the consumption of polluted fish, agricultural products, and cattle raised in such an environment.

Process (b) appears to be a more roundabout way in comparison process (a) and may seem to be an absolutely indirect way of affecting human health. However, in case of the existence of an organism (food) there is the possibility of bioaccumulation or biomagnification via the food chain. Thus, even if chemical concentration proves to be low in the environment, safety is not necessarily guaranteed and the situation is of even greater concern compared to process (a).

Therefore, the system of chemical safety inspection of Japan is especially focused on process (b) but is applicable to process (a) as well.

3. Causes of effects on human health or the environment through processes (a) and (b), elucitated in paragraph (2), may be indicated as follows:

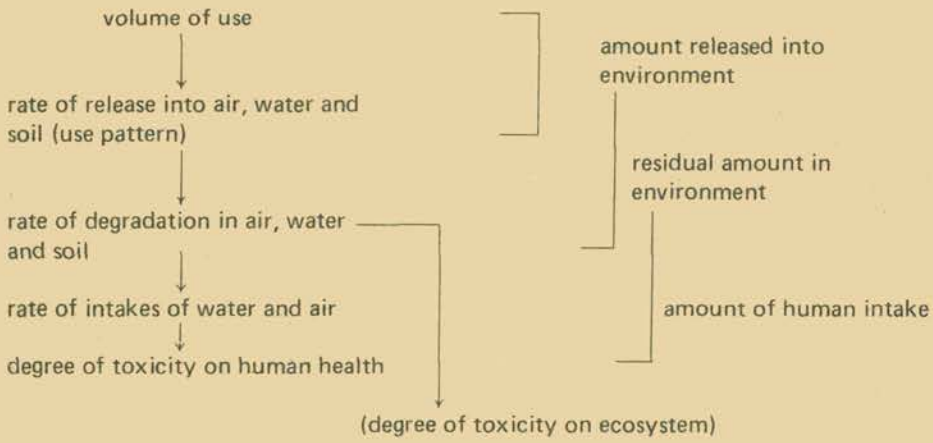


Fig. 1: (a) Effects through General Environmental Exposure

Taking into consideration the consistency of the amount of food, water, or air intake in the above two schemes and disregarding them for the time being, the following factors may be considered as common causes for affecting man and the ecosystem in both schemes:

a) volume of use
b) rate of release into environment (use pattern)
c) rate of degradability in environment
d) degree of toxicity on man and environment

Furthermore, for process (b), an addition would be:

e) rate of accumulation in organisms (food)

must be included.

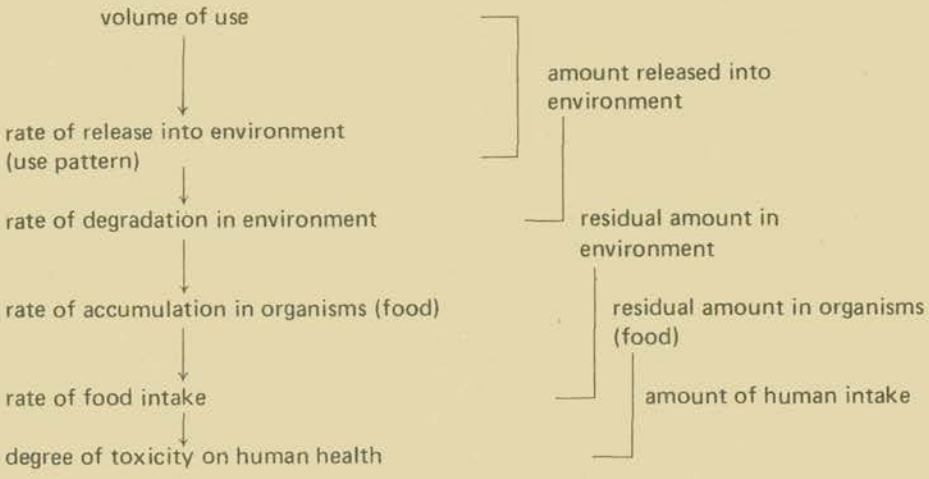


Fig. 2: (b) Effects through Indirect Human Exposure through Food Chain

3. As a result of detailed study of these different causes, we arrived at the following three basic stages of examination which enable a rational selection of questionable chemicals. These three stages which we are presently following are:

a) Stage 1: Preliminary inspection from the standpoint of volume of use, use pattern available information, etc. (selection of existing chemicals which require testing).

b) Stage 2: Testing and evaluation of the fate of chemicals in the environment (degradation, accumulation) selected in Stage 1.

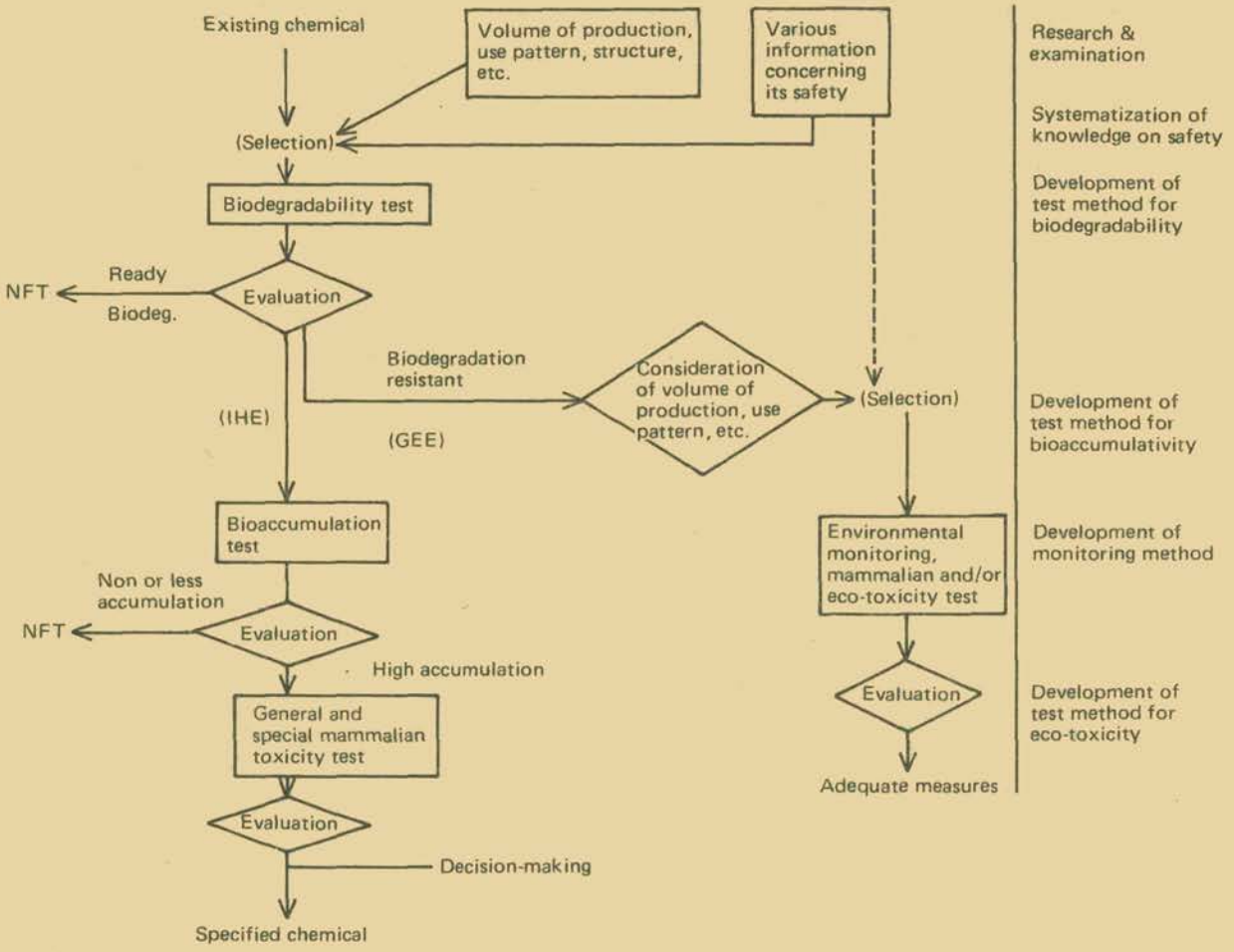
c) Stage 3: Evaluation of health and natural environmental effects of chemicals selected in Stage 2.

3. Flow Scheme of the Test

1. The safety examination of existing chemicals in Japan can be illustrated in the following scheme (see page 150).

2. The left half of the scheme is directly related to the aforementioned regulation – the Chemical Substances Control Law. This part of the scheme is significant for selecting (out of approximately 20,000) chemicals which fall under legal regulation as specified chemicals. In this connection, MITI and the Ministry of Health and Welfare are carrying out a costeffective yet efficient safety examination through the introduction of the step-sequence testing scheme, namely the flow of biodegradability test – bioaccumulation test – and general and specific mammalian toxicity tests.

3. When the persistency of chemicals is made evident by a biodegradability test, special consideration for safety, especially in terms of general environmental exposure, is given. This implies that the primary screening of chemicals activity in the environment also utilizes an effective application of results of biodegradation test. And for degradation resistant chemicals, with consideration of both causes affecting the exposures such as the volume of production, use pattern, etc. and already known toxicity voluntary entrepreneurial measures such as environmental monitoring, eco-



NFT; non further test

Fig. 3: Flow Scheme for the Safety Test of the Existing Chemical

toxicity test, etc. are carried out in accordance with MITI's guidance. Taking into account the possibility of not only mathematically analyzing the exposure of all existing chemicals, but also of directly monitoring existing chemicals in the environment, in contrast with new chemicals, it can be concluded that the application of environmental monitoring of existing chemicals is effective way in the late stage of safety examination just before controlling. In Japan, such areas which do not fall under the jurisdiction of the Chemical Substances Control Law are filled by voluntary research and environmental monitoring in private enterprises under MITI's guidance.

4. Moreover, for the rationalization and improved efficiency of this scheme, MITI has been updating and developing new testing and monitoring methods etc. This contributes to the safety examination of not only existing chemicals but also new chemicals.

Knowledge collected through such a safety examination, in particular, has proved to be useful in analyzing the correlation between safety and the chemical structure or physicochemical properties. Results of this analysis have been utilized in an effective selection of chemicals from existing ones which may require testing as well as in examining new chemicals.

5. Our system of chemical safety examination in relation to chemical effects on man via the environment and on the environment itself as explained above may be summarized as below:

a) The stepwise scheme allows cost-effective examination by selection those chemicals requiring expensive tests through a comparatively low cost biodegradability test.
b) Results of environmental monitoring are utilized in relation to other various test results in the late stage of examination just before controlling.
c) The systematization of collected information and knowledge are utilized in the selection of chemicals for safety examination.
d) Research and development of testing methods, etc. are promoted for the efficiency of examination.

4. List of Existing Chemicals and Selection of Chemicals for Safety Examination

1. List of Existing Chemicals

I. MITI has prepared and announced a list of existing chemicals which differentiates new from existing chemicals. Chemicals registered on the list of existing chemicals are those which were actually commercially manufactured or imported at the time of promulgation of the Chemical Substances Control Law but exclude those which were manufactured or imported for tests and research use and those manufactured or imported as reagents. Moreover, those chemicals which had been commercially manufactured or imported in the past but were discontinued or could not be considered so at the time of promulgation of the law are not registered on the list of existing chemicals and are required to be handled as new chemicals.

II. The actual compiling of the list of existing chemicals was accomplished by ministerial (MITI) adjustment and approval of filings of commercially manufactured or imported chemicals submitted from all business circles. Filings of chemicals were required to be accompanied by the following information:

a) name of manufacturer or importer
b) name of chemical (IUPAC or commercial name)
c) structural or rational formula
d) physicochemical properties

e) composition
f) volume of manufacture of import
g) utilization
h) manufacturing process
i) analytical method
j) other information, knowledge available concerning safety

However, in actuality, it is almost impossible to acquire all such information. Some, among registered chemicals on the list, are missing data on physicochemical properties or the manufacturing process. Moreover, volume of manufacture or import as well as utilization, etc. change according to social and economic situations. Thus, such aspects undergo an extensive survey of existing chemicals every three years and serve as reference for the selection of existing chemicals for the safety examination. All information except for the names of chemicals submitted at the time of filling are handled confidentially and names are merely publicized.

2. Selection of Existing Chemicals for Examination

I. The government is deemed to be responsible for the safety examination of all existing chemicals. However, safety testing and evaluation of all existing chemicals require both a tremendous sum of money and time. Thus, prior to testing, studies on the following aspects are performed to select only those which necessitate testing:

a) volume of manufacture and import
b) utilization
c) structure
d) physicochemical properties

In other words, chemicals with a large volume of production of import, those utilized in open-systems, chemicals necessary for systematizing for the safety-structure correlation or safety-physicochemical properties correlation are selected.

II. Such a selection is made due to the fact that chemicals produced or imported in large quantity and simultaneously used in open systems are released in the environment in a large absolute quantity. This implies the magnitude of their impact on the environment and man. Along with increasing knowledge on chemical safety, information which verifies an intimate relationship between chemical structure, physicochemical properties, and chemical safety (biodegradability, bioaccumulation, etc.) is becoming more and more available. The systematically arranged information allows for a safety evaluation of untested chemicals as well as for an increased precision of safety evaluation of test results.

III. Furthermore, based upon such information available on the chemical structure and physicochemical properties, chemicals deemed to have significant impact on the environment and/or man are preferentially selected. Toxicity information and results from environmental monitoring are also considered for the selection of chemicals subject to safety testing.

IV. Likewise, MITI is not testing a constant number of existing chemicals from a fixed list, but, rather, is selecting chemicals to be tested in accordance with the above criteria every year. This is due to the annually increasing information on safety which allows for further clarifications of relations between the safety and chemical structure or physicochemical properties as well as due to the acquisition of the latest information on toxicity, environmental monitoring, etc. The effective safety examination of

existing chemicals, extremely receptive to social situations, is made possible through the selection of new chemicals to be tested based upon updated knowledge.

5. Testing, Evaluation, etc.

1. Testing Institutes

I. Safety testing is practiced by various forms of institutes in Japan – some publicly run, others independent and yet other institutes under the administration of chemical manufacturers, etc. However, nationally administered tests on biodegradability, bioaccumulation, etc., for existing chemicals are carried out by a public and independent institute of high reliability and quality known as Chemicals Inspection and Testing Institute, Japan (CITI).

II. CITI, not only carries out tests for biodegradability, bioaccumulation, etc. under national subsidies, but also promotes research and development concerning chemical safety. Of the entire staff, inclusive of those in the research and development section and those in the new chemicals testing section, approximately 100 are working full-time concerning the inspection of existing chemicals. 90% of the staff are university graduates with 1/3 of them possessing either an M.A. or a Ph. D. Thus, a high quality of test result is guaranteed.

III. The man power needed for the testing of existing chemicals by MITI method is as follows:

biodegradability test 1 sample one man/month
bioaccumulation test 1 sample three-four man/month

The major task of such tests is devoted to the development of analytical procedure and its degree of difficulty determines the amount of man power.

IV. Other Japanese laboratories, comparable to CITI, also have been carrying out tests of high quality, for they too have highly educated staffs.

2. Evaluation of Test Results, etc.

I. Although test results acquired through a highly reliable institute (CITI) are very precise and of high quality, MITI does not neglect to provide further care and attention through the Chemical Products Council in evaluating such results.

The Chemical Products Council, comprised of experienced intellectuals (university professors) of chemistry, biology, analytical chemistry, sanitary science, medicine, etc., impartially evaluates test results from various aspects and also indicates additional testing when necessary prior to arriving at a final conclusion.

II. Results of evaluation are publicized by MITI.

When chemicals are found to be degradation-resistant and seem to remain in the environment, MITI asks the related industries to draw up voluntary adequate measures, as has been formerly mentioned, such as collection of information for safety, performing of safety test, environmental monitoring, etc.

6. Results of Examination of Existing Chemicals

I. Summary

Results of safety examinations for biodegradability and bioaccumulation administered by MITI are shown below:

Table 1. Results of Examination of Existing Chemicals

Financial Year	'73	'74	'75	'76	'77	'78	'79	'80	Total
[A] Biodegradation Test									
number of designated chemicals	10	108	109	124	68	1	90	121	631
evaluated	5	39	84	82	55	48	56	61	430
well degradability	0	21	37	25	14	12	27	24	160
degradation resistant	5	18	47	57	41	36	29	37	270
[B] Bioaccumulation Test									
number of designated chemicals	10	18	38	76	73	38	36	39	328
evaluated	0	8	13	28	46	38	43	25	201
low level of bio-accumulation	0	6	13	27	43	32	39	25	185
medium level of bioaccumulation	0	0	0	1	1	6	4	0	12
high level of bioaccumulation	0	2	0	0	2	0	0	0	4

631 chemicals have been designated to undergo tests for biodegradability.

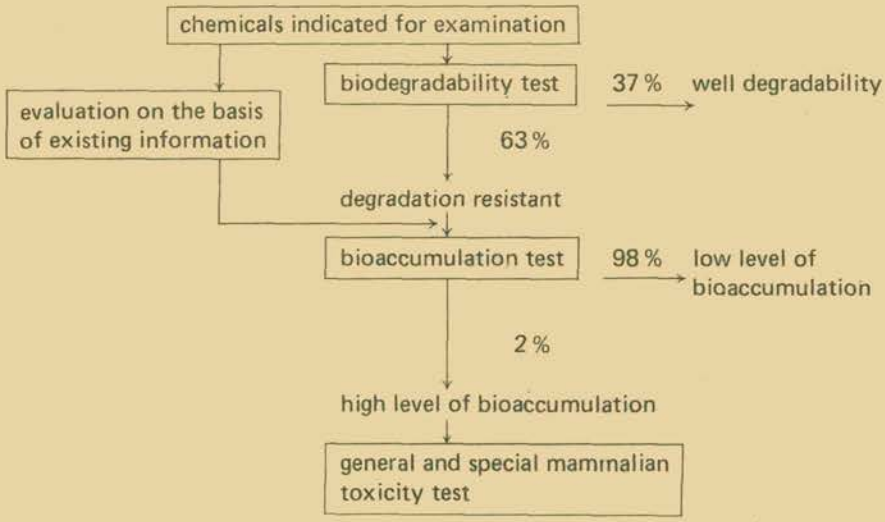


Fig. 4 *Effectiveness of Biodegradation Test and Bioaccumulation Test as Screening Test*

328 chemicals which proved to be degradation resistant in the biodegradability test or evaluated to be so from information available but its bioaccumulation potential is unknown were required to undergo bioaccumulation tests for clarification. Results of

biodegradability tests show 160 chemicals to be of well degradability and 270 chemicals to be resistant to biodegradation. Bioaccumulation results show 185 chemicals to have low levels of bioaccumulation, 12 to have medium, and 4 to have high levels of bioaccumulation.

II. Three chemicals, namely polychlorinated biphenyl (PCB) hexachlorobenzene (HGB), polychlorinated naphthalene (PCN), have proved to be degradation resistant, high in levels of bioaccumulation and chronically toxic from the results of examination of existing chemicals in the past eight years. They have been designated as specified chemicals (PGB in June 7, 1974; HGB and PCN in August 14, 1979) under the Chemical Substances Control Law and their production and import are restricted and their production, import and use are only approved for closed utilization where they cannot be substituted, but are yet indispensable. The production and import of these three chemicals have not yet been actualized until today and only PCB is used for special purpose. However the approval for the use of PCB has been extremely limited (for trains, transformers, etc.) under the regulation of technological standards. Results from such an examination of existing chemicals have thus served to draw up necessary adequate measures for potentially environmental pollutants for the purpose of protecting environment and human health.

III. Likewise, an efficient selection of chemicals has resulted in a limited number of chemicals for chronic toxicity tests, which requires both time and money, and a large number of chemicals for tests which can be completed over a short period at low cost. If, all tests (for biodegradability, bioaccumulation, and chronic toxicity) were given to a chemical, a significant amount of time and expense for safety examination must be given for testing for chronic toxicity as is evident below.

	Period	**Expense**
biodegradability test	1–2 months	¥ 300,000–¥ 1 million
bioaccumulation test	3–5 months	¥ 2 million–¥ 5 million
chronic toxicity test	2–4 years	¥ 50 million–¥ 100 million

MITI, on the contrary, employs a more efficient system of safety inspection which curbs the necessary time and expense to a minimum by performing bioaccumulation tests on chemicals which are proved to be degradation resistant after a biodegradability test; this is followed by a chronic toxicity test for chemicals which are proved to have high levels of bioaccumulation after the preceding test.

Based upon the actual record of safety examinations by MITI, tests on 100 chemicals in the MITI system would require ¥ 256 million as illustrated below.

On the other hand, when all three tests are given to all 100 chemicals, the necessary expense increases twenty-fold to ¥ 5,230 million. (¥ 300,000 + ¥ 2 million + ¥ 50 million) x 100 chemicals = ¥ 5,230 million. Likewise the amount of time required for all the tests have been extensively curtailed in the MITI system.

Thus, the MITI system which follows a step-by-step evaluation procedure is an essential method of examination in terms of economy and efficiency.

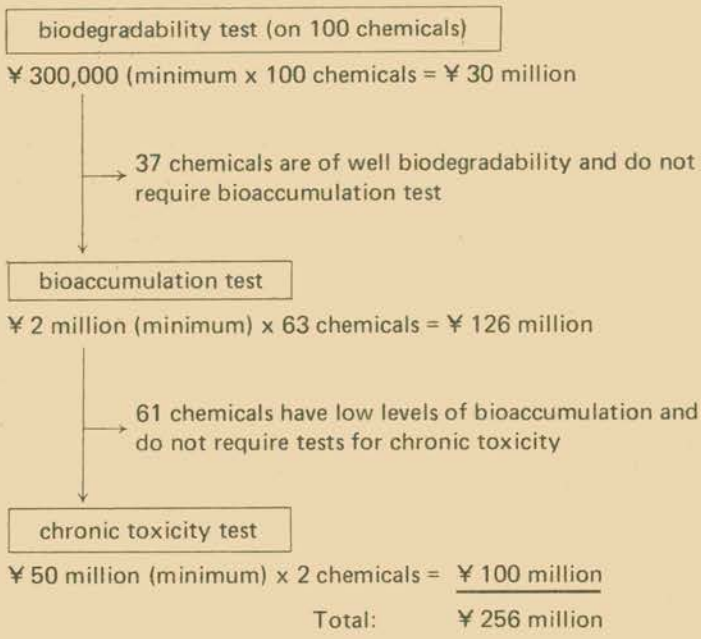


Fig. 5. Cost of Safety Examination by the MITI Scheme

7. Systematization of Collected Data

1. Effective Utilization of Existing Data

The basic and most significant problem for the safety examination of existing chemicals is the efficient use of limited resources (man power, etc.) and budget. For this purpose, a step system testing scheme and a systematization of collected data (elucidated below) are being carefully studied and applied to reap optimum results from minimum testing. In other words, such a systematization makes possible and adequate and efficient screening of chemicals based on such basic data as their structure and physicochemical properties prior to acutal testing (as mentioned in section 4. of this paper) and this even allows for the omission of some tests in some cases.

I. Structure-Activity Correlations

Chemical structure is a fundamental and most easily acquired data. But this minimum information can lead to the knowledge of chemical activity in the environment (biodegradation, bioaccumulation eco-toxicity, etc.), when the systematization of structure-activity correlations is practiced. In Japan, results of tests for degree of biodegradability, etc. on more than 400 chemicals are being considered to be utilized for systematization. A large volume of collected information, as shown below as some examples, has been utilized for the annual selection of existing chemicals examination.

a) biodegradability-structure correlations
   * effects of ramification of aliphatic compounds on biodegradability
   * effects of substituents of aliphatic compounds on biodegradability
   * effects of substituents of aromatic compounds on biodegradability
   * effects of structure of heterocyclic compounds on biodegradability

b) bioaccumulations-structure correlations
   * effects of substituents on bioaccumulation potential
   * effects of molecular mass on bioaccumulation potential

Furthermore, continued study of a different approach is also scheduled. This approach is based on polar and non-polar analysis (two-dimensional matrix) of a chemical structure which is suggested as a means of predicting biodegradability and bioaccumulation potential, eco-toxicity potential from the structural formula of chemicals.

II. Physicochemical Properties-Activity Correlations

Basic physicochemical properties such as solubility, etc. are comparatively easy to acquire as well as chemical structures of existing chemicals. Measurements of such simple properties, if necessary, are also feasible. Thus, like the usefulness of the chemical structure, a systematization of physicochemical properties and activity can serve as a reference for the selection of chemicals for examinations. Moreover the tests for physicochemical properties like solubility, etc. as a prior step towards other tests may also lead to an improved efficiency as well as a curtailed testing expenses.

In this connection, the systematization of data, as shown below as some examples on relations between physicochemical properties, degradation, bioaccumulation and eco-toxicity is presently being undertaken.

a) relations between bioaccumulation and physicochemical properties: correlation of water solubility, Po/w and degree of bioaccumulation
b) relations between eco-toxicity and physicochemical properties: correlation of water solubility, Po/w and eco-toxicity (effects on fish, daphnia, and algae)

III. Correlations among Biological Test Results

Improved efficiency for examination calls for another significant point – the extraction of maximum data from a single test. Taking this into account, a test result may be utilized for the screening of other tests once correlations of effects are made clear. A clarification of these correlations in the field of bioaccumulation and eco-toxicity, in particular, is deemed to be promising.

A systematization of correlations of test results is promoted in our country as follows:

a) correlations of bioaccumulation potential, and fish toxicity
b) correlations among eco-toxicities (fish-daphnia-algea)

2. Establishment of the Data Bank

MITI has thus been promoting the safety examination of existing chemicals since 1973. However, recent increases in the volume of knowledge stemming from safety testing and increasing information on chemical safety along with rising chemical safety recognition on a world-wide scale demand a system capable of responding promptly to the information and knowledge of safety so that efficient examination of existing chemicals can be promoted. Under such circumstances, MITI, with its computer installations, is diligently endeavoring to develop efficient information systems for collection, arrangement, and retrieval as mentioned below:

a) development of a survey system for volume of production, utilization, etc. of existing chemicals
b) development of a chemical structure retrieval system
c) development of a data retrieval system for physicochemical properties, biodegradability, bioaccumulation, toxicity, etc.
d) development of a retrieval system for literatures concerning chemicals safety.

Such a computerized data bank system would not only improve speed and efficiency for selection of existing chemicals to be examined but also avails information on relations between safety and chemical structure of physicochemical properties. Moreover, this type of system is also anticipated to predict safety properties from chemical structure, physicochemical properties, etc. These systematized data can be used for the evaluation of new chemicals as well as for the safety examination of existing chemicals. Thus necessary expenses for confirmation of safety is curtailed in such a system. Moreover, systematized knowledge on safety is also deemed to be of great significance for the purpose of further research and development in regard to chemicals safety.

8. Conclusion

Examination of existing chemicals which may effect on the environment and human health via the environment has been promoted in Japan as explained in the former pages. The following suggestions for similar activities in the OECD may be summarized from our past experiences.

I. The "systematization of knowledge", presently undertaken in Japan, is deemed to be essential for the selection of chemicals for testing, such a selection will be possible by the screening of existing chemicals through minimum information (structural formula, etc.). In this connection, it is advised at first that specialists study this particular point in detail rather than selecting existing chemicals.

II. It is deemed to be more efficient to select gradually chemicals to be tested every year considering the additional new information than to fix the list of chemicals to be tested at first. And also it seems to harmonize better with the every year situation of each country such as budget, man-power, etc.

III. In cases of testings, a step-sequential-testing scheme as done in Japan make it possible to minimize expenses. Especially for general environmental exposure (GEE) and indirect human exposure (IHE) it is most efficient to start biodegradation testing which is comparatively cheap. It is also important in case of existing chemicals unlike new chemicals to consider the feasibility of monitoring the real environment at the final stage of examination just before the administration makes final decision to control.

IV. Research and development of the systematization of formerly mentioned information and knowledge, the establishment of step-system, etc. are all indispensable elements to be promoted simultaneously for the implementation of the safety inspection of existing chemicals. A positive attitude for research and development in this particular area in each country is certainly expected.

ANNEX 1

Notification of New Chemicals

Items \ Year	'74	'75	'76	'77	'78	'79	'80	Total
Notified substances	210	82	95	140	180	253	222	1,182
manufacture	114	45	70	76	140	160	152	757
import	96	37	25	64	40	93	70	425
Designated as safe	29	28	57	111	144	228	197	794
biodegradable	12	15	24	26	38	53	33	201 (46 *)
non or less accumulative	16	13	33	85	106	175	164	592 (32 *)
non-toxic	1	0	0	0	0	0	0	1

* percentage of chemicals whose safety are confirmed based on their structures, physicochemical properties, etc. without biodegradability test and/or bioaccumulation test

Notification of New Chemicals in Small Quantities

Items \ Year	'74	'75	'76	'77	'78	'79	'80	Growth rate (%) '80/'79	'81	Growth rate (%) Mar. '81/Mar. '80
Notified substances	714	773	931	949	1,170	(1,318) 1,722	(1,475) 1,833	6.4	(1,660)	12.5
manufacture	415	469	576	545	617	(688) 915	(768) 937	2.4	(869)	13.2
import	299	304	355	404	553	(630) 807	(707) 896	11.0	(791)	11.9

Technical Appendix

Some Examples of Systematization of Knowledge

1. Chemical Structure and Safety

Table 1 illustrates the biodegradability of aliphatic compounds arranged from the aspect of structures. From this Table, it is evident that aliphatic compounds with quaternary carbon are resistant to degradation whereas compounds having only primary and secondary carbons demonstrate highly degradable behavior. Both good degradation and degradation resistant cases are evident in those with tertiary carbon atoms. This phenomenon implies that biodegradation by microorganisms becomes less effective as carbon-hydrogen bond is changed to carbon-carbon bond. Thus, the existence of a quaternary carbon is a key factor for evaluation in terms of predicting biodegradability.

Table 2 summarizes effects of different substituents in a bezene ring on biodegradation. It is evident from this Table that biodegradability of a substituted benzene depends on the type of its substituent. Compounds substituted whith one or two substituents, such as $-CH_3$, $-OH$, $-NH_2$, or $-SO_3H$, generally show highly biodegradability, whereas those even with one substituent of $-Cl$ or $-NO_2$ have been proved to be degradation resistant. Compounds possessing a mixture of both types of substituents (good biodegradability: $-CH_3$, $-NH_2$, $-OCH_3$, $-SO_3H$ and degradation resistant: $-Cl$, $-NO_2$) are generally deemed to show degradation resistance. But in some cases, biodegradability, either good or resistant, seems to depend on the positioning of substituents in the ring (ex. nitrophenol and nitrobenzoic acid.) This implies that not only the types and the number of substituents but their position also affect the biodegradability of a compound. Substituents in the ortho or para positions show good degradability and those in the meta positions has been proved to be biodegradation resistant for nitrobenzoic acid. On the contrary, nitrophenol shows a completely opposite positional behavior. This implies the relation with orientation created from the resonance effects of electrons in the molecule. More knowledge on these phenomena may be acquired for systematization in order to further detailed and precise understandings of relations between chemical structure and biodegradability.

Figure 1 illustrates relations between the number of chlorine atoms in benzene and naphthalene rings with bioaccumulation factor. This figure clarifies the exponential magnification of bioaccumulation factor along with the increase in number of chlorine atoms.

2. Physicochemical Properties and Safety

Figures 2 and 3 summarize the correlations of the degree of water solubility and partition coefficient with magnification of bioaccumulation. It is evident from these figures that the magnification of bioaccumulation is related to the degree of water solubility as well as to the partition coefficient of water/n-octanol and that such factors may be referred to predicting bioaccumulation potential.

Figure 4 illustrates the relationship of degree of water solubility of chemicals with algae growth inhibitant. Figure 5 plots toxic effects on daphnia against partition coefficient of water/n-octanol. It can be learned from these figures that there also exist correlations of degree of water solubility and the partition coefficient for water/n-octanol not only with chemical bioaccumulation but also with toxicity to aquatic organisms. Likewise, correlations with other tests data, when arranged and system-

atized, are also deemed to serve as knowledge of great importance in terms of predicting chemical safety.

3. Concept Diagram of Organic Compounds and Safety

The concept diagram of organic compounds has been formulated by Dr. Fujita and his co-workers in Japan. This diagram basically studies the structure of an organic compound in terms of two parameters – polar and non-polar as shown below:

(i) a polar parameter determined by the type of substituent
(ii) a non-polar parameter determined by the number of carbon atoms and type of substituent.

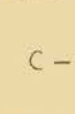
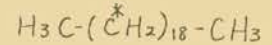
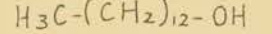
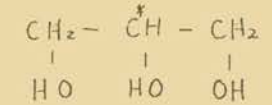
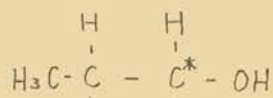
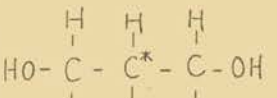
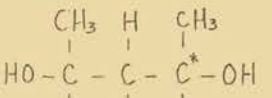
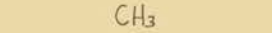
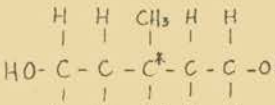
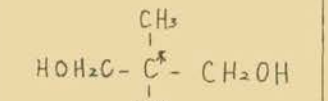
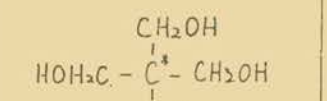
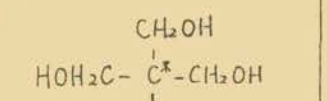
The calculation scheme of these parameters, as elucidated in Table 3, is determined from physicochemical properties of chemicals and other data obtained from past experiences.

Prof. Arai, a member of Chemicals Council, shows that when polar and non-polar values are calculated and plotted on the matrix, positions of the chemicals of common characteristics are situated within a constant area on the matrix as shown in Figure 6. Special attention may be given to the area of chemicals of a idiosyncratic nature – of degradation resistant and of high levels of bioaccumulation. The application of this matrix enables us to predict biodegradability, bioaccumulation, etc. merely through a simple calculation of two parameters based on the structural formula of a chemical. Thus, further, studies are under consideration.

Acknowledgement

I would like to express my gratitude to Chemicals Inspection and Testing Institute Japan, for the advice on technical analysis, and I also would like to express my sincere thanks to Professor Arai, University of Tokyo, for giving me suggestion about Concept Diagram of Organic Compounds and Safety.

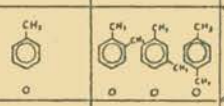
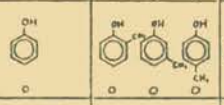
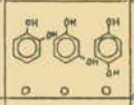
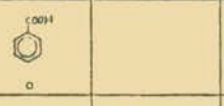
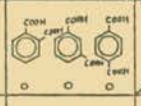
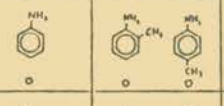
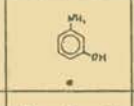
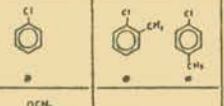
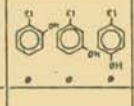
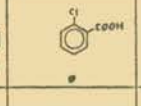
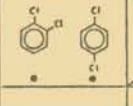
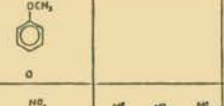
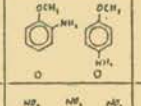
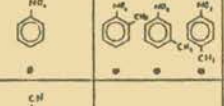
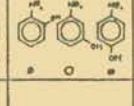
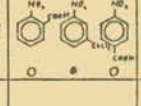
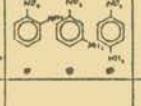
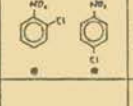
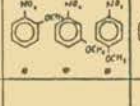
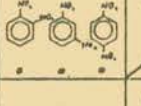
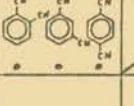
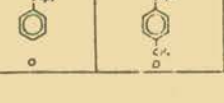
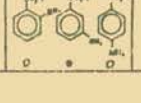
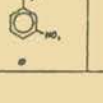
Table 1. Degradability of aliphatic compounds

degradable		degradation resistant	
			
    	  	 	   

o : degradable

● : nondegradable

Table 2. Biodegradability of mono & disubstituted benzens

first substituent \ second substituent	none	$-CH_3$	$-OH$	$-COOH$	$-NH_2$	$-Cl$	$-OCH_3$	$-NO_2$	$-CN$	$-SO_3H$
$-CH_3$	 o	o o o								
$-OH$	 o	o o o	 o o o							
$-COOH$	 o		 o	 o o o						
$-NH_2$	 o	o o	 ●							
$-Cl$	 ●	● ●	 ● ● ●	 ●	 ●	 ● ●				
$-OCH_3$	 o				 o o					
$-NO_2$	 ●	● ● ●	 ● o ●	 o ● o	 ● ● ●	 ● ●	 ● ● ●	 ● ● ●		
$-CN$	 o								 ● ● ●	
$-SO_3H$	 o	o			 o ● o			 ●		

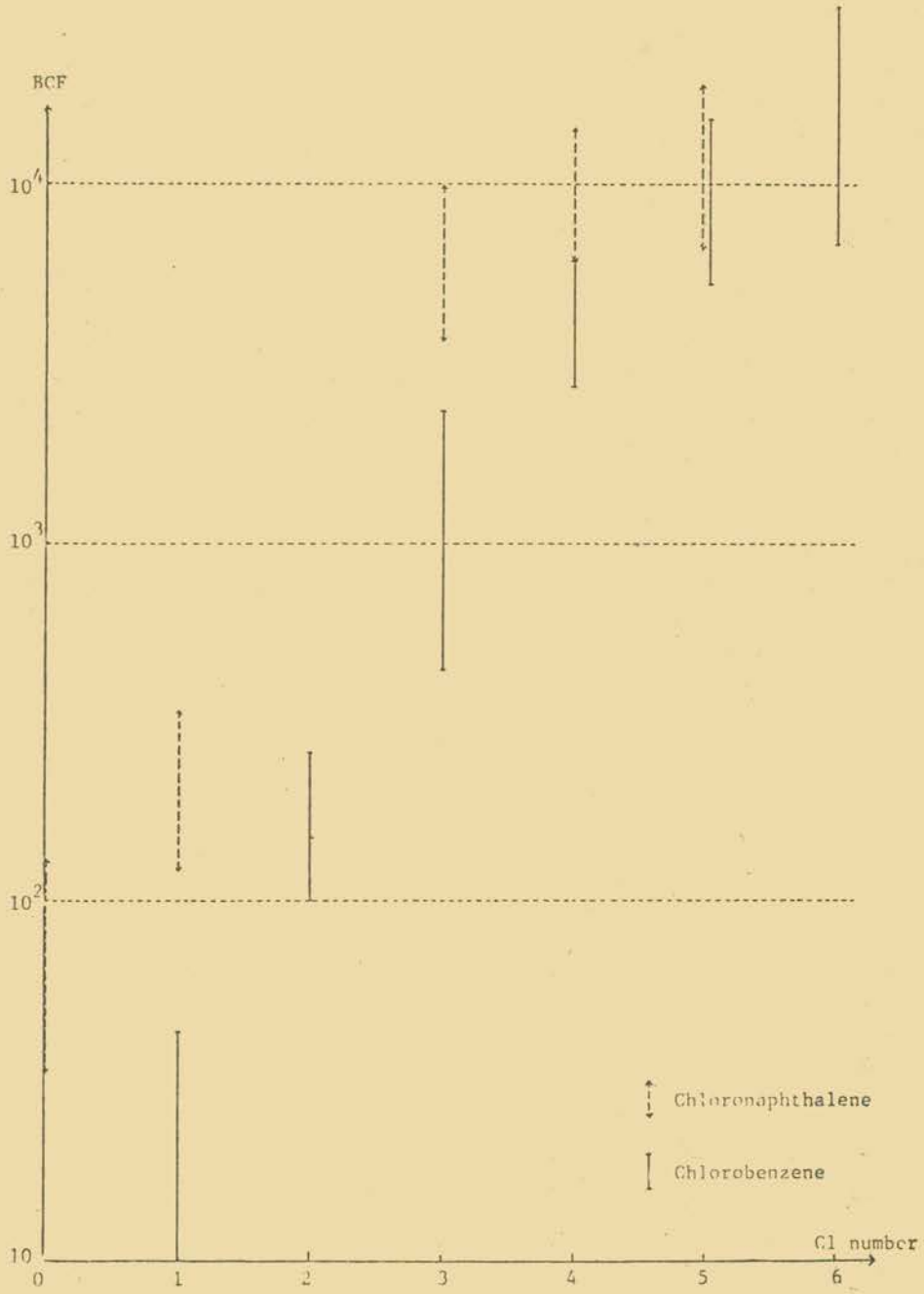

BCF
10^4
10^3
10^2
10
Chloronaphthalene
Chlorobenzene
Cl number
0
1
2
3
4
5
6

Fig. 1

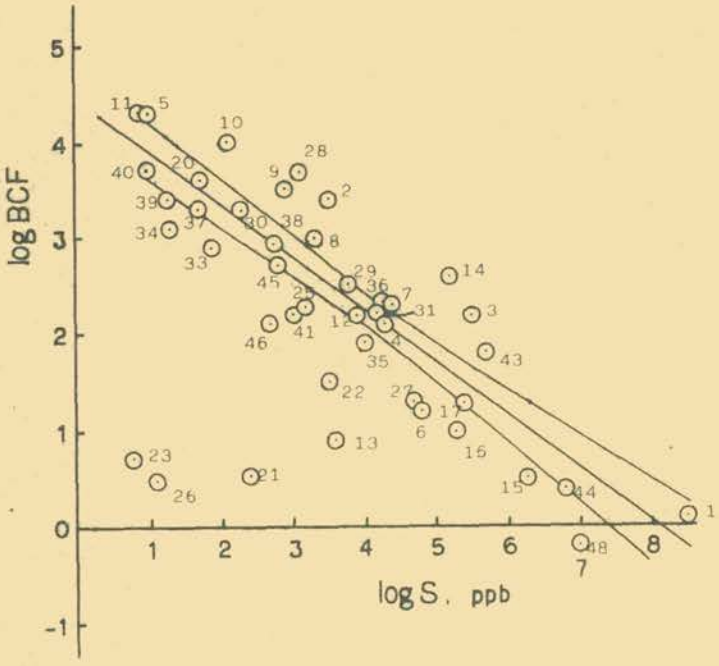


Fig. 2. Correlation between BCF and water solubility

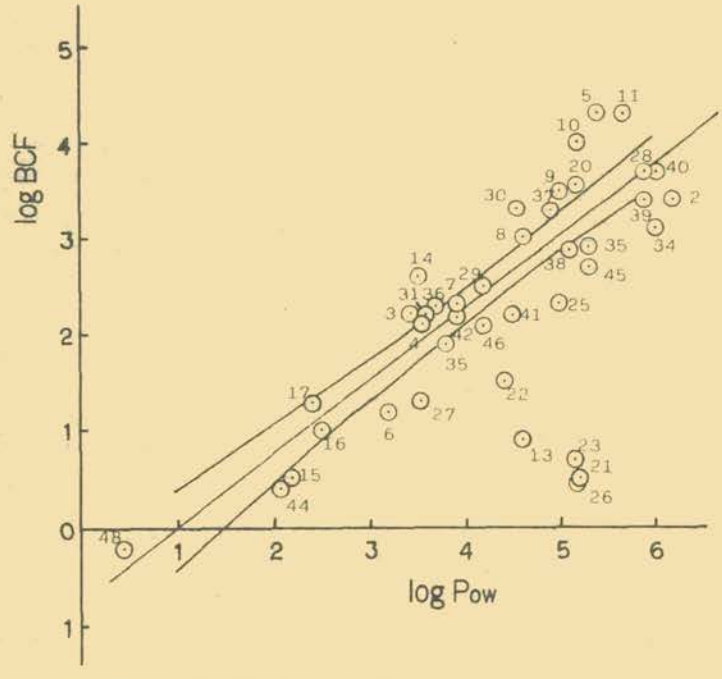


Fig. 3. Correlation between BCF and Pow

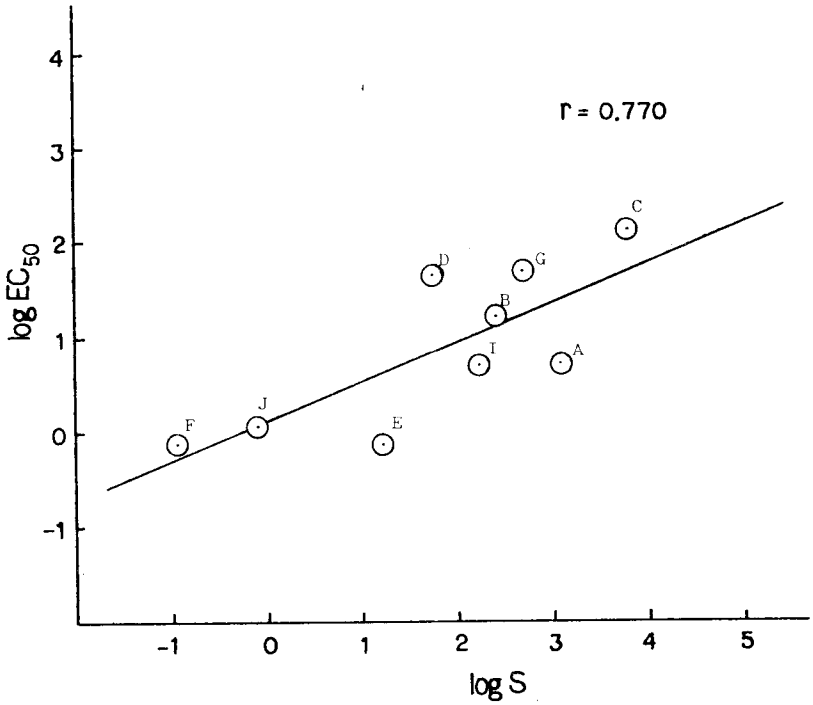


Fig. 4. Correlation between algae growth inhibition and water solubility

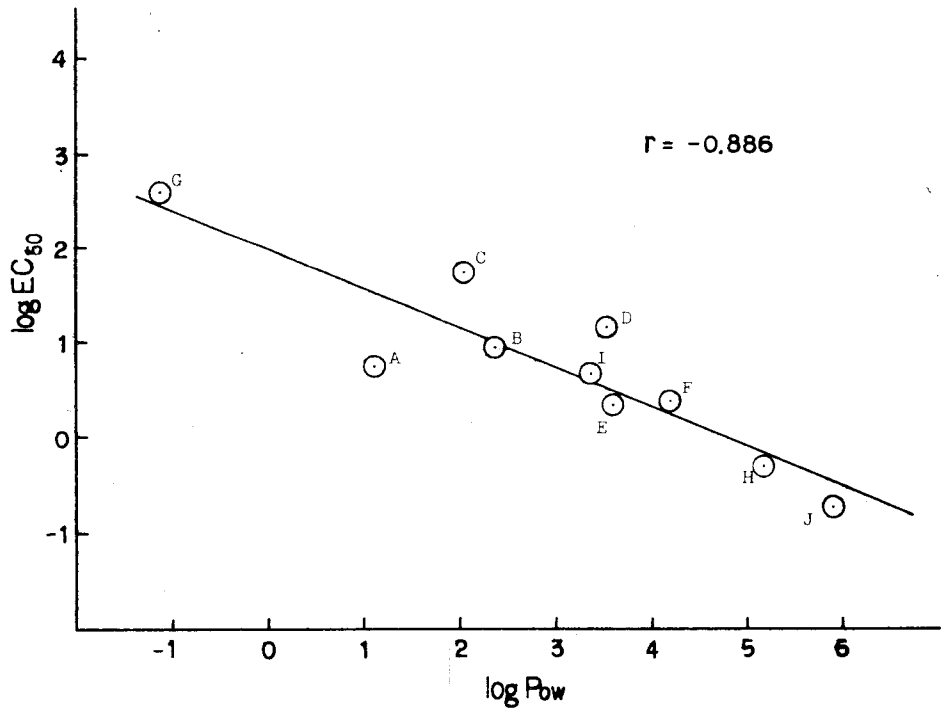


Fig. 5. Correlation between Daphnia EC-50 and Pow

Table: Test compound

No.	Name
1	Pentaerythritol
2	2,3,3,3,2′,3′,3′,3′-Octachlorodipropylether
3	Cyclohexane
4	1;2,4-Trimethylbenzene
5	2,4,6-Tribromo(2-methyl-2,3-dibromopropyl) ether
6	Monochlorobenzene
7	o-Dichlorobenzene
8	1,2,3-Trichlorobenzene
9	1,2,3,4-Tetrachlorobenzene
10	Pentachlorobenzene
11	Hexachlorobenzene
12	p-Dibromobenzene
13	Hexabromobenzene
14	2,4,5-Trichlorophenol
15	Nitrobenzene
16	p-Chloronitrobenzene
17	o-Nitrotoluene
18	4-Ethoxyaniline
19	4-Methylphenyl-1,3-diamine
20	2,4,6-Trinitro-5-t-butyl-1,3-xylene
21	Diheptyl Phthalate
22	Dibutyl Phthalate
23	Dioctyl Phthalate
24	Diisodecyl Phthalate
25	2,2-Bis(4-hydroxy-3,5-dibromophenyl)propane
26	Decabromodiphenyl
27	2,2-Bis(4-hydroxyphenyl)propane
28	1,1-Bis(p-chlorophenyl)-2,2,2-trichloroethanol
29	Diphenylether
30	2,4,6-Trichlorophenyl-(4-nitrophenyl)ether
31	Diphenylamine
32	N,N′-Diphenylguanidine
33	N,N′-Diphenyl-p-phenylenediamine
34	Xylylphenylethane
35	Naphthalene
36	Tetrahydronaphthalene
37	Anthracene
38	Monoisopropylnaphthalene
39	Diisopropylnaphthalene
40	Triisopropylnaphthalene
41	2-(N-Phenylamino)naphthalene
42	2-Naphthylaminosulfonic Acid
43	Acid Red 114
44	Quinoline
45	O,O′-Diethyl-o-(3,5,6-trichloro-2-pyridil)phosphothioate
46	Carbazol
47	Pigment Red 53
48	N-Hexamethylolmelamine Polyalkylether
49	Polyoxypropylene
50	Polyvinylalcohol

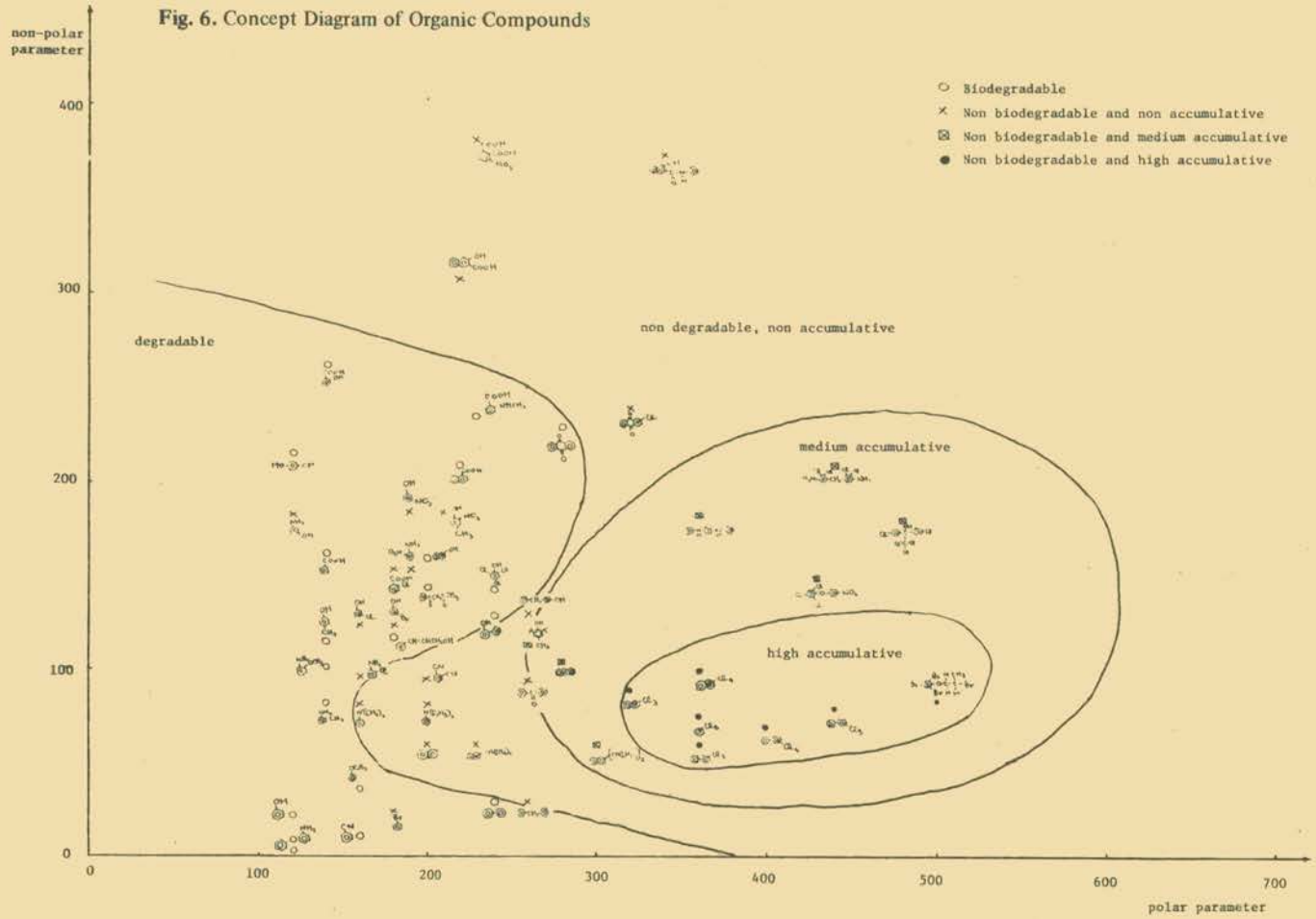
Table: Test compound

No.	Name
A	4-Ethoxyaniline
B	o-Nitrotoluene
C	Quinoline
D	Bisphenol A
E	Diphenylamine
F	Diphenylether
G	Acid Red 114
H	2,4,6-Trinitro-5-t-butyl-1,3-xylene
I	2,4,5-Trichlorophenol
J	1,1-Bis(p-chlorophenyl)-2,2,2-trichloroethane
K	Polyvinylalcohol

Table 3. Calculation of Polar Parameter based on Substituent

Substituent	Polar-parameter	Substituent (amphoteric)	Non-polar parameter	Polar-parameter
Light metal	500	R_4BiOH	80	250
Heavy metal	400	R_4SbOH	60	250
$-AsO_3H_2$, $-AsO_2H$	300	R_4AsOH	40	250
$-SO_2-NH-CO-$, $-N=N-NH_3$	260	R_4POH	20	250
$\equiv N-OH$, $-SO_3H$, $-NH-SO_2-NH-$	250	$>SO_2$	40	110
$-CO-NH-CO-NH-CO-$	250	CSSH	120	80
$\equiv S-OH$, $-CO-NH-CO-NH-$	240	$-S-CN$	90	80
$-SO_2-NH-$	240	$-CSOH$, $-COSH$	80	80
$-CS-NH-$, $-CO-NH-CO-$	230	$-NCS$	90	75
$=N-OH$, $-NH-CO-NH-$	220	$-NO_2$	70	70
$=N-NH-$, $-CO-NH-NH-$	210	$-Bi<$	80	70
$-CO-NH-$	200	$-Sb<$	60	70
$-COOH$	150	$-As<$, $-CN$	40	70
Lactone	120	$-P<$	20	70
$-CO-O-CO-$	110	$-CSSR$	130	50
Anthracene, Phenanthrene (nucleus)	105	$-CSOR$, $-COSR$	80	50
$-OH$	100	$-NO$	50	50
$>Hg$	95	$-O-NO_2-$	60	40
$-NH-NH-$, $-O-CO-O-$	80	$-NC$	40	40
$-N<$ (amine character)	70	$-Sb=Sb-$	90	30
$>CO$	65	$-As=As-$	60	30
$-COOR$	60	$-P=P-$, $-NCO$	30	30
Naphthalene, Quinoline (nucleus)	60	$-O-NO$, $-SH$, $>S$	40	25
$>C=NH$	50	$=S$	50	10
$-N=N-$	30	$-I$	80	10
$-O-$	20	$-Br$	60	10
Benzene (nucleus)	15	$-Cl$	40	10
Nucleus	10	$-F$	5	5
$\equiv$	3	Iso →	−10	0
$=$	2	Tert. →	−20	0

Fig. 6. Concept Diagram of Organic Compounds



Environment Agency Japan

Background Paper on the Experience of the Environmental Monitoring of Chemical Substances in Japan

I. General Environmental Safety Inspection System

The countermeasures for existing chemicals are very important parts of the environmental policies in Japan also. The Environment Agency carries out the environmental monitorings of chemicals from 1974 to obtain useful data for taking proper measures to meet the situation at need, if the pollution can be discovered at very early stage.

In 1978, we had set up the general environmental safety inspection system for aiming

1. to survey effectively and comprehensively much numbers of existing chemicals from viewpoint of the protection of the environmental pollution
2. to arrange as much as possible scientific data which should be requested in taking administrative measures based on the survey results
3. to undertake the environmental survey of such chemicals as considered to be harmful to man and the environment
4. and to contribute easily the information obtained from this inspection system to the international activities in the relative fields.

It is, frankly speaking, very difficult to select the objective substances for the surveys under such situation as there are little available information, less suitable analysis methods.

Outline of the inspection system is figured in Annex I.

The starting step is to make a priority list of the candidate chemicals for the environmental monitorings for which criteria we had prepared is described in chapter IV in this presentation paper. There have been selected about 2,000 chemicals.

II. The Environmental Monitoring

The environmental monitorings are proceeded in three types of survey. The first one is the general environmental survey, the second is the precision environmental survey, and the last is the atomospheric investigation. Surveying points are not established near the exhaust ports, etc. of factories or places of business, because the object of the surveys is general environment.

The necessity of the environmental monitoring

1. The results of laboratory testing for chemicals give us various information to know the indications of chemical-behavior in the environment and the potential hazardous nature of chemicals to man and the environment.
2. However, when we are threatened to decide which chemical should be controlled and to what extent the exposure of the chemical should be reduced, it is absolutely necessary to confirm the level of the chemical in the environment so that we can estimate the risk of the chemical which is the function of both exposure and toxicity.
3. With regard to new chemicals which are not released into the environment yet at the stage of notification, we can not but to estimate the risk of chemical with some amounts of laboratory testing data as is listed in MPD.
4. On the other hand, when we need to check the potential risk of existing chemicals which more or less really exist in the environment, the environmental level of the

chemicals could be valuable information for decision making in gathering further information and conductivity further testings.

5. The results of environmental monitoring of chemicals are remarkably useful for the following points, if there have been established reliable analytical methods for environmental samples.

(i) Validation of exposure-analysis which is based on the prediction of the environmental fate of chemicals with physical chemical data,
(ii) determination of the reasonable dose of candidate chemicals for laboratory human and environmental effects testings,
(iii) confirmation of risk with both human and environmental effects data and environmental monitoring data,
(iv) checking for effects of countermeasures taken to clean up the environment.

When in selecting a chemical substance at first time, it is objective for the general environmental survey at 2 or 3 surveying points, and sampling is undertaken from water and sediment.

With regard to the general environmental survey, about 50 chemicals are chosen from the priority list mentioned above in taking into consideration the scientific information, which are published in Japan and in abroad, especially on the residual property in the environment, the production scale as well as the toxicity to human health and the environment.

Subsequently, the detected chemicals in the general environmental survey should be objectives for the precision survey in next year generally which are conducted at more than 40 surveying points covered almost all of Japanese islands (Fig. I), and sampling is undertaken from water, sediment and fish.

In 1979, we had detected organic silicon compounds, chlorinated parafine and ethylenediamintetraacetic acid (EDTA) at range of concentration 10.1-2.1 ppm, 9.4-0.7 ppm and 7.1-1.3 ppm in only water samples respectively, so, they were objectives for the precision survey in last year with exception of EDTA due to the difficulty of the analysis method especially for the sample from sea water.

Annex II indicates the distribution of the maximum concentration of chemical substances detected by the environmental surveys in 1974–1979, and Annex III is a summary of the results of the environmental surveys for the same period.

These results give us the suggestions as follows:

(i) Such chemicals as are required to have physical and chemical stability, for instance, plasticizers to be added to plastics or rubber, antioxidants, stabilizers, antiflaming agents, incombustibilizing agents or substances to be used as heat transfer media are high in residual property in the environment (BHT, 2-mercaptobenzothiazole, chlorinated paraffine, etc.).
(ii) Even if a chemical substance superior in biodegradability, it is possible that the substance shows a high residual property in the environment in case a large amount of the substances is used in open system and discharge surpasses the degradability in the environment (phtalicesters and LAS, etc.).
(iii) As it is unexpected that a substance to be regulated is directly discovered from the results of every year's survey, we requested to confirm potential injurious substances early and evaluate environmental danger by them while monitoring their concentration levels in the environment so that we can take necessary measures to meet with the danger as occasion demands.

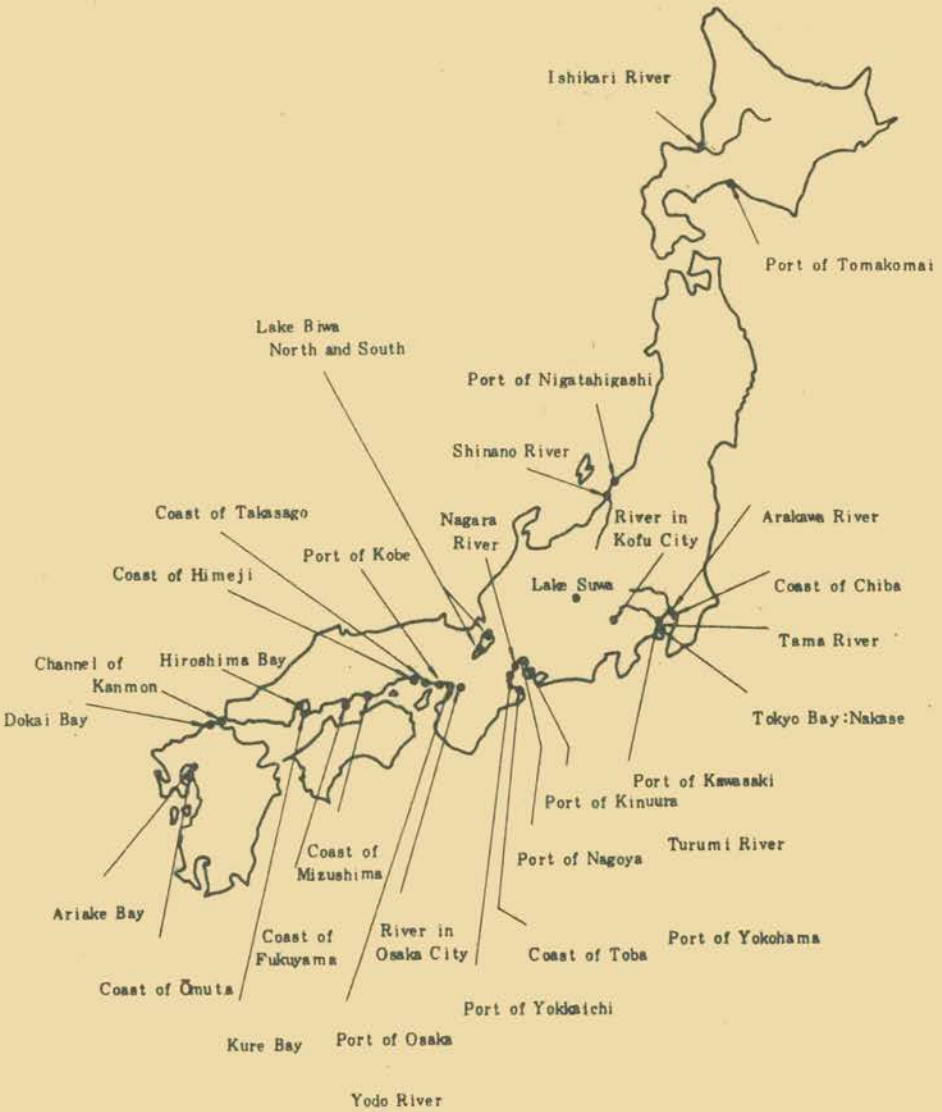


Fig. I. Areas for precision and general environmental examinations

III. Wildlife Monitoring Surveys of Environmental Pollution

In addition to the environmental monitorings, we are carrying out the wildlife monitoring surveys of chemical substances from 1978. The concentration of chemicals to be determined in such environmental media, as water, air, sediment is generally very low, but it is well known that in bodies of such animals as bird, fish, chemical substances are sometimes accumulated, concentrated to higher level compared with the level of same substance in the environment. By measuring systematically and periodically the levels of pollutants in such animals, it will become possible to obtain data

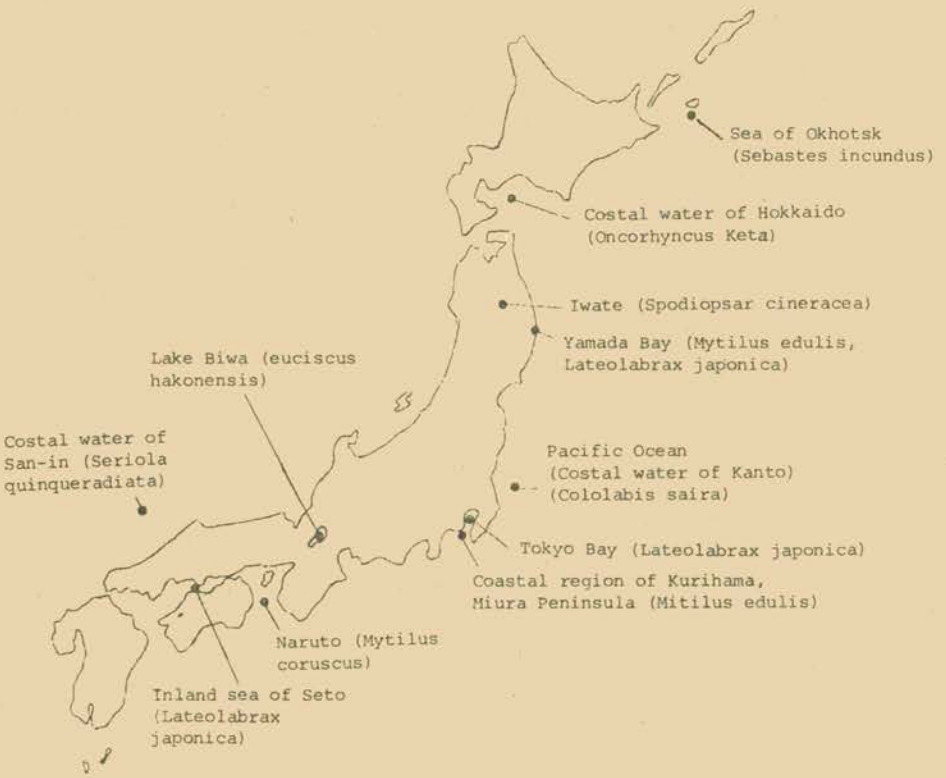


Fig. II. An outline of the areas and animal species selected for the wildlife monitoring survey of environmental pollution in 1979.

which can be used effectively for various purposes such as the monitoring of the change in the level of substances considered to cause potential hazards to human health and various ecosystems and their behavior in the environment. From standpoint of monitoring the environmental pollution by chemical substances, however, there are some problems remaining unsolved with regard to the continuity of data. The present survey is carried out, giving special consideration to the following points;

(i) It was decided to carry out this survey continuously in the future. There were selected the sampling points such as that they would make it possible to determine the average level of pollution in the areas around the Japanese islands (Fig. II).

(ii) The animals species to be used as the objects of survey and measurement were determined, considering their effectiveness and usefulness as the indices of environmental pollution and also their capability of international comparison.

(iii) As for the chemical substances to be investigated, those which have been pointed out as potentially hazardous mainly on the basis of previously available information and which would require continuous observation of the change in their concentration levels over a long period in the future were selected.

The results obtained from the wildlife monitorings realised in 1979 are summarised in Annex IV.

IV. Priority List for the Environment Survey

1. Outline of priority list

In making up this list, the selection was made from among the existing chemical substances with special reference to the four types of substance given below. However, the presently available information on the toxicity, production and the form of use of such individual substances is often fragmental and the choice had to be made on the basis of the rather limited information available at the present time and therefore, this list is considered to be of such nature that it should be reappraised as such information is further expanded in the future.

a) Substances which have been found or reported to possess a degree of toxicity higher than a definite level
b) Substances which are judged to have a property similar to a) above in view of their chemical structure
c) Substances which are considered to be stable or highly accumulated in the environment
d) Substances which are produced industrially in considerable amounts and have the possibility of being emitted into the environment

On the basis of the four basic categories a)–d), the choice of the substances was made by the more concrete criteria of judgement as given below.

For category a),

(i) Substances which have been found to have a degree of toxicity over a definite level with reference to LD_{50} and the like and those which are reported to have the possibility of being mutagenic, teratogenic or carcinogenic and are actually produced (including those which were produced in past. (The same shall apply hereinafter)).
(ii) Substances which are expected to turn into such substanced as described above and are actually produced.

For category b),

(i) Organic halogenated compounds which are actually produced.
(ii) Organic phosphorus compounds which are actually produced.
(iii) Chemical compounds such as amino compounds, azo compounds and nitroso compounds substituents containing noticeable for the viewpoint of their ecological effects and are actually products.

For category c),

(i) Substances which are judged to be difficult to degrade or easy to accumulate from the results of investigations carried out in the past.
(ii) Substances which are reported to be present in the environment from the results of surveys conducted in the past.
(iii) Substances such as fire retardants and heat transfer media which are used for their chemical stability and those which are used as substitutes for PCB.

For category d),

(i) Substances which are industrially produced in considerable quantities.
(ii) Substances contained in relatively large quantities in industrial products.

Of the above, the following substances have been excluded.

(i) Substances which are produced in large quantities but do not deserve to be noticed from the viewpoint of environmental pollution, such as those which are not physiologically active. (Alumina, Methane, etc.)

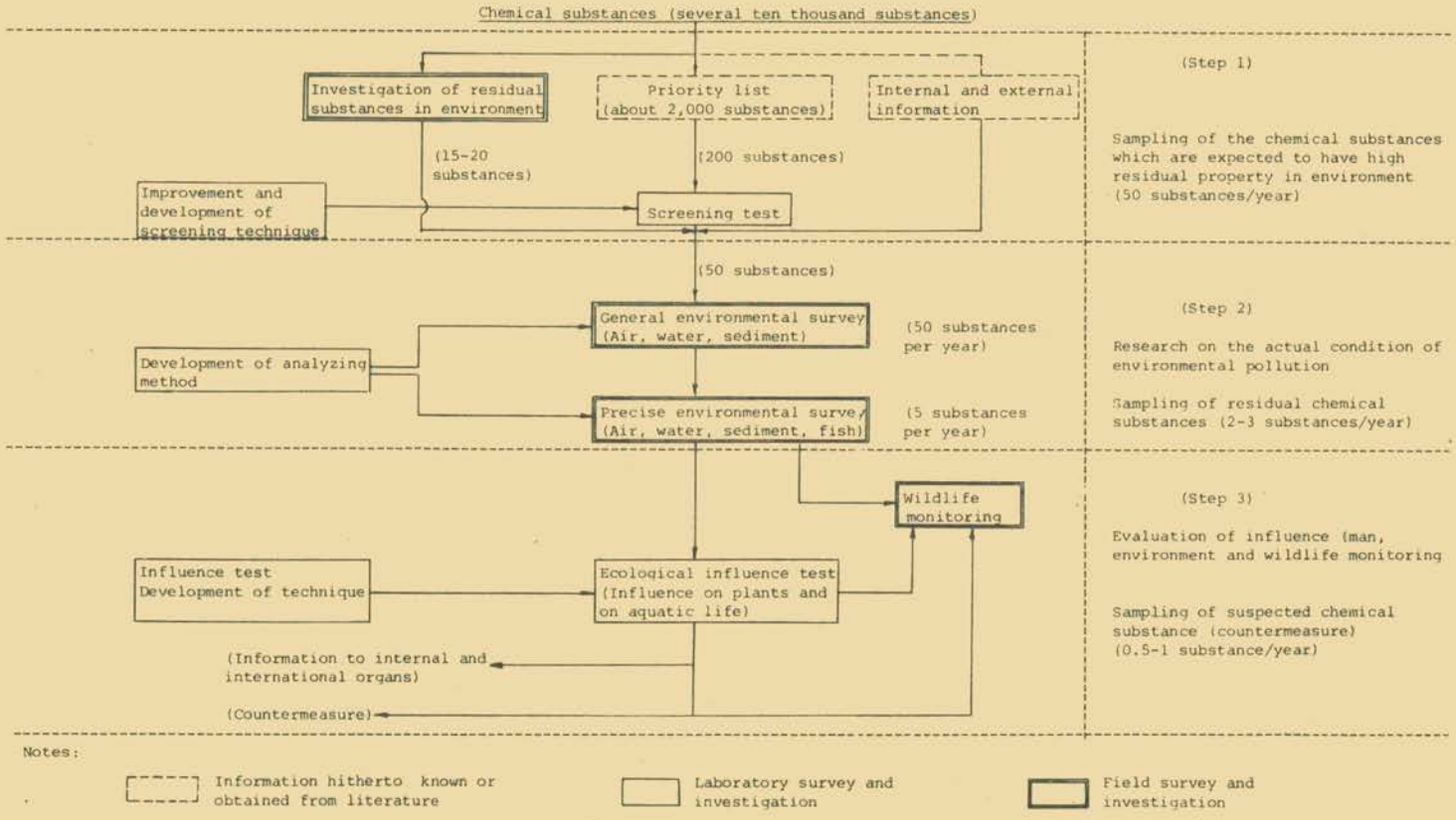
(ii) Substances which are known to have physiological activity and ecological effects but negligible judging from the form in which they are used at the present time. (Sodium chloride, ethanol, etc.)

(iii) Substances whose uses are limited to medical and pharmaceutical products, reagents, food additives, etc.

The following are the inventories of chemical substances used mainly as references in selecting the substances to be placed on the list according to the above conditions.

1. The list of existing chemical substances (Substances specified by Article 2 of Supplementary Provisions of the Chemical Substances Control Law)
2. List of publicized chemical substances (Existing Chemical substances specified by Para. 2, Article 57 of the Occupational Safety and Health Law)
3. Registry of Toxic Effects of Chemical Substances, 1977 edition (National Institute for Occupational Safety and Health)

ANNEX I. General environmental safety inspection system for chemical substance



ANNEX II. Distribution of the Maximum Concentrations of Chemical Substances Detected by Environmental Surveys in 1974–1979.

[Water Quality]

(Unit: ug/ml)

Range of Detection	< 0.0001	0.0001 ≦ < 0.001	0.001 ≦ < 0.01	0.01 ≦
Chemical Substances Detected	m-Anisidine 3,5-Xylidine 1,2,3-Trichlorobenzene 1,3,5-Trichlorobenzene HCB* PCN* 2-Mercaptobenzothiazole	p-Anisidine Anion active agent N-Ethylaniline Ethylene Vinyl chloride o-Chloroaniline m-Chloroaniline p-Chloroaniline 2,4-Dichloroaniline 3,4-Dichloroaniline 2,6-Dinitrotoluene Terephthalic acid Dimethyl terephthalate Dodecachlorododecahydrodimethanodiberzo-cyclooctene 1,2,4-Trichlorobenzene Tris(chloroethyl) phosphate Tributyl phosphate* m-Toluidine p-Toluidine o-Nitroanisole o-Nitrotoluene m-Nitrotoluene p-Nitrotoluene p-Nitrophenol α-BHC* Di-i-heptyl phthalate* Propylene Pentachlorophenol	o-Anisidine p-Dichlorobenzene N.N-Dimethylaniline Tetrachloroethylene 1,1,1-Trichloroethane m-Nitroanisole Nitrobenzene*	Aniline LAS (Straight chain) Carbon tetrachloride Trichloroethylene Trichloromethane o-Toluidine Diethyhexyl phthalate* Di-n-octyl phthalate Di-n-butyl phthalate* Di-i-butyl phthalate* Polyoxyethylene alkylphenyl ether
Total (Cumulative Total)	7 (7)	28 (35)	7 (42)	11 (53)

[Sediment]

(Unit: μg/g dry)

Range of Detection	< 0.01	0.01 ≦ < 0.1	0.1 ≦ < 1.0	1.0 ≦
Chemical Substances Detected	p-Anisidine Ethylene Methyl chloride p-Octyl phenol p.p'-DDT p.p'-DDE Dicyclopentadiene o-Dinitrobenzene 2,6-Dinitrotoluene 2,4,6-Trichlorophenol	o-Anisidine m-Anisidine N-Ethylaniline p-Cresol 2,3-Xylidine 2,5-Xylidine 3,4-Xylidine 3,5-Xylidine o-Chloroaniline m-Chloroaniline 2,4-Dichloroaniline m-Dichlorobenzene p-Dichlorobenzene p.p'-DDD m-Dinitrobenzene 1,2,3-Trichlorobenzene 1,2,4-Trichlorobenzene 1,3,5-Trichlorobenzene Tris(chloroethyl) phosphate o-Toluidine m-Toluidine p-Toluidine α-Naphthylamine o-Nitroanisole m-Nitroanisole m-Nitrotoluene p-Nitrotoluene Nonylphenol α-BHC* β-BHC γ-BHC	Aniline p-Chloroaniline Diisopropulnaphthalene 3,4-Dichloroaniline N.N-Dimethylaniline o-Terphenyl m-Terphenyl p-Terphenyl Trioctyl phosphate Tris(isopropylphenyl) phosphate Tributyl phosphate* Tris(butoxyethyl) phosphate o-Nitroanisole o-Nitrotoluene HCB* Pentachlorophenol	Acetaldehyde LAS (Staight chain) Anthracene Ethylenediaminetetroacetic acid Chlorinated paraffine Caprolactam Dibutylhydroxytoluene (BHT) Tricresyl phosphate Nitrobenzene* Phenanthrene Diethylhexyl phthalate* Di-n-octyl phthalate Di-n-butyl phthalate* Di-i-butyl phthalate* Di-i-heptyl phthalate* PCN* PCT Polyoxyethylene alkylphenyl ether

(To be continued)

[Sediment]

Chemical Substances Detected		δ-BHC 1-Phenyl-1-(3,4-dimethylphenol)ethane Phenol Pentachlorobenzen N-Methylaniline 2-Mercaptobenzothiazole Organic silicon compounds		
Total (Cumulative Total)	10 (10)	38 (48)	16 (64)	18 (82)

[Fishes and Shellfishes]

(Unit: μg/g wet)

Range of detection	0.001 ≦ < 0.01	0.01 ≦ < 0.1	0.1 ≦
Chemical Substances Detected	o.p'-DDT p.p'-DDT m-Terphenyl 1,3,5-Trichlorobenzene Tributyl phosphate* β-BHC HCB*	Diisopropylnaphthalene Dibutylhydroxytoluene (BHT) p.p'-DDD Tris(dichloropropyl) phosphate p-Nitroanisole α-BHC* γ-BHC pentachlorobenzene	p.p'-DDE 1,2,4-Trichlorobenzene Tris(chloroethyl) phosphate Nitrobenzene* 1-Phenyl-1-(3,4-dimethylphenyl)ethane Diethylhexyl phthalate* Di-n-butyl phthalate* Di-i-butyl phthalate* Di-i-heptyl phthalate* PCN* PCT
Total	7 (7)	8 (15)	11 (26)

(Note) This table shows the maximum concentrations of chemical substances detected by material group, and these results do not mean that substances other than the listed ones are completely absent from the environment or all the water, sediment, fishes and shellfishes of the regions surveyed are contaminated to such degrees. The number of the kinds of chemical substances detected by the surveys in 1973 to 1979 was 54/288 in water, 82/270 in sediment and 26/88 in fishes and shellfishes (The denominater is the number of substances searched.)

* The substances (9 kinds) detected in every group of the test materials (water, sediment, and fishes and shellfishes).

ANNEX III. A Summary of the Results of Environmental Surveys for Chemical Substances (in 1974 to 1979)

[B/A: Polluted cases/samples,
Unit: ppm except the case of atmos. (ppb)]

No.	Substance	Year	Example of detection and range of detection			
			Water quality	Sediment	Fishes	Others
			B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
1	Acrylamide	'75	0/95 – (0001)			
2	Acrylonitrile	'77	0/8 – (002~005)	0/8 – (04~05)		
3	Acrolein	'78	0/21 – (0001~0011)	0/15 – (002~01)		
4	Adiponitrile	'78	0/21 – (001)	0/21 – (01~08)		
5	Acetaldehyde	'77	0/4 – (001)	3/4 2~4 (25)		
6	Acetonitrile	'77	0/8 – (012~02)	0/8 – (2~24)		
7	Azobisisobutyronitrile	'79	0/15 – (001)	0/15 – (01)		
8	o-Anisidine	'76	14/68 00002~00018 (00002~00008)	27/68 0003~0079 (0003~0004)		
9	m-Anisidine	'76	5/68 0000014~0000028 (000001~00002)	6/68 00004~0019 (00002~0001)		
10	p-Anisidine	'76	4/68 0000004~0000012 (000004~00002)	12/68 0001~0004 (00007~0004)		
11	Aniline	'76	40/68 000002~0026 (000004~00002)	48/68 00007~050 (0008)		
12	o-Aminobiphenyl	'77	0/4 – (000005)	0/4 – (002)		
13	Sodium alkylbenzenesulfonate (Straight chain)	'77	0/51 028~29 (001)	51/51 10~240 (1)		
14	Sodium alkylbenzenesulfonate (branched chain)	'77	0/51 – (001)	0/51 – (1)		
15	Aldrin	'74	0/60 – (00001)	0/60 – (001)	0/60 – (0005)	
16	Anthracene	'76	0/24 – (00001)	6/20 001~028 (001)		
		'77	0/8 – (0000002~0003)	6/8 0015~12 (0004)		
17	Isophthalonitrile	'77	0/8 – (0001~0005)	0/8 – (01~1)		
18	Isobutyronitrile	'77	0/8 – (0001)	0/8 – (01)		
19	Isoprene	'78	0/12 – (0001)	0/12 – (0001)		
20	Isopropylbenzene	'77	0/4 – (0002)	0/4 – (0004)		
21	Anion active agent	'74	26/68 00014 (000005)			
22	N-Ethylaniline	'76	2/68 000048~000058 (00001~00006)	26/68 0003~0088 (0002~0008)		
23	Ethylbiphenyl	'76	0/68 – (00006~002)	0/50 – (014~20)	0/20 – (012~05)	
24	2-Ethylhexanol	'79	0/80 – (0000002~02)	0/80 – (000008~2)		
25	2-Ethylhexyl adipate	'78	0/80 – (00004~0025)	0/80 – (002~1)		
26	Ethylenediaminetetraacetic acid	'79	0/18 – (001~002)	5/24 28~13 (02~20)		
27	Ethylbenzene	'77	0/8 – (0002)	0/8 – (0004)		
28	Ethylmorpholine	'79	0/88 – (0001~008)	0/88 – (001~01)		
29	Ethylene	'77	1/4 00001 (000005~0005)	0/4 00003~00004 (0005)		

[B/A: Polluted cases/samples.
Unit: ppm except the case of atmos. (ppb)]

No.	Substance	Year	Example of detection and range of detection			
			Water quality	Sediment	Fishes	Others
			B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
30	Ethylene glycol	'77	0/6 — (0.1~0.4)	0/6 — (1~20)		
31	2-Ethoxyethanol	'76	0/48 — (0.08~0.1)	0/20 — (0.4)		
32	Epichlorohydrin	'77	0/8 — (0.01)	0/8 — (0.04)		
33	Allyl chloride	'77	0/4 — (0.005)			
34	Ethyl chloride	'77	0/8 — (0.00004)	0/8 — (0.0007)		
		'79				* 0/44 0.48~20 ppb (0.006~2)
35	Vinyl chloride	'75	5/100 0.0041 (0.0005~0.048)			
		'79				* 1/45 0.02~40 ppb (0.002~2)
36	Benzyl chloride	'76	0/60 — (0.08~0.1)	0/58 — (0.4~10)	0/8 — (10)	
37	Methyl chloride	'77	0/4 — (0.00001)	2/8 0.0001~0.0008 (0.00005)		
		'79				* 30/45 0.28~22 ppb (0.02~1)
38	Chlorinated paraffine	'79	0/51 — (0.01)	24/51 0.7~10 (0.5)		
39	Endrin	'74	0/40 — (0.0001)	0/40 — (0.01)	0/40 — (0.005)	
40	Octanol	'79	0/27 — (0.005~0.05)	0/27 — (0.8~1)		
41	p-Octylphenol	'77	0/4 — (0.00004~0.00015)	2/4 0.004 (0.004~0.058)		
42	Caprolactam	'77	0/4 — (0.001~0.005)	1/4 1.6 (0.1~1)		
43	Carbazole	'76	0/20 — (0.0002)	0/20 — (0.02)		
44	2,8-Xylidine	'76	0/48 — (0.001~0.01)	6/48 0.004~0.038 (0.001~0.004)		
45	2,5-Xylidine	'76	0/48 — (0.0002~0.0005)	2/48 0.004~0.027 (0.001~0.004)		
46	3,4-Xylidine	'76	0/48 — (0.00004~0.0007)	8/48 0.001~0.048 (0.001~0.004)		
47	3,5-Xylidine	'76	1/48 0.00004 (0.00002~0.0002)	5/48 0.002~0.01 (0.0005~0.001)		
48	o-Xylene	'77	0/8 — (0.002)	0/8 — (0.004)		
49	m-Xylene	'77	0/8 — (0.002)	0/8 — (0.004)		
50	p-Xylene	'77	0/8 — (0.002)	0/8 — (0.004)		
51	o-Cresol	'77	0/8 — (0.0002~0.01)	0/8 — (0.02~0.1)		
52	m-Cresol	'77	0/8 — (0.0002~0.01)	0/8 — (0.02~0.1)		
53	p-Cresol	'77	0/8 — (0.0002~0.01)	5/8 0.02~0.04 (0.02~0.1)		
54	o-Chloroaniline	'76	12/120 0.000028~0.00085 (0.00002~0.1)	29/118 0.0007~0.098 (0.0002~1.0)	0/2 — (1.0)	
55	m-Chloroaniline	'76	10/120 0.000018~0.00084 (0.00004~0.1)	34/121 0.0003~0.047 (0.0001~1.2)	0/2 — (1.0)	
56	p-Chloroaniline	'76	9/120 0.000024~0.00089 (0.00002~0.1)	33/121 0.0001~0.27 (0.0005~1.2)	0/2 — (1.0)	
57	Chlorocyclohexane	'77	0/4 — (0.00002~0.01)	0/6 — (0.0001~2)		

*: Atmosphere

[B/A: Polluted cases/samples,
Unit: ppm except the case of atmos. (ppb)]

No.	Substance	Year	Example of detection and range of detection			
			Water quality	Sediment	Fishes	Others
			B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
58	o-Chlorotoluene	'79	0/18 — (0.0000004~0.001)	0/18 — (0.0001~0.02)		
59	p-Chlorotoluene	'79	0/18 — (0.0000004~0.001)	0/18 — (0.0001~0.02)		
60	1-Chloronaphthalene	'77	0/4 — (0.0003~0.008)	0/4 — (0.01~0.4)		
61	2-Chloronaphthalene	'77	0/4 — (0.0003~0.008)	0/4 — (0.01~0.4)		
62	1-Chloro-2,4-dinitrobenzene	'78	0/24 — (0.0002~0.0005)	0/15 — (0.007~0.147)		
63	4-Chloro-2-nitroaniline	'78	0/24 — (0.0001~0.0008)	0/15 — (0.02~0.022)		
64	o-Chloronitrobenzene	'75	0/95 — (0.001)			
65	m-Chloronitrobenzene	'75	0/95 — (0.001)			
66	p-Chloronitrobenzene	'78	0/24 — (0.00005~0.00007)	0/15 — (0.002~0.025)		
67	Chloropicrin	'79	0/24 — (0.0000005~0.0001)	0/24 — (0.00025~0.005)		
68	o-Chlorophenol	'78	0/24 — (0.0002~0.004)	0/24 — (0.1~4)		
69	m-Chlorophenol	'78	0/24 — (0.002~0.04)	0/24 — (0.1~4)		
70	p-Chlorophenol	'78	0/24 — (0.002~0.04)	0/24 — (0.05~4)		
71	Chloroprene	'77	0/4 — (0.002)			
72	Chlorobenzene	'76	0/68 — (0.001~0.2)	0/61 — (0.4~4)	0/2 — (10)	
73	o-Dianisidine	'77	0/4 — (0.0005)	0/8 — (0.008)		
74	Diisodecyl adipate	'78	0/30 — (0.0008~0.1)	0/30 — (0.04~1)		
75	Diisobutylene	'75	0/12 — (0.00018~0.0004)	0/12 — (0.00081~0.00078)		
76	Diisopropylnaphthalene	'75	0/108 — (0.00217~0.0005)	0/108 0.001~0.19 (0.01~0.25)	2/34 0.020~0.048 (0.021~0.23)	
		'77	0/117 — (0.00091~0.01)	6/117 0.001~0.1 (0.001~0.04)	7/88 0.00052~0.0017 (0.0002~0.03)	
77	m-Diisopropylbenzene	'77	0/8 — (0.004)	0/8 — (0.01)		
78	p-Diisopropylbenzene	'77	0/8 — (0.004)	0/8 — (0.01)		
79	Dietanolamine	'79	0/12 — (0.0005~0.0004)			
80	N,N-Diethylaniline	'77	0/4 — (0.001~0.001)	0/4 — (0.2~1)		
81	Diethylbiphenyl	'76	0/68 — (0.0005~0.02)	0/50 — (0.2~2.0)	0/20 — (0.1~0.5)	
82	Carbon tetrachloride	'74	0/40 — (0.000002~0.0005)			** 2/18 0.0101~0.0105 (0.000002~0.0005)
		'75	105/855 0.00002~0.0018 (0.00001~0.0008)			** 17/108 0.0000022~0.0084 (0.000002~0.0008)
		'79				* 42/45 0.048~20 ppb (0.008~8)
83	Dioxane	'76	0/60 — (0.1)	0/20 — (0.4)		
84	Cyclohexane	'79	0/17 — (0.00005~0.0002)	0/17 — (0.0001~0.0004)		
85	N-Cyclohexyl-2-benzothiazolylphenamide	'77	0/18 — (0.00005~0.0008)	0/18 — (0.002~0.02)		

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No.	Substance	Year	Example of detection and range of detection			
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			B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
86	2,4-Dichloroaniline	'76	7/68 0.000082~0.00065 (0.00007~0.0008)	12/68 0.0003~0.024 (0.0003~0.001)		
87	3,4-Dichloroaniline	'76	4/68 0.00074~0.00042 (0.00004~0.0008)	21/68 0.0045~0.11 (0.0008~0.008)		
88	1,1-Dichloroethane	'77	0/3 — (0.0005)	0/3 — (0.008)		
		'79				* 0/24 — (0.2~10) ppb
89	1,2-Dichloroethane	'76	0/60 — (0.04~0.2)	0/48 — (1.0~24)	0/16 — (0.7)	
		'79				* 0/16 0.06~10 ppb (0.008~10)
90	trans-1,2-Dichloroethylene	'77	0/3 — (0.0008)	0/3 — (0.009)		
91	cis-1,2-Dichloroethylene	'77	0/3 — (0.0006)	0/3 — (0.008)		
92	1,1-Dichloroethylene	'79	0/21 — (0.0000028~0.0008)	0/21 — (0.0008~0.002)		
93	3,3'-Dichloro-4,4'-diaminodiphenylmethane	'79	0/80 — (0.0002~0.02)	0/80 — (0.001~0.6)		
94	2,2'-Dichlorodiethylether	'77	0/4 — (0.002~0.005)	0/4 — (1.5~24)		
95	p,p'-Dichlorodiphenylethane (pp'DDE)	'74	0/55 — (0.00000088~0.0001)	22/58 0.0001~0.0078 (0.01)	48/48 0.0008~0.181 (0.0002~0.005)	
96	p,p'-Dichlorodiphenyltrichloroethane (pp'DDT)	'74	0/55 — (0.00000088~0.0001)	20/58 0.0008~0.0078 (0.01)	1/48 0.0009~0.0018 (0.002~0.0005)	
97	p,p'-Dichlorodiphenyldichloroethane (pp'DDD)	'74	0/55 — (0.00000087~0.0001)	20/55 0.0018~0.0158 (0.01)	21/48 0.0008~0.0015 (0.0008~0.005)	
98	o,p'-Dichlorodiphenyltrichloroethane (op'DDT)	'74	0/55 — (0.00000087~0.0001)	0/50 — (0.0008~0.01)	0/49 0.0014~0.0021 (0.0008~0.005)	
99	Dichlorodiphlorosethane (Flon 12)	'76				* 41/115 0.1~28 ppb (0.25~1)
		'77				* 28/87 0.048~0.78 ppb (0.018~2)
100	2,3-Dichlorophenol	'78	0/24 — (0.0002~0.04)	0/24 — (0.005~4)		
101	2,4-Dichlorophenol	'78	0/24 — (0.0002~0.04)	0/24 — (0.005~4)		
102	2,5-Dichlorophenol	'78	0/24 — (0.0002~0.04)	0/24 — (0.005~4)		
103	2,6-Dichlorophenol	'78	0/24 — (0.0002~0.04)	0/24 — (0.005~4)		
104	3,4-Dichlorophenol	'78	0/24 — (0.001~0.04)	0/24 — (0.02~4)		
105	3,5-Dichlorophenol	'78	0/24 — (0.001~0.04)	0/24 — (0.02~4)		
106	1,2-Dichloropropane	'76	0/60 — (0.04~0.2)	0/40 — (1.0~24)		
107	o-Dichlorobenzene	'75	0/95 — (0.0008~0.008)	0/95 — (0.02~0.5)	0/75 — (0.02~0.5)	** 0/24 — (0.2~1)
108	m-Dichlorobenzene	'75	0/95 — (0.0001~0.002)	0/95 0.01~0.05 (0.01~0.5)	0/75 — (0.02~0.5)	** 0/24 — (0.1~1)
109	p-Dichlorobenzene	'75	0/95 0.0005~0.001 (0.0002~0.002)	1/95 0.08 (0.02~0.5)	0/75 — (0.02~0.5)	** 0/24 — (0.2~1)
110	3,3'-Dichlorobenzidine	'79	0/21 — (0.0000~0.007)	0/21 — (0.0008~0.2)		
111	Dichloropentadiene	'78	0/12 — (0.0000016~0.0002)	0/12 0.000087~0.00098 (0.0000043~0.0008)		
112	2,4-Dinitrotoluene	'76	0/10 — (0.000008~0.0001)	0/50 — (0.00005~0.01)	0/16 — (0.008)	
113	2,6-Dinitrotoluene	'76	1/10 0.000054 (0.0000025~0.00008)	4/55 0.002~0.0050 (0.0007~0.01)	0/16 — (0.008)	

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			Water quality	Sediment	Fishes	Others
			B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
114	3,4-Dinitrotoluene	'76	0/18 — (0.00005~0.00007)	0/59 — (0.002~0.01)	0/16 — (0.004)	
115	o-Dinitrobenzene	'76	0/18 — (0.0005)	1/54 0.0008 (0.0002~0.01)	0/16 — (0.004)	
116	m-Dinitrobenzene	'76	0/18 — (0.0001~0.0002)	1/54 0.08 (0.007~0.02)	0/16 — (0.01)	
117	Diphenylamine	'76	0/88 — (0.0004~0.005)	0/28 — (0.02~0.74)	0/28 — (0.15~0.2)	
118	Diphenylguanidine	'78	0/42 — (0.002~0.05)	0/42 — (0.1~0.5)		
119	Dibutyldiglycol adipate	'78	0/80 — (0.0002~0.02)	0/88 — (0.04~2)		
120	Dibutylhydroxytoluene (BHT)	'76	0/48 — (0.0004~0.005)	16/48 0.006~1.8 (0.01~0.04)		
		'77	0/117 — (0.0001~0.002)	17/117 0.008~0.22 (0.002~0.04)	7/85 0.006~0.068 (0.004~0.12)	
121	1,2-Dibromoethane	'76	0/60 — (0.0002~0.07)	0/40 — (0.005~0.1)	0/28 — (0.09)	
122	Dibromocresylglycidylether	'77	0/15 — (0.00005~0.0002)	0/15 — (0.004~0.2)		
123	Dibenzyltoluene	'77	0/15 — (0.1~0.4)	0/15 — (0)~4)		
124	2,2'-Dibenzothiazyldisulfide	'77	0/12 — (0.005)	0/12 — (0.05~0.1)		
125	2,4-Dimethylaniline	'77	0/6 — (0.01~0.02)	0/6 — (0.2~1)		
126	3,4-Dimethylaniline	'77	0/6 — (0.01~0.02)	0/6 — (0.2~4)		
127	N,N-Dimethylaniline	'76	0/48 0.0011~0.0017 (0.0002~0.0024)	0/48 0.011~0.21 (0.004~0.05)		
128	Dimethylformamide	'78	0/24 — (0.1~0.2)	0/24 — (0.1~0.8)		
129	4,4'-Dimetoxydiphenylamine	'77	0/6 — (0.02~0.05)	0/6 — (1)		
130	Methyl bromide	'76	0/60 — (0.001~0.01)	0/60 — (0.02~0.2)	0/20 — (0.01~0.2)	
131	Ethyl bromide	'76	0/60 — (0.1~0.4)	0/40 — (1.5~2)	0/20 — (0.1~1)	
132	Triphenyl hydride	'77	0/15 — (0.1~0.2)	0/15 — (0.5~1)		
133	Styrene	'77	0/8 — (0.02)	0/8 — (0.04)		
134	o-Terphenyl	'76	0/68 — (0.0002~0.02)	15/68 0.0007~0.08 (0.0001~0.2)	0/1 — (0.1)	
		'77	0/117 — (0.0002~0.02)	18/117 0.001~0.1 (0.0001~0.1)	0/98 — (0.0006~0.1)	
135	m-Terphenyl	'76	0/68 — (0.0001~0.1)	21/68 0.001~0.2 (0.001~1)	0/1 — (0.1)	
		'77	0/117 — (0.0001~0.01)	18/117 0.001~0.1 (0.0001~1)	1/98 0.0024 (0.001~1)	
136	p-Terphenyl	'76	0/68 — (0.0002~0.1)	21/68 0.001~0.2 (0.001~1)	0/1 — (0.1)	
		'77	0/117 — (0.0001~0.01)	1/117 0.0004~0.1 (0.001~1)	0/98 — (0.0006~1)	
137	Thioures	'77	0/6 — (0.01~0.1)	0/6 — (0.1~1)		
138	Dieldrin	'74	0/60 — (0.001)	0/60 — (0.01)	0/68 — (0.005)	
139	Decanol	'79	0/27 — (0.02~0.05)	0/27 — (0.1~1)		
140	Decabromodiphenylether	'77	0/15 — (0.0002~0.0005)	0/15 — (0.05~0.07)		

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			B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
141	Tetrachloroethylene	'74	3/60 0008 (00002~0002)			** 0/18 — (00003~0002)
		'75	78/895 000016~00093 (000006~00002)			** 3/114 00002~00002 (000006~00002)
		'79				* 22/45 002~15 ppb (0004~013)
142	Tetrachloroisophthalonitrile	'77	0/8 — (001)	0/8 — (01)		
143	1,1,2,2-Tetrachloroethane	'76	0/60 — (0001~005)	0/40 — (005~19)	0/10 — (02)	
144	1,2,3,4-Tetrachlorobenzene	'75	0/100 — (000005)	0/100 — (001)	0/95 — (005)	** 0/18 — (005)
145	1,2,3,5-Tetrachlorobenzene	'75	0/100 — (000005)	0/100 — (001)	0/95 — (005)	** 0/18 — (005)
146	1,2,4,5-Tetrachlorobenzene	'75	0/100 — (000005)	0/100 — (005)	0/95 — (005)	** 0/18 — (005)
147	2,3,4,6-Tetrachlorophenol	'78	0/21 — (000004~00008)	0/21 — (0002~002)		
148	Tetrahydrothiophen-1,1-dioxide	'76	0/60 — (000018~0001)	0/55 — (0007~0200)	0/1 — (002)	
149	Tetrahydronaphthalene	'77	0/8 — (00001~0001)	0/6 — (0004~01)		
150	Tetrahydrofuran	'79	0/28 — (00002~0026)	0/28 — (00001~0022)		
151	Tetrabromobisphenol A	'77	0/15 — (000002~000004)	0/15 — (00018~0007)		
152	1,1,2,2-Tetrabromoethane	'76	0/60 — (00002~00005)	0/40 — (0001~001)	0/20 — (0001~00005)	
153	Terephthalic acid	'75	4/100 00002~00007 (000002~0005)			
154	Dimethyl terephthalate	'75	1/100 000016 (0000002~00005)			
155	Telodrin	'74	0/45 — (00001)	0/40 — (001)	0/40 — (0004)	
156	Dodecachlorododecahydrodimetanodibenzocyclooctene	'76	4/60 00004~00006 (00002~00003)	0/58 — (001~002)	0/2 — (0018)	
157	Triethanolamine	'78	0/12 — (00008~00018)			
158	Triethylbiphenyl	'76	0/68 — (00003~004)	0/50 — (03~10)	0/20 — (010~20)	
159	Trioctyl phosphate	'75	0/100 — (000004~000050)	8/100 002~0100 (0002~010)	0/94 — (001~010)	
160	Tricresyl phosphate	'75	0/100 — (000005~00015)	1/100 015 (001~025)	0/94 — (002~025)	
		'76	0/114 — (0000005~00025)	8/114 104~216 (000025~04)	0/93 — (000025~015)	
161	1,1,1-Trichloroethane	'74	0/60 — (00001~0002)			** 0/18 — (00001~0002)
		'75	48/895 00004~00054 (0000005~00004)			** 0/114 — (000005~00004)
		'79				* 26/48 002~071 ppb (0002~018)
162	1,1,2-Trichloroethane	'76	0/60 — (0004~005)	0/40 — (02~10)	0/10 — (04)	
163	Trichloroethylene	'74	1/60 0005 (0001)			** 0/18 — (00002~0002)
		'75	75/895 000028~0012 (00002~0001)			** 0/114 00002~0001 (00001~00001)
		'79				* 21/48 0018~58 ppb (0002~012)
164	2,4,6-Trichlorophenyl-4'-nitrophenylether	'78	0/18 — (0000004~000008)	0/18 — (00002~0002)		

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165	2,4,5-Trichlorophenol	'78	0/21 – (0.00002~0.00008)	0/21 – (0.001~0.008)		
166	2,4,6-Trichlorophenol	'78	0/21 – (0.0000008~0.0001)	1/21 0.0008 (0.0005~0.01)		
167	1,2,3-Trichloropropane	'76	0/19 – (0.1~0.2)	0/44 – (0.2~1)	0/15 – (1)	
168	1,2,3-Trichlorobenzene	'75	0/95 – (0.00004~0.0003)	0/95 – (0.002~0.1)	0/15 – (0.005~0.1)	** 0/24 – (0.000005~0.0002)
		'79	2/111 0.00005~0.00067 (0.000001~0.00004)	16/111 0.0004~0.058 (0.00001~0.1)	0/28 – (0.0001~0.1)	
169	1,2,4-Trichlorobenzene	'75	0/95 – (0.00004~0.0004)	0/95 0.002~0.02 (0.002~0.1)	2/15 0.1~0.2 (0.005~0.1)	** 0/24 – (0.000005~0.0004)
		'79	8/111 0.00001~0.0001.2 (0.000001~0.0004)	22/111 0.0005~0.008 (0.0001~0.1)	1/28 0.0005~0.008 (0.0001~0.1)	
170	1,3,5-Trichlorobenzene	'75	0/95 – (0.00002~0.0002)	0/95 – (0.001~0.1)	0/15 – (0.002~0.1)	** 0/24 – (0.000003~0.0002)
		'79	1/111 0.00002 (0.000001~0.0004)	14/111 0.0004~0.0247 (0.0001~0.1)	1/28 0.012 (0.0001~0.1)	
171	Trichloromethane (Chloroform)	'74	21/26 0.0014~0.0276 (0.001)			** 6/15 0.021~0.118 (0.0002)
		'75	84/259 0.00009~0.017 (0.00005~0.001)			** 25/114 0.0001~0.048 (0.00005~0.001)
		'79				* 21/44 0.028~0.50 ppb (0.02~1)
172	Trichloromonophloromethane (Flon 11)	'76				* 80/115 0.002~0.45 ppb (0.002)
		'77				* 71/97 0.02~0.9 ppb (0.01~1)
173	o-Tolidine	'77	0/6 – (0.0002)	0/6 – (0.002)		
174	Tris(isopropylphenyl) phosphate	'78	0/24 – (0.00005~0.002)	2/24 61 (0.01~0.1)		
175	Tris(chloroethyl) phosphate	'75	8/48 0.0001~0.00004 (0.00001~0.0001)	1/20 0.070 (0.02)	0/20 – (0.02)	
		'78	0/114 – (0.00001~0.001)	0/114 – (0.001~0.05)	2/28 0.005~0.14 (0.001~0.05)	
176	Tris(dichloropropyl) phosphate	'75	0/100 – (0.00002~0.0002)	0/100 – (0.002~0.05)	1/84 0.018~0.028 (0.002~0.05)	
		'78	0/114 – (0.0001~0.0005)	0/114 – (0.001~0.02)	0/28 – (0.001~0.02)	
177	Tris(dibromopropyl) phosphate	'75	0/20 – (0.02)	0/20 – (0.4~1.6)	0/20 – (1)	
178	Tris(butoxyethyl) phosphate	'75	0/100 – (0.00002~0.0002)	1/88 0.02~0.54 (0.002~0.1)	0/14 – (0.002~0.1)	
		'78	0/114 – (0.0001~0.001)	0/114 – (0.002~0.1)	0/28 – (0.0005~0.1)	
179	1,3,5-Tris(2'-hydroxyethyl)-isocyanuric acid	'79	0/18 – (0.005~0.01)	0/18 – (0.002~0.07)		
180	Tridecyl alcohol	'77	0/4 – (0.1)	0/4 – (1)		
181	Triphenyl phosphate	'75	0/100 – (0.00002~0.0002)	0/100 – (0.002~0.05)	0/100 – (0.002~0.05)	
182	Tributyl phosphate	'75	16/100 0.0002~0.00071 (0.00001~0.0001)	84/100 0.001~0.05 (0.001~0.025)	51/84 0.002~0.028 (0.002~0.025)	
		'77	84/117 0.000006~0.00058 (0.000004~0.0005)	48/117 0.0019~0.24 (0.001~0.1)	27/85 0.0011~0.0008 (0.002~0.1)	
183	2,4,6-Tribromophenyl(2-methyl-2,3-dibromopropyl)ether	'79	0/21 – (0.0001~0.0005)	0/21 – (0.02~0.05)		
184	Tribromomethane	'76	0/40 – (0.0002~0.02)	0/40 – (0.001~0.05)	0/20 – (0.001~0.005)	
185	1,2,3-Trimethylbenzene	'76	0/20 – (0.001)	0/20 – (0.01)		

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186	1,2,4-Trimethylbenzene	'76	8/20 — (0.0001)	8/20 — (0.01)		
187	1,3,5-Trimethylbenzene	'76	8/20 — (0.0001)	8/20 — (0.01)		
188	o-Toluidine	'76	5/48 0.00014~0.0020 (0.0001~0.0004)	21/48 0.002~0.013 (0.002~0.01)		
189	m-Toluidine	'76	4/48 0.0000094~0.000024 (0.000008~0.00002)	21/48 0.002~0.056 (0.001~0.004)		
190	p-Toluidine	'76	11/48 0.000002~0.00018 (0.000002~0.00002)	25/48 0.0007~0.020 (0.0004~0.0006)		
191	2,3-Toluidinediamine	'78	0/24 — (0.001~0.02)	0/24 — (0.7~11)		
192	2,4-Toluidinediamine	'78	0/24 — (0.002~0.005)	0/24 — (1.8~22)		
193	Toluene	'77	0/8 — (0.002)	0/8 — (0.004)		
194	o-Toluenesulfonamide	'77	0/4 — (0.01)	0/4 — (0.005~0.048)		
195	p-Toluenesulfonyl chloride	'77	0/4 — (0.004~0.01)	0/4 — (0.1~0.25)		
196	Naphthalene	'76	0/20 — (0.0001)	0/20 — (0.01)		
197	Sodium salt of β-naphthalene-sulfonic acid-formalin condensate	'79	0/21 — (0.01~0.1)	0/21 — (0.2~20)		
198	α-Naphthylamine	'76	0/48 — (0.0001~0.0007)	7/48 0.0007~0.0048 (0.0002~0.01)		
		'79	0/111 — (0.000014~0.0005)	8/111 0.00056~0.0055 (0.0004~0.01)	0/98 — (0.0007~0.05)	
199	1-Naphtol	'77	0/4 — (0.0004~0.0045)	0/4 — (0.04~0.29)		
200	2-Naphtol	'77	0/4 — (0.0004~0.005)	0/4 — (0.04~0.29)		
201	o-Nitroanisole	'76	8/70 0.000035~0.00069 (0.00002~0.00004)	1/58 0.010 (0.001~0.01)	0/10 — (0.002)	
202	m-Nitroanisole	'76	5/42 0.0001~0.0014 (0.00005~0.0001)	1/20 0.015 (0.002~0.004)	0/10 — (0.002)	
203	p-Nitroanisole	'76	0/10 — (0.00008~0.0002)	0/59 — (0.004~0.02)	1/10 0.018 (0.004)	
204	Sodium 4-nitrochlorobenzenesulfonate	'79	0/80 — (0.002~0.02)	0/80 — (0.05~0.4)		
205	4-Nitrosodiphenylamine	'77	0/4 — (0.001~0.005)	0/4 — (0.25~1)		
206	o-Nitrotoluene	'76	8/70 0.00015~0.00079 (0.00002~0.0002)	16/59 0.0004~0.014 (0.0002~0.002)	0/10 — (0.002)	
207	m-Nitrotoluene	'76	8/70 0.00085~0.00086 (0.00005~0.0002)	21/59 0.014~0.019 (0.0004~0.01)	0/10 — (0.004)	
208	p-Nitrotoluene	'76	1/70 0.0001 (0.00004~0.0004)	8/59 0.011~0.028 (0.002~0.01)	0/10 — (0.002)	
209	o-Nitroaniline	'78	0/24 — (0.0002~0.0005)	0/15 — (0.007~0.167)		
210	m-Nitroaniline	'78	0/24 — (0.0002~0.001)	0/15 — (0.01~0.238)		
211	p-Nitroaniline	'78	0/24 — (0.0007~0.001)	0/15 — (0.02~0.238)		
212	o-Nitrophenol	'78	0/80 — (0.0004~0.01)	0/80 — (0.02~0.5)		
		'79	0/111 — (0.0001~0.0005)	0/111 — (0.01~0.76)	0/98 — (0.01~0.5)	
213	m-Nitrophenol	'78	0/80 — (0.000008~0.01)	0/80 — (0.0004~0.5)		
		'79	0/111 — (0.000004~0.0005)	0/111 — (0.002~0.2)	0/98 — (0.01~0.2)	

[B/A: Polluted cases/samples,
Unit: ppm except the case of atmos. (ppb)]

No.	Substance	Year	Example of detection and range of detection			
			Water quality	Sediment	Fishes	Others
			B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
214	p-Nitrophenol	'78	1/80 0.001 (0.0004~0.01)	0/80 — (0.02~0.5)		
		'79	0/111 — (0.0004~0.005)	0/111 — (0.002~0.1)	0/80 — (0.01~0.2)	
215	1-Nitropropane	'79	0/18 — (0.01~0.2)	0/18 — (0.1~1.0)		
216	2-Nitropropane	'79	0/18 — (0.1~0.2)	0/18 — (0.1~1.0)		
217	Methyl dichloride	'79				★ 21/48 0.1~1.5 ppb (0.004~1.0)
218	Nitrobenzene	'76	21/76 0.001~0.014 (0.0002~0.0004)	15/67 0.001~1.8 (0.002~0.035)	10/10 0.03~0.6 —	
		'77	22/115 0.0018~0.0088 (0.001~0.02)	19/117 0.003~1.5 (0.01~1)	3/35 0.03~0.005 (0.001~0.2)	
219	Sodium m-nitrobenzenesulfonate	'77	0/4 — (0.004~0.01)	0/4 — (0.1~0.78)		
220	Carbon bisulfide	'77	0/6 — (0.0000004~0.0001)	0/6 — (0.0015~0.01)		
221	Neopentylglycol	'77	0/4 — (0.2~0.4)	0/4 — (?)		
222	Nonanol	'79	0/17 — (0.003~0.005)	0/17 — (0.2~1)		
223	Nonylphenol	'76	0/6 — (0.005)	0/6 — (0.25)		
		'77	0/8 — (0.0004)	4/8 0.05~0.07 —		
224	1,1-Bis(p-chlorophenyl)-2,2,2-trichloroethanol	'78	0/24 — (0.0002~0.0003)	0/24 — (0.008~0.011)		
225	2,2-Bis(4-hydroxyphenyl)propane (bisphenol A)	'76	0/50 — (0.00005~0.0001)	0/50 — (0.0002~0.005)	0/10 (0.005) —	
226	Biphenyl	'76	0/48 — (0.0002~0.01)	0/50 — (0.05~1.0)	0/25 — (0.04~0.25)	
227	Biphenylether	'76	0/48 — (0.0004~0.005)	0/25 — (0.1~0.74)	0/25 — (0.15~0.25)	
228	Phenanthrene	'77	0/8 — (0.0002~0.005)	8/8 0.009~2.8 —		
229	1-Phenyl-1-(3,4-dimethylphenyl)ethane	'75	0/100 — (0.0001~0.005)	18/100 0.025~0.8 (0.05~0.25)	0/84 — (0.05~0.25)	
		'77	0/117 — (0.0002~0.005)	12/117 0.002~0.008 (0.001~0.05)	1/88 0.0005~0.8 (0.0005~0.05)	
230	N-Phenyl-2-naphthylamine	'76	0/10 — (0.002~0.04)	0/40 — (0.1~0.5)	0/10 — (0.5~1.0)	
231	o-Phenylphenol	'76	0/80 — (0.00002~0.0125)	0/80 — (0.02~0.08)		
232	m-Phenylphenol	'76	0/80 — (0.00002~0.02)	0/80 — (0.05~2.5)		
233	p-Phenylphenol	'76	0/80 — (0.00002~0.02)	0/80 — (0.05~2.5)		
234	o-Phenylenediamine	'79	0/24 — (0.0005~0.02)	0/24 — (1.0~5.0)		
235	m-Phenylenediamine	'79	0/24 — (0.0005~0.02)	0/24 — (1.0~5.0)		
236	p-Phenylenediamine	'79	0/24 — (0.0005~0.02)	0/24 — (1.0~5.0)		
237	p-Phenetidine	'77	0/6 — (0.001~0.005)	0/6 — (0.5~1)		
238	Phenol	'77	0/8 — (0.0002~0.01)	4/8 0.08~0.04 (0.01~0.1)		
239	Butadiene	'77	0/6 — (0.0001~0.005)	0/6 — (0.0005~0.005)		
240	n-Butanol	'79	0/80 — (0.1~1.0)	0/80 — (1.0~100)		

*: Atmosphere

[B/A: Polluted cases/samples,
Unit: ppm except the case of atmos. (ppb)]

No.	Substance	Year	Example of detection and range of detection			
			Water quality	Sediment	Fishes	Others
			B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
241	sec-Butanol	'79	0/88 — (81~10)	0/36 — (10~100)		
242	tert-Butanol	'79	0/88 — (81~10)	0/88 — (10~100)		
243	Total phthalic acid ester	'75	54/118 0.0068~0.077 (0.005~0.010)			
244	Diethylhexyl phthalate	'74	174/875 0.00008~0.018 (0.00001~0.002)	224/370 0.0008~0.017 (0.0003~0.002)	56/852 0.01~10 (0.02~1.0)	** 69/111 0.0006~0.018 (0.0006~0.002) *** 1/4 88 (0.06)
		'75	58/115 0.0002~0.011 (0.0001~0.002)			
245	Di-n-octyl phthalate	'74	4/855 0.001~0.041 (0.0005~0.050)	1/881 0.72~44 (0.05~5)	0/252 — (0.005~25)	** 1/105 0.12 (0.005~0.050) *** 0/4 (0.01~10)
246	Di-i-decyl phthalate	'74	0/250 — (0.0005~0.010)	0/227 — (0.0005~0.14)	0/252 — (0.005~1.00)	** 0/98 — (0.0005~0.010) *** 0/4 — (0.01)
247	Di-n-butyl phthalate	'74	208/875 0.0005~0.058 (0.0003~0.004)	154/370 0.001~28 (0.001~0.28)	111/252 0.18~1.95 (0.01~0.87)	** 68/111 0.0018~0.052 (0.0001~0.004) *** 0/4 — (0.1~5)
		'75	75/115 0.0018~0.021 (0.0001~0.003)			
248	Di-i-butyl phthalate	'74	88/875 0.0014~0.0012? (0.0001~0.001)	57/850 0.0078~0.78 (0.003~0.1)	22/252 0.15~0.47 (0.003~0.2)	** 11/111 0.0015~0.0044 (0.0005~0.001) *** 0/4 — (0.1~5)
249	Di-i-heptyl phthalate	'74	28/875 0.0012~0.011 (0.0005~0.010)	80/850 0.008~0.48 (0.003~1)	13/252 0.14~0.36 (0.005~0.50)	** 22/111 0.0018~0.0085 (0.0003~0.010) *** 0/4 — (0.1~10)
250	o-Phthalonitrile	'77	0/4 — (0.001~0.005)	0/4 — (0.1~1)		
251	p-tert-Butylphenol	'76	0/48 — (0.002~0.005)	0/48 — (0.1~0.5)		
252	2-Butoxyethanol	'76	0/60 — (0.03~0.1)	0/20 — (0.4)		
253	Propylene	'77	2/4 0.0001 (0.00005~0.0005)	0/4 — (0.0002~0.001)		
254	Propylene glycol	'77	0/4 — (0.2~0.4)	0/4 — (2~3)		
255	Bromochloroethane	'76	0/60 — (0.0002~0.001)	0/40 — (0.005~0.05)	0/20 — (0.005~0.01)	
256	Hexachloroethane	'76	0/60 — (0.0001~0.005)	0/40 — (0.01~0.3)	0/10 — (0.3)	
257	β-Hexachlorocyclohexane	'74	4/60 0.0001 (0.0001)	5/60 0.01 (0.01)	18/60 0.005~0.015 (0.005)	
258	γ-Hexachlorocyclohexane	'74	0/60 — (0.0001)	4/60 0.03~0.05 (0.01)	2/60 0.005~0.007 (0.005)	
259	δ-Hexachlorocyclohexane	'74	0/60 — (0.0001)	3/60 0.01 (0.01)	2/60 0.007~0.013 (0.005)	
260	ε-Hexachlorocyclohexane	'74	0/60 — (0.0001)	4/60 0.01 (0.01)	0/60 — (0.005)	
261	Hexachlorobenzene	'74	0/60 — (0.0001)	0/60 — (0.01)	4/60 0.005~0.007 (0.005)	
		'75	0/880 — (0.0000001~0.00001)	37/869 0.0002~0.12 (0.0001~0.0005)	110/369 0.0001~0.028 (0.0001~0.0005)	
		'78	8/77 0.00000016~0.00000045 (0.00000016)	63/76 0.00011~0.140 (0.00011)	73/75 0.0002~0.0126 (0.00016)	

**: Rain water
***: Plankton

[B/A: Polluted cases/samples,
Unit: ppm except the case of atmos. (ppb)]

No.	Substance	Year	Example of detection and range of detection			
			Water quality	Sediment	Fishes	Others
			B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
242	Hexabromobenzene	'77	9/15 – (0.00004~0.0004)	2/15 – (0.1~0.1)		
243	Heptanol	'79	0/27 – (0.005~0.05)	0/27 – (0.5~1)		
244	Benzene	'77	0/8 – (0.02)	0/8 – (0.04)		
245	Benzenenitrile	'77	0/4 – (0.001~0.005)	0/4 – (0.1~1)		
246	Pentachlorophenol	'74	2/55 0.002 (0.001)	10/58 0.01~0.04 (0.1~0.5)		
247	Pentachlorobenzene	'75	0/189 – (0.0005)	0/106 – (0.1)	2/96 0.15~0.025 (0.1)	** 0/20 – (0.0001)
		'79	0/111 – (0.0000005~0.00004)	20/111 0.0001~0.0113 (0.0001~0.01)	2/28 0.001~0.002 (0.0001~0.01)	
248	Benzidine	'77	0/4 – (0.0000115)	0/4 – (0.005)		
249	Polychloroterphenyl	'74	0/60 – (0.0001~0.001)	0/60 – (0.005)	2/11 0.05~0.1 (0.05~0.2)	
		'76	0/166 – (0.0001~0.001)	21/151 0.001~0.08 (0.01~0.2)	0/89 – (0.01~0.2)	
		'78	0/72 – (0.0000025~0.00025)	37/76 0.001~0.7 (0.01~1.0)	8/68 0.0002~0.0003 (0.0002~0.1)	
250	Polychloronaphthalene (PCN)	'76	0/148 0.00016~0.00045 (0.00002~0.0002)	28/108 0.003~0.07 (0.002~0.2)	1/89 0.05 (0.02~0.05)	
		'78	2/75 0.0000085~0.00004 (0.000001~0.001)	15/75 0.02~1.0 (0.02~0.05)	2/46 0.002~0.180 (0.002~0.025)	
251	Polyoxyethylenealkylphenylether	'77	2/18 0.18~0.26 (0.1)	2/15 1.2~2.6 (1.0)		
		'78	25/105 0.15~0.9 (0.1)	69/88 2.1~4.5 (2)		
252	Formaldehyde	'75	0/102 – (0.1~0.5)			
253	Methyl methacrylate	'79	0/24 – (0.000005~0.001)	0/24 – (0.0001~0.01)		
254	Ethyl methacrylate	'79	0/24 – (0.0000005~0.001)	0/24 – (0.0001~0.01)		
255	Butyl methacrylate	'79	0/24 – (0.0000005~0.001)	0/24 – (0.0001~0.01)		
256	N-Methylaniline	'76	0/48 – (0.0005~0.0005)	11/48 0.002~0.012 (0.002~0.002)		
257	Methylethyl ketone oxime	'78	0/21 – (0.01~0.02)	0/18 – (0.1~0.7)		
258	α-Methylstyrene	'77	0/8 – (0.004)	0/8 – (0.01)		
259	o-Methylstyrene	'77	0/8 – (0.004)	0/8 – (0.01)		
260	m-Methylstyrene	'77	0/8 – (0.004)	0/8 – (0.01)		
261	p-Methylstyrene	'77	0/8 – (0.004)	0/8 – (0.01)		
262	2-Methylnaphthalene	'76	0/28 – (0.0002~0.001)	0/28 – (0.02~0.1)		
263	1-Methylnaphthalene	'76	0/28 – (0.0002~0.001)	0/28 – (0.02~0.1)		
264	2-Methoxyethanol	'76	0/60 – (0.02~0.1)	0/20 – (0.4)		
265	Mercaptobenzimidazole	'78	0/46 – (0.00025~0.005)	0/88 – (0.01?~0.5)		
266	2-Mercaptobenzothiazole	'77	2/18 0.0005(1)~0.005(1) (0.0005?)	2/18 0.002?~0.05? (0.0005?~0.02)		
		'78	0/117 – (0.00001~0.01)	2/111 0.045~0.05? (0.002?~1.2)	0/90 – (0.02?~1)	

**: Rain water

[B/A: Polluted cases/samples,
Unit: ppm except the case of atmos. (ppb)]

No.	Substance	Year	Example of detection and range of detection			
			Water quality	Sediment	Fishes	Others
##7	2-(Morpholinothio)benzothiazole	'77	B/A Range of detection (Limit of detection) 0/12 — (0.0005~0.0004)	B/A Range of detection (Limit of detection) 0/12 — (0.01~0.1)	B/A Range of detection (Limit of detection)	B/A Range of detection (Limit of detection)
##8	Mono-(α-methylbenzyl)phenol	'78	0/45 — (0.0005~0.1)	0/45 — (0.01~1)		
##9	Morpholine	'79	0/88 — (0.01~0.5)	0/88 — (0.1~0.5)		
##0	Organic silicon compound	'79	0/120 — (0.1)	21/120 21~182 (10)		
##1	Organic tin compound	'75	0/80 — (0.1~0.5)			

ANNEX IV. A Summary of the Results of Wildlife Monitoring Surveys in 1979 (Average values in ppm)

	Oncorhynchus keta (Coast of Hokkaido)	Sebastes iracundus (Sea of Okhotsk)	Cololabis saira (Pacific Ocean)	Lateolabrax japonica (Yamada Bay)	Lateolabrax japonica (Tokyo Bay)	Lateolabrax japonica (Inland Sea of Seto)	Seriola quinqueradiata (Coast of San-in)	Leuciscus hakonensis (Lake Biwa)	Mytilus edulis (Miura Peninsula)	Mytilus edulis (Yamada Bay)	Mytilus coruscus (Naruto)	Spodiopsar cineracea (Outskirts of Kofuka City)
Organochlorine compounds												
1 PCB	nd	0.03	0.01	0.05	0.42	0.68	0.22	0.08	0.07	0.02	0.03 (0.04)	0.02
2 PCN	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd (nd)	nd
3 HCB	0.003	–	0.003	–	0.002	0.001	0.007	0.002	nd	nd	nd (nd)	–
4 α-BHC	–	nd	0.003	0.002	0.002	0.002	0.021	0.003	nd	nd nd	0.036 (0.09)	0.003
5 β-BHC	–	nd	nd	nd	nd	nd	0.017	0.030	nd	na	0.005 (nd)	0.009
6 γ-BHC	–	nd	–	nd	nd	nd	0.006	0.001	nd	nd	0.003 (0.009)	nd
7 δ-BHC	nd	nd	nd	nd	nd	nd	–	nd	nd	nd	nd (nd)	–
8 Aldrin	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd (nd)	nd
9 Dieldrin	0.001	nd	nd	0.001	0.012	0.005	0.003	0.004	0.005	nd	0.043 (0.076)	0.002
10 Endrin	nd	nd	nd	nd	nd	–	nd	–	–	nd	0.024 (0.12)	nd
11 OP-DDT	nd	–	0.001	–	nd	nd	0.029	nd	nd	nd	nd (nd)	nd
12 PP'DDT	–	0.017	0.002	0.004	0.002	0.028	0.151	nd	0.005	0.002	0.007 (0.016)	nd
13 OP'DDE	–	nd	nd	nd	0.003	nd	nd	nd	–	nd	nd (nd)	nd
14 PP'DDE	0.001	0.009	0.003	0.006	0.022	0.037	0.109	0.030	0.004	0.001	0.006 (0.020)	0.235
15 OP'DDD	nd	nd	nd	nd	–	nd	nd	nd	–	nd	nd (nd)	0.004
16 PP'DDD	–	0.002	0.001	0.003	0.007	0.008	0.025	0.012	0.002	0.001	0.001 (nd)	nd
(Heavy metals)												
17 Selenium	0.31	1.11	0.29	0.37	0.22	0.25	0.45	0.24	0.52	0.25	0.40 (0.39)	0.48
18 Arsenic	0.3	2.4	1.3	1.7	1.2	2.7	1.6	–	1.6	1.7	2.3 (3.7)	nd
19 Lead	nd	nd	nd	nd	nd	nd	na	nd	0.28	0.11	0.24 (0.13)	0.30
20 Cadmium	nd	nd	nd	nd	nd	nd	nd	nd	0.16	0.22	0.27 (0.63)	6.39
21 Nickel	nd	nd	nd	nd	nd	nd	nd	nd	0.52	0.06	0.17 (0.20)	nd
22 Zinc	3.20	3.43	7.96	4.54	4.70	5.12	4.39	7.13	41.5	18.5	24.7 (13.4)	8.91
23 Mercury	0.02	0.55	0.06	0.23	0.03	0.16	0.36	6.10	6.02	–	(–)	–

(Note) 1 Parenthesized values in the column of Mytilus coruscus were obtained in 1953.
2 nd: The substance could not be detected, because its concentration was below the detection limit;
–: The average value could not be calculated, because test result was nd in one or more samples.

ANNEX V. Appearance Patterns of Detected Chemical Substances (in 1978 and 1979)

Substance \ Species	Fishes																Shellfishes						Birds	
	Oncorhynchus keta (Cost of Hokkaido)		Sebastes iracundus (Sea of Okhotsk)		Cololabis saira (Pacific Ocean)		Lateolabrax japonica (Yamada Bay)		Lateolabrax japonica (Tokyo Bay)		Lateolabrax japonica (Inland Sea of Seto)		Seriola quinqueradiata (Coast of San-in)		Leuciscus hakonensis (Lake Biwa)		Mytilus edulis (Miura Peninsula)		Mytilus edulis (Yamada Bay)		Mytilus coruscus (Naruto)		Spodiopsar cineracea (Outskirts of Morioka City)	
	1978	1979	1978	1979	1978	1979	1978	1979	1978	1979	1978	1979	1978	1979	1978	1979	1978	1979	1978	1979	1978	1979	1978	1979
(Organochlorine compounds)																								
1. PCB	–	–	○	○	○	○	○	○	○	○		○	○	○		○	○	○	○	○	○	○	○	○
2. PCN		–		–		–		–		–		–		–		–		–		–		–		–
3. HCB	○	○	○	○	○	○	○	○	○	○		○	○	○		○	–	–	–	–	–	–	–	○
4. α-BHC	○	○	○	–	○	○	○	○	○	○		○	○	○		○	○	–	○	○	○	○	○	○
5. β-BHC	○	○	–	–	○	–	○	–	–	–		–	○	○		○	○	–	–	–	–	○	○	○
6. γ-BHC	○	△	–	–	○	△	○	–	–	–		–	○	○		○	○	–	–	–	○	○	○	△
7. δ-BHC	–	–	–	–	–	–	–	–	–	–		–	△	△		–	–	–	–	–	–	–	△	○
8. Aldrin	–	–	–	–	–	–	–	–	–	–		–	–	–		–	–	–	–	–	–	–	△	–
9. Dieldrin	○	○	–	–	○	–	○	○	○	○		○	○	○		○	–	○	○	–	○	○	–	○
10. Endrin	–	–	–	–	–	–	–	–	–	–		△	–	△		○	–	△	–	–	○	○	–	–
11. o,p'-DDT	○	△	○	△	○	○	–	△	–	–		–	○	○		–	△	–	–	–	–	–	△	–
12. p,p'-DDT	–	○	○	○	○	○	○	○	○	○		○	○	○		–	○	○	○	○	○	○	○	–
13. o,p'-DDE	–	–	–	–	–	–	–	–	○	○		–	–	–		–	–	–	–	–	–	△	○	–
14. p,p'-DDE	○	○	○	○	○	○	○	○	○	○		○	○	○		○	○	○	○	○	○	○	○	○
15. o,p'-DDD	–	–	–	–	–	–	–	–	–	–		–	○	–		–	–	–	–	–	–	–	–	○
16. p,p'-DDD	–	○	–	○	○	○	○	○	○	○		○	○	○		○	○	○	○	○	–	○	○	–
(Heavy metals)																								
17. Selenium	○	○	○	○	○	○	○	○	○	○		○	○	○		○	○	○	○	○	○	○	○	○
18. Arsenic	○	○	○	○	○	○	○	○	○	○		○	○	○		△	○	○	○	○	○	○	–	–
19. Lead	–	–	–	–	–	–	–	–	–	–		–	–	–		–	○	○	○	○	○	○	○	○
20. Cadmium	–	–	○	–	○	–	–	–	–	–		–	–	–		–	○	○	○	○	○	○	○	○
21. Nickel	–	–	–	–	–	–	–	–	–	–		–	–	–		–	○	○	○	○	○	○	○	○
22. Zinc	○	○	○	○	○	○	○	○	○	○		○	○	○		○	○	○	○	○	○	○	○	○
23. Mercury	○	○	○	○	○	○	○	○	○	○		○	○	○		○	○	○	△	○	○	○	○	○

(Note) ○ : Detected in not less than half the number of samples.
△ : Detected in less than half the number of samples.
– : Detected in no sample.

The number of the samples of each species collected in each spot: 5 in fishes and shellfished, and 6 in birds.

Marilyn Bracken

U.S. Experiences in the Selection of Existing Chemicals for Testing and Control Under TSCA

I am pleased to have this opportunity to share with you some of the techniques, experiences, and policies of the United States Government in selecting existing chemicals for testing and control under the Toxic Substances Control Act (TSCA).

As many of you know, TSCA required the Environmental Protection Agency (EPA) to develop an inventory of chemical substances in the United States. This inventory lists all chemicals manufactured, processed, or imported into the United States with the exception of certain categories of chemicals (such as those used solely as drugs, pesticides, food and food additives, cosmetics and devices). These latter chemicals are addressed under other United States laws and are not under the jurisdiction of the Toxic Substances Control Act. This chemical inventory defines the universe of "existing chemicals" for consideration under TSCA. Any chemical which is not on this inventory is by definition a "new chemical" and is subject to the premanufacture notification requirement of TSCA. The TSCA Inventory currently contains approximately 55,000 chemicals.

Which such a large number of existing chemicals to consider, a scheme for selecting the chemicals on which to focus Agency efforts is clearly crucial. A chemical selection, or "priority-setting" scheme is needed for two main purposes – to identify those chemicals which may pose risks of injury to human health or the environment but which, for a lack of information, we do not know whether they do, and to identify those chemicals for which existing information indicates that they do pose such risks. The former are candidates for testing, and the latter are candidates for control. Of course, in practice, this distinction is rarely absolutely clear. Some chemicals may be candidates for testing and for control simultaneously. In some cases, a chemical may clearly pose a risk of one type (for example acute health effects) and may possibly pose a risk of another type (for example cancer); in this case the chemical could be controlled to protect against the risk of acute effects while it is tested for carcinogenic effects. In other cases, a chemical's full risk potential may be unknown but it may nonetheless warrant a limited control action – such as labelling – while the testing to determine the true risk is undertaken.

I will focus, in today's talk, on the priority setting system used to select chemicals for testing. Most of our experience is in this area, and the system we are developing to select chemicals as candidates for control is based on this testing-oriented system.

The Toxic Substances Control Act provides authority to the Environmental Protection Agency to require industry to test the chemicals they manufacture or process if the Agency can make certain findings about the chemicals. These are that (1) the chemicals may pose an unreasonable risk *or* there is substantial human or environmental exposure to the chemicals and (2) there is insufficient information to determine whether they do in fact pose an unreasonable risk, *and* (3) the testing required will develop the information necessary to make such a determination.

The TSCA established a group of scientists from a number of government agencies dealing with chemicals and their safety, the TSCA Interagency Testing Committee (ITC), to recommend to the EPA chemicals and categories of chemicals for priority consideration in the development of testing rules. The ITC may designate up to

50 chemicals or categories of chemicals as recommendations at any one time. The Committee is required to revise its priority list at least every six months. There are currently 45 chemicals or categories of chemicals on the Committee's priority list. The list is shown in Figure 1. At this time all of the Agency's efforts in developing testing rules are focussed on the ITC recommendations, although the Agency has identified additional candidates for testing.

The experience of the ITC recommending chemicals for testing is worth discussing in some detail. The ITC developed what it calls a "scoring system" for screening large numbers of chemicals to identify candidates that may warrant receiving priority for testing. The basis for this scoring system is contained in large part in TSCA which directs the ITC to consider several factors in deciding which chemicals to recommend for testing. These factors are:

- production volume of the chemical
- extent of environmental release
- extent of occupational exposure
- extent of general population exposure
- relationship to other chemicals known to have adverse health or environmental effects
- any existing data on health or environmental effects
- extent to which testing can generate data on which to reasonably determine or predict health or environmental effects
- availability of testing facilities and personnel to conduct the testing.

The Committee's (ITC's) first step was to identify a "universe" of chemicals from which to choose priorities. ITC decided to compile a "list of lists" – grouping together many previously generated lists of chemicals known as or suspected of posing risks to health or the environment. This resulted in an INITIAL LISTING of about 3650 chemicals and categories of chemicals. This list was then reviewed to eliminate chemicals not within the jurisdiction of TSCA (including chemicals used exclusively as pesticides, drugs, foods, food additives, and a few other categories). Chemicals that were not likely to be in commercial production were also excluded from the Initial Listing. These exclusions resulted in what was called a MASTER FILE of about 1700 substances (Figure 2).

These 1700 chemicals in the Master File were then put through a first order screening. They were scored for exposure-related factors (leaving aside any toxicity factors at this point). These factors were:

- annual production volume of the chemical
- extent of environmental release of the chemical
- occupational exposure (including both the number of exposed individuals and the duration of the exposure)
- general population exposure

Availability of information on which to assign scores for each of these factors was obviously key to making the system work. In addition to production volume, the most important information on a chemical was use information. Knowing what a chemical's uses are allowed an estimation of the above factors and was especially important in estimating environmental release and general population exposure. Use information was available for only approximately 700 of the 1700 chemicals on the Master File, so only these 700 were scored for the above exposure factors. By combining the scores for each of the factors the Committee ranked the 700 scored chemicals on the basis of potential exposure.

TSCA SECTION 4(E) PRIORITY LIST

ACETONITRILE
ACRYLAMIDE
ALKYL EPOXIDES
ALKYL PHTHALATES
ALKYLTIN COMPOUNDS
ANILINE AND BROMO, CHLORO AND/
OR NITRO ANILINES
ANTIMONY (METAL)
ANTIMONY SULFIDE
ANTIMONY TRIOXIDE
ARYL PHOSPHATES
BENZIDINE-BASED DYES
BENZYL BUTYL PHTHALATE
BUTYL GLYCOLYL BUTYL PHTHALATE
CHLORINATED BENZENES, MONO- AND DI-
CHLORINATED BENZENES, TRI-, TETRA-, AND PENTA-
CHLORINATED NAPHTHALENES
CHLORINATED PARAFFINS
2-CHLOROTOLUENE
CRESOLS
CYCLOHEXANONE
o-DIANISIDINE-BASED DYES
DICHLOROMETHANE
1,2-DICHLOROPROPANE
DIETHYLENETRIAMINE
FLUOROALKENES
GLYCIDOL AND ITS DERIVATIVES
HALOGENATED ALKYL EPOXIDES
HEXACHLORO-1,3-BUTADIENE
HEXACHLOROCYCLOPENTADIENE
HEXACHLOROETHANE
HYDROQUINONE
ISOPHORONE
MESITYL OXIDE
4,4'-METHYLENEDIANILINE
METHYL ETHYL KETONE
METHYL ISOLBUTYL KETONE
NITROBENZENE
PHENYLENEDIAMINES
POLYCHLORINATED TERPHENYLS
PYRIDINE
QUINONE
o-TOLIDINE-BASED DYES
TOLUENE
1,1,1-TRICHLOROETHANE
XYLENE

Figure 1

STEPS IN THE ITC SELECTION PROCESS OF PRIORITY CHEMICALS

EXCLUDES:
- DRUGS
- FOOD ADDITIVES
- PESTICIDES
- NON-COMMERCIAL CHEMICALS

SCREENING FOR:
- POTENTIAL FOR HUMAN AND ENVIRONMENTAL EXPOSURE

ELIMINATION OF CHEMICALS:
- REGULATED
- WELL CHARACTERIZED
- CONSIDERED INERT
- POORLY CHARACTERIZED NATURAL PRODUCTS
- INSUFFICIENT INFORMATION

SCREENING FOR:
- HEALTH EFFECTS
- ENVIRONMENTAL EFFECTS
- TESTING NEEDS

Figure 2

This rank-ordered list of 700 was further reduced by eliminating certain categories of chemicals from the list. These eliminations were done primarily on the basis of the professional judgment of the Committee member. The categories of chemicals eliminated were those:

- of known toxicity (which would therefore not be appropriate candidates for *testing*) including those already adequately regulated (for example, vinyl chloride and mercury compounds);
- which were essentially inert materials (e.g. certain polymers) or which were reasonably well characterized as having low toxicity (e.g., methane);
- covered by testing requirements under food, drug and cosmetic or pesticide legislation (e.g., citric acid); or
- which were poorly characterized natural products (e.g., asphalt) whose consideration should be *deferred* pending better characterization for testing purposes.

The Committee then added to its list any chemicals from the original Master File of 1700 or other additional sources which members of the Committee, in their professional judgment, felt should be included on a list of chemicals to be recommended for testing. At this point, the Committee also grouped chemicals into structurally-related categories. Some of the chemicals were already categorized from their initial listings. These categorizations were either retained or modified, based on the Committee's judgment. In addition the Committee formed several other structurally-related categories. Categorization was perceived as essential in order that similar substances be similarly addressed, and in order to keep the size of the list manageable. As a result of these categorizations and the exclusions described earlier, the Committee developed what it called a PRELIMINARY LIST. This list contained approximately 330 entries, 15 % of which were chemical categories.

This list of 330, having been scored and ranked for exposure, and having been weeded of all chemicals which were either not under TSCA's jurisdiction or which were, in the Committee's view, simply not good candidates for testing, was then scored on the basis of toxicity factors. The aim of the toxicity scoring was to consider, as required by TSCA:

- the extent to which a chemical is related to other chemicals known or suspected of posing risks,
- the extent of existing data on a chemical's effects on health and the environment, and
- the extent to which testing could develop data on which the effects of a chemical could be reasonably determined or predicted

Each of the 330 chemicals was scored for seven "biological activity" factors. These were:

- carcinogenicity
- mutagenicity
- teratogenicity
- acute toxicity
- other toxic effects (such as reproductive effects or organ – specific toxicity)
- bioaccumulation
- ecological effects

Scoring was performed by a panel of experts available through the Committee's contractor, on the basis of summary information and the knowledge and professional judgment of the experts. They were careful to differentiate between whether they

believed a chemical *did cause* the effect in question, or whether they thought it *might cause* that effect; in other words between known and suspected effects. If data existed to show that a chemical caused an effect, the score was in the former category; if the available data were not sufficient, but the chemical was suspected to cause the effect, the score was in the latter category.

On the basis of these "biological effects" scores and the exposure scores prepared earlier, the Committee ranked the chemicals on the PRELIMINARY LIST in several different ways using different criteria for each ranking. Separate lists for each toxicity factor were prepared, in order of the average score the chemical received for that factor. These lists identified those chemicals most in need of testing for a single effect. Additional lists were prepared which considered all of the toxicity factors, ordered by the sum of the average scores for all of the toxicity factors. These lists identified chemicals which needed testing for a number of different effects. To each of these lists the Committee added an exposure index, based on the exposure scores. Human exposure was differentiated from environmental exposure. The human exposure index was based on the scores for production volume, occupational exposure, and general population exposure. The environmental exposure index, used in combination with the bioaccumulation and ecological effects scores, was based on the scores for production volume and environmental release. The Committee also developed a list of the chemicals they felt may have adverse effects on health or the environment due to likely contaminants or degredation products of the chemicals being considered.

In preparing these rank-ordered lists, and throughout the entire review process, the Committee devoted particular attention to chemicals which were suspected of having carcinogenic, teratogenic, or mutagenic effects in human beings. TSCA requires such an emphasis; several parts of the statute, including that which directs the Interagency Testing Committee, indicate that priority attention should be paid to chemicals which may cause these kinds of risks. One way in which the Committee gave special attention to these effects was to assign individual scores for each of these effects, while other types of toxicity (for example "other toxic effects" or "ecological effects") were considered in a more summary fashion. To date, approximately 1300 chemicals have been scored for exposure and 700 for biological effects.

On the basis of these rankings the Committee selects chemicals for in-depth study and the preparation of dossiers or Hazard Information Reviews. These reports summarize information obtained from the open literature, and other non-confidential sources, relating to relevant chemical and physical properties, production volume, uses, environmental release, and exposure to the substances under consideration as well as information on the nature and findings of previous studies of its human health and environmental effects. Information on the biological activity of other similar chemical substances is also included when available. To date, these detailed reviews have been prepared for approximately 200 chemicals or chemical categories selected in three separate scoring exercises.

After reading, reviewing, and discussing these Hazard Information Reviews, the Committee decides which chemicals and categories of chemicals to recommend to the Environmental Protection Agency for priority consideration for testing under section 4 of TSCA. The ITC has designated 46 such chemicals and categories to date, as I indicated earlier. One, chloromethane, has been responded to and removed from the list which now stands at 45.

The work of the Committee is ongoing as it is required to review and update its list of recommendations every six months. Two continuing challenges for the Committee are

how to refine the scoring system and how to update the scores assigned several years ago to reflect current information.

Before I discuss EPA's own priority setting efforts, I'd like to make a few comments about what happens after the ITC has made its priority selections and EPA develops testing rules on those chemicals. TSCA requires EPA to write requiring industry to test the chemicals that the Committee has recommended, or to make public its reason for not doing so. Authority is granted to require such testing only if certain findings about the chemical or category can be made, those which I mentioned earlier regarding potential for unreasonable risk of human or environmental exposure, insufficiency of available information to determine the health or environmental effects of the chemical, and capability of testing to develop information on which the health or environmental effects can be determined or predicted.

In July 1980 EPA proposed its first set of testing rules requiring the testing of chloromethane and chlorinated benzenes for several different health effects. The second set of testing rules, which will require testing of nitrobenzene, dichloromethane, and 1,1,1 trichloroethane (for both health and environmental effects), is under the final stages of review within EPA. Proposal is expected very shortly. These chemicals were all recommended by the ITC.

However, translating the Committee's recommendations into testing rules which support the required findings has not been easy. One of the largest challenges facing the Agency is how to address the ITC's recommendations of chemical categories. While EPA wholeheartedly agrees that requiring the testing of chemical *categories*, rather, than simply individual chemicals, is a useful approach if we are to make any progress in determining the characteristics of the thousands of untested and inadequately tested existing chemicals, doing so raises numerous complex issues. The Agency's goal in requiring testing of a structurally-related category of chemicals is to characterize all members of the category with minimal testing costs. Requiring testing of each member of the category in essence resorts to treating each member of the category as an individual chemical and does not accomplish the Agency's goal. The Agency prefers to employ a sampling approach – requiring testing of members of the category, the results of which are to be extrapolated to the other members of the category. Determining a scientifically representative sample for testing is very tricky, however, precisely because so little is known about the chemicals. And yet if the sample is not scientifically representative, the Agency may not be able to extrapolate the testing of the sample to the other members of the category. This could in turn undermine the original category definition. Furthermore, different member of a structurally-based chemical category may have vastly different production volumes, uses, exposures, etc., and these must all be taken into account. This category issue is one of several faced by EPA as it develops its testing program.

A major characteristic of EPA's testing program is the extensive involvement of industry members. Industry members frequently possess important information on the chemicals which the ITC has recommended to the EPA. EPA sees the need to involve industry at a very early stage in the process of reviewing ITC recommendations, so that the Agency may be fully aware of all pertinent information on a chemical or category and industry's view of that information. Furthermore, EPA encourages voluntary industry testing of the chemicals recommended by the ITC – an approach which demands fewer Agency and industry resources and obviates the need for rule-making. Under EPA's current system, shortly after the ITC issues a set of recommendations the Agency holds what is called a "Scoping Workshop" in which industry and government

and any other interested parties trade information and views on the testing needs of the recommended chemicals. In many cases, EPA will hold additional meetings with industry to discuss the terms of the testing which industry is planning to do voluntarily. In these meetings the specific tests which industry would perform are discussed, along with the conditions they would agree to concerning EPA test standards and good laboratory practices. The industry has, in several cases, formed a consortium of members who manufacture or process a chemical in question, and this consortium negotiates with the Agency. Two such groups which are making considerable progress toward defining the terms of voluntary testing are the phthalates consortium and the chlorinated paraffins consortium. Others are not far behind. EPA believes the future of voluntary testing is very promising and, presuming conditions can be agreed to, is happy to avoid testing regulations.

I wanted to make these few comments on our experience in developing testing rules to show the kinds of efforts required to implement the ITC's priority recommendations. The careful, state-of-the-art chemical scoring system used by the ITC has its limitations, and is after all, simply a scheme for setting priorities – vastly important but generally the first step in the process.

I'd like to mention briefly EPA's own priority-setting activities. EPA is developing a scoring system for identifying both chemicals which are candidates for control and for testing. This system, near completion, is an extension of the ITC system. It is relatively simple, uses readily available information, includes some objective guidelines and relies on expert judgment. Like the ITC system, chemicals will be scored first for exposure. A subset of those will then be scored for biological activity. Scoring for biological activity is more expensive and complex and should logically be done on this subset of chemicals for which there is some indication of human or environmental exposure. The scores will reflect the adequacy of the data on which they are based. Also, to differentiate between candidates for control and for testing, the scores will indicate whether the toxicity is known or suspected. Once the system is in place, EPA hopes to be able to score between 1000 and 5000 chemicals per year.

The first large set of chemicals to be scored will be those which are currently subject to a proposed information gathering rule under TSCA. This rule, which will apply to 1000 to 2000 chemicals, requires reporting of rudimentary exposure information – the kind of information to feed the exposure section of the scoring system. EPA will identify chemicals for scoring from a variety of different sources: from the open literature and from the notices of substantial risk which the Agency receives from the chemical industry, and from numerous other sources.

EPA prepares assessments of the chemicals it identifies as potential priorities through this scoring system. The Agency has developed a system for performing different levels of assessments, from very preliminary ones through more detailed ones. Those assessments have been published and made available to the public as the Hazard Assessment Series.

While our scoring systems are essential for setting priorities among the many untested and uncontrolled chemicals in production, EPA is careful to reserve resources to deal with chemicals that come to our attention in a less systematic manner, which is so often the case. This is both so that we may be responsive to public concern, and, as we say, to "keep the system honest". Priority setting is a mixture of art and science, and we are looking to refine our art and improve our science.

We are also looking at how to integrate the ways in which priorities are set in each of the Environmental Protection Agency's different programs. EPA administers seven

different environmental statutes. This toxics integration effort is intended to ensure that the Agency addresses the worst health and environmental problems in a cost-effective manner and is not inconsistent among its different programs. We plan to have an interim report to the Administrator on this subject this fall.

We are eager to learn of the experiences of other countries in tackling these same problems. We also hope that our experience can be useful to others as they plan and develop their own systems.

Jan W. Huismans and Michel Gilbert

The International Register of Potentially Toxic Chemicals: Its Usefulness for the Selection of Priority Existing Chemicals for Assessment and Hazard Control

Abstract

One of the objectives assigned to the International Register of Potentially Toxic Chemicals (IRPTC) concerns the development of central files containing adequate information for an understanding of health and environmental hazards caused by toxic substances.

During 1978, IRPTC has endeavoured to identify and define the attributes (characteristics) of chemicals which were actually used or considered to be necessary by both national and international institutions to evaluate the potential hazards of chemicals in their various uses. Detailed unequivocal Instructions for the selection and presentation of data for the Register were then developed and this work, although still continuing and susceptible of further improvement, made it possible to start developing data profiles on chemicals. A List of high priority chemicals was assembled: the preparation of data profiles on these substances was initiated last year and is being pursued.

At that stage of IRPTC's development, a substantial contribution from Network Partners in national and international organisations and industry was sought to substantiate the compilation of data for the Register and also to ensure global data coverage.

In the meantime, the problem of storage of the information was addressed. A Data Base Management System was chosen which would allow the most efficient data retrieval from the Register data bank. Access to bibliographic on-line information system was also arranged since such facilities are indispensable for the identification of the most recent sources of information relevant to the data profiles under development and for their updating.

It is believed that the content of the IRPTC data profiles is sufficiently comprehensive to permit assessment of hazards posed by chemical substances to human health and the environment. Data profiles contain information on, *inter alia*, physical and chemical properties, production and use, pathways into the environment, chemobiokinetics, toxicity to mammals and man, effects on non-mammalian organisms and plants, waste management, spills, treatment of poisoning, analysis, and national and international recommendations and legal instruments for the control of chemicals.

Constant attention is given by IRPTC to the completeness, accuracy and precision of the information and data collected. Presentation of the information in a condensed format makes it easy to read and understand for a worldwide user community. Not only does this facilitate the compilation and dissemination of objective information, but it also encourages the active participation of Network Partners which was foreseen for IRPTC from its inception.

The usefulness of the IRPTC as an information tool at the disposal of its users, its potential as an instrument for selection of priority chemicals, and some mutually beneficial aspects of participation in an interactive global data handling network are briefly discussed.

Introduction

The International Register of Potentially Toxic Chemicals (IRPTC) has systematically been developed by UNEP since 1976.

The mandate for the Register is based on a recommendation adopted by the United Nations Conference on the Human Environment, Stockholm, June 1972.

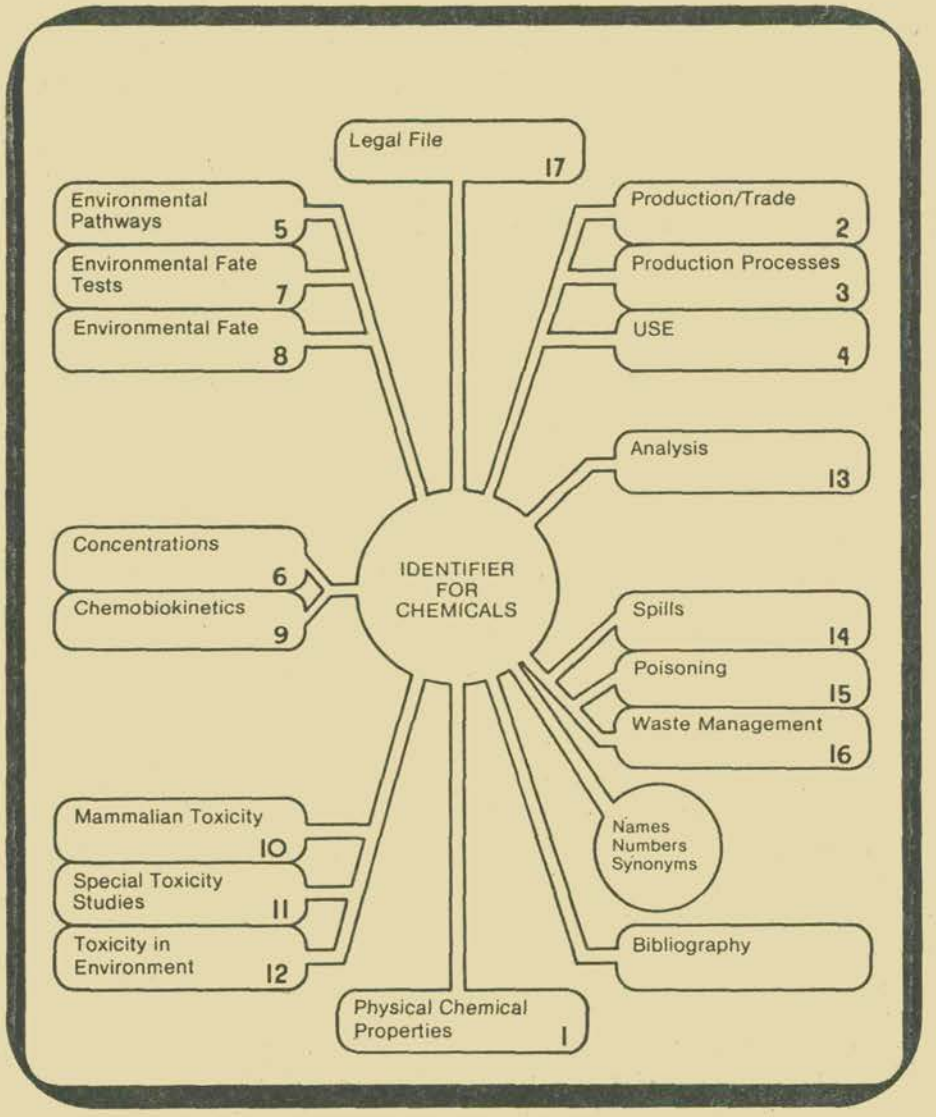
The main principles that guided the IRPTC since its inception are:

a) It should increase the capability of the United Nations System to provide awareness and advance warning of deleterious effects to human health and well-being from man-made pollutants;
b) The content, scope, and operation of the Register should be so organized as to fulfill the information requirements of worldwide users, in particular policy makers at the national level:

c) It should be built on existing and planned national and international systems and it should be able to request information from those systems which have chosen to cooperate with IRPTC;
d) Governments and organizations wishing to participate in IRPTC should be prepared to establish and maintain the necessary mechanisms for such interaction.

At the heart of the IRPTC Programme is the process of data profile development. Data profiles for chemicals enable the expert user worldwide to identify what is known about a chemical substance in terms of its chemical, physical, environmental and

Table 1. File structure of the IRPTC Data Bank



toxicological characteristics relevant for hazard assessment. They also provide information on production and trade, use, spills treatment of poisoning and waste management, as well as on recommendations and regulatory instruments for hazard control. Rather than merely providing bibliographical references or narrative summaries, data profiles furnish the user with extracted, factual, numerical and non-numerical information together with the sources from which it was obtained. This allows for easy reading by worldwide user community with differing linguistic capabilities.

The Data Profile Concept

The data elements considered to be relevant to the IRPTC have been grouped into seventeen files or attributes (Table 1) which together constitute a data profile.

Each file is divided, when appropriate, into subfiles which in turn contain data records. Each record represents a complete item of information and is accompanied by a cited reference. However, in order to contribute significantly to a better understanding of the potential hazards posed by chemicals to man and the environment, no record should be considered on its own merits but merely as part of a whole body of scientific evidence (a profile indeed) compiled to permit the 'best-informed' judgment of decision-makers. The development and dissemination of these *data profiles* are the most important objectives of the IRPTC Programme Activity Centre.

Detailed unequivocal instructions for the selection and presentation of data for the Register were developed and this work, although still susceptible of further improvement, is now being extensively used for data profile production by IRPTC and its Network Partners.

Table 2. Carcinogenicity Subfile

A complete record in this register subfile may include the following fields:

Test Description

- study type
- organism
- route
- sex
- lifestage
- number of organisms exposed
- number of organisms in the control group
- species/strain/system description
- exposure dose/concentration
- exposure period
- exposure type
- intermittence of exposure
- exposure frequency
- exposure comment
- purity grade and/or percentage
- impurities
- vehicle/solvent
- particle size, formulation and adjuvants
- isotope
- labelled compound/label site
- test conditions
- test method

Test Results

- organ/system/tissue affected
- effect
- sex affected
- reversibility/persistence of the effect
- time of onset of the effect
- number of exposed affected
- number of controls affected
- effect comment
- general comments
- evaluations and appraisals

Reference

- secondary reference
- primary reference

As an illustrative example, a full record of the subfile 'Carcinogenicity' is shown in Table 2. The following main entries are included: exposure dose or concentration; exposure period and route of administration; organism, sex and life stage, with numbers in control and experimental groups; target organ(s) with number in control and experimental groups showing the effects described; a reference; an evaluation is also entered with its reference. The effect(s) are reported as described in the author's conclusions. Eventually an inconclusive observation or a 'no effect found' result are also reported.

To qualify for entry into the Register, evaluations must have been issued by expert panels, e.g. representing the United Nations, international, governmental or non-governmental scientific organizations. Evaluations prepared by individual or joint authors, without the review of an expert panel are not included.

Sources of Information and Reliability of Data

The identification of all pertinent sources of information and the ascertainment of their reliability are imperative for the Register.

The importance of the reliability of data entered into the IRPTC data bank cannot be over-emphasized. Information which has been evaluated by international and national groups of experts are reported by preference; secondary documents containing evaluated information, however, do not exist for the great majority of chemical substances. In such cases IRPTC will use primary sources of data carefully selected and reviewed according to the data selection and presentation instructions, an improved version of which will be published by IRPTC later in 1981. In addition, IRPTC will seek advice, as appropriate, from individual consultants and also from panels of experts. The International Programme on Chemical Safety sponsored by ILO, UNEP and WHO with its highly specialized lead institutions can be of very great help in this respect.

The reader's own requirements and the severity of his own criteria and judgement are, and will remain, the decisive issues on this matter of data reliability. An information system on chemicals should at the best indicate the type (evaluated or non-evaluated) of information that it contains. The IRPTC system of citing references uses a special sign to call the reader's attention to the fact that evaluated information is quoted.

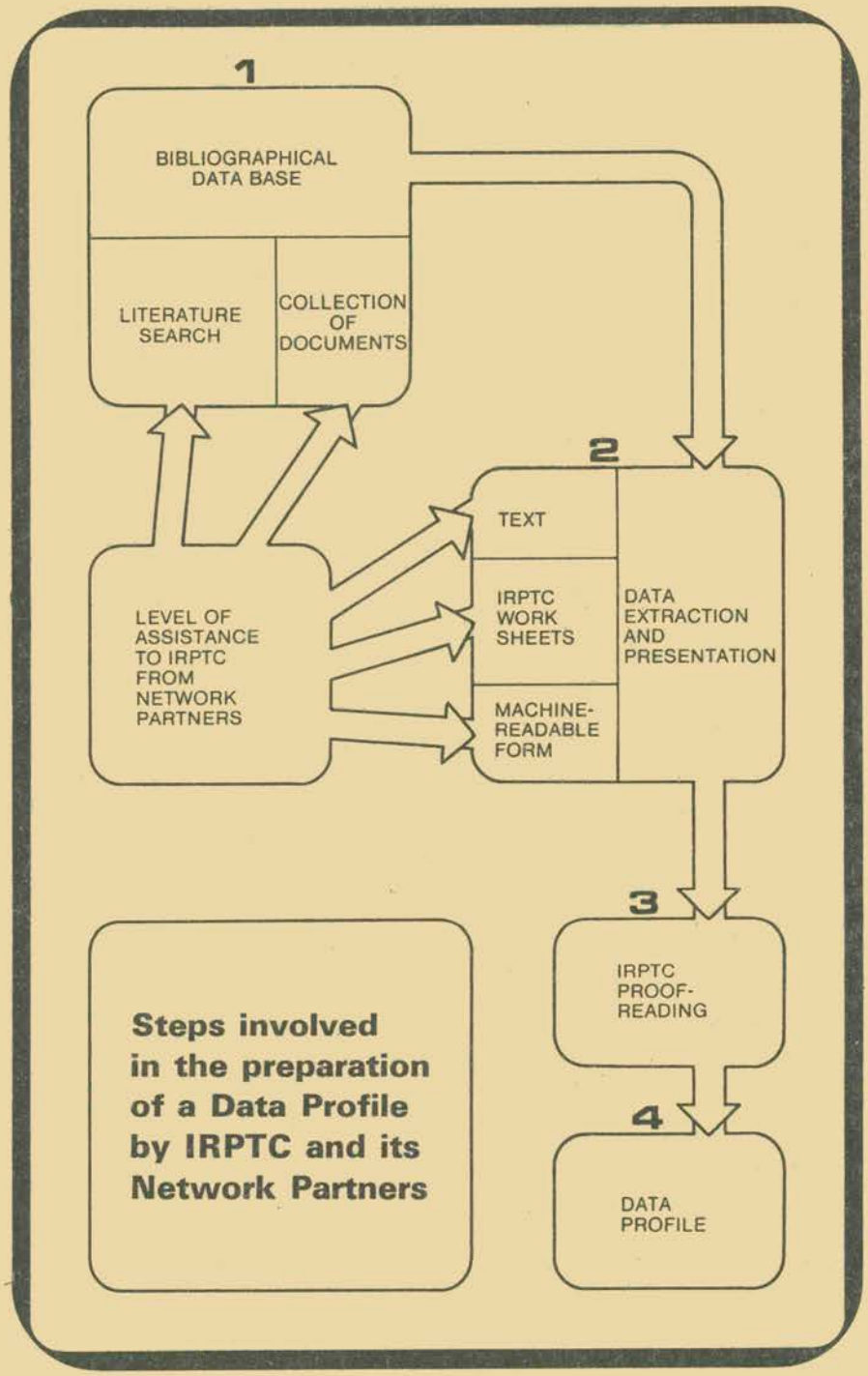
Users

National authorities responsible for protection of human health and the environment represent the most important user group of IRPTC. Decisions to regulate or control chemicals must be based on 'best-informed' judgement. Clearly, the task of mastering the mass of information publicly available from the scientific literature and reports prepared by international, national or industrial organizations on the many chemicals in use is a very difficult one indeed.

The International Register aims at providing its readers with a reliable, up-to-date and comprehensive description of the information necessary to assess the risk presented by chemicals to man and his environment.

The scientists involved in experimental research can hardly expect from a computerized data bank like IRPTC such detailed information that it will obviate the necessity of reading the original sources of data. However, the scientific community can use the Register to identify priority chemical substances which may have the

Table 3


1
BIBLIOGRAPHICAL DATA BASE
LITERATURE SEARCH
COLLECTION OF DOCUMENTS
2
TEXT
IRPTC WORK SHEETS
MACHINE-READABLE FORM
DATA EXTRACTION AND PRESENTATION
LEVEL OF ASSISTANCE TO IRPTC FROM NETWORK PARTNERS
3
IRPTC PROOF-READING
4
DATA PROFILE
Steps involved in the preparation of a Data Profile by IRPTC and its Network Partners

potential for being noxious and for which little or no pertinent research has been performed to elucidate this potential. This is also of interest to both government and industry in the allocation of efforts for chemical research. Moreover, the compiled information may eventually lead to a primary understanding of some cause-effect relationships between physical and chemical characteristics of chemicals on the one hand and their biological properties on the other.

List of Chemicals

In view its ongoing activity of data profiles development, IRPTC prepared a first list of selected substances on which data are compiled systematically. It is extremely difficult for an information system such as an environmental chemicals data bank to select chemicals for priority treatment. The development of such a list can be based on two approaches.

Selection criteria can be used for each chemical, such as: production statistics, main uses, toxicity to man, ecotoxicity, persistence and biodegradability, etc. After data collection, the application of a scoring system to each of the criteria would lead eventually to a list of chemicals ranked as a function of their impact on man and the environment.

The second approach for the preparation of a priority list, followed by IRPTC, is a more pragmatic one. The motivating idea behind it is to collect data on chemicals for which concern has been expressed at the national or international level. This includes listings of chemicals widely used, lists of poisons, lists of chemicals to which wide sectors of the population or workers are exposed, lists of pesticides, etc. In preparing an integrated list which gradually will grow, IRPTC felt that it had identified the major part of the chemicals of international significance. The list at present includes approximately 330 chemicals of which 160 are agrochemicals and is available from IRPTC/ Programme Activity Centre in Geneva, or from the IRPTC National Correspondents. The list is by definition open-ended and will undergo considerable expansion, based *inter alia* on the suggestions made by National Correspondents, by the International Programme on Chemical Safety and by the IRPTC contributing Network Partners.

As regards the development of data profiles, it is planned that 250 of these chemicals will be covered by the end of 1981.

Network Partners

In order to work out data profiles using the most reliable and complete information, IRPTC is developing working relationships with 'Network Partners'. From the beginning of its activities, the identification of partners and the implementation of effective collaboration has been a priority task for IRPTC. The potential partners can be identified as:

- the IRPTC National Correspondents
- some national and international institutions
- industries and external contractors.

In collaborating with IRPTC on the data collection undertaking, the contributing Network Partners can play a very important role by ascertaining the completeness, accuracy and precision of the information collected.

Several mechanisms for a collaborative production of data profiles can be envisaged and various levels of assistance to IRPTC are suggested in Table 3. Obviously, it is essential to adhere to the IRPTC instructions in order to achieve maximal compatibility between the central files and those held by Network Partners.

A most efficient cooperation would consist of the preparation of data profiles using either machine-readable worksheets, now under development, or more textual worksheets presently used by IRPTC staff. The study and review of data profiles prepared by IRPTC could also be most helpful: in this case, the amount of the contributing partner's work could be rather limited, depending on the extent of information contained in his own files. A third useful possibility would permit IRPTC to compare its chemical-related sources of information with the Network Partner's bibliographical data bases.

Working relationships are being developed with Network Partners including members of International Groups of Chemical Manufactures who would be willing to review some of the IRPTC data profiles on chemicals. The crucial question of treatment of unpublished data, in particular proprietary information of a confidential nature is being studied at the moment. It is our firm opinion that for the majority of problems that might arise in this area, IRPTC will be able to provide a satisfactory solution.

Data Management

Rapid growth of documentation received from many sources – IRPTC National Correspondents, national and international organizations, industry, direct acquisitions by IRPTC, material related to the query-answer service – necessitates optimal access to the relevant information it contains. On the other hand, data profiles have to be processed and stored using an adequate software package allowing easy updating and retrieval of information. The terminals now in use in IRPTC's offices are connected to the equipment (IBM 370/158) of the International Computing Centre (ICC), Geneva.

Access to relevant on-line information systems has been established. These connections are indispensable tools for the development of the Register (Data Profiles and their updating) and operation of the queryanswer service. As well as its own library, IRPTC extensively uses the documentation available in the libraries of the International Labour Office, the United Nations and the World Health Organization.

Having reached the stage of computerization of the data compiled on chemicals, IRPTC had to make a choice of a Data Base Management System which can be adapted to provide the services required by the International Register of Potentially Toxic Chemicals.

The paramount criteria taken into consideration for supporting the implemented action were the following: ease of use; optimal facility for udating; friendly command and query language; linkage between files.

Other criteria not directly relevant to the technical characteristics of the packages have also been scrutinized: possibility of linking to an international network; (automatic) exchange of information with existing data banks.

Considering the above-mentioned parameters and the electronic data processing facilities available in ICC, IRPTC has decided to implement its information bank through a Data Base Management System called 'ADABAS'.

A unique and unequivocal identifier is used for each substance, although access can also be provided through a subfile containing names, synonyms, and widely accepted numbering systems. Each file contains various types of information which are used as entry points in the data base.

At the moment, considerable effort is being devoted in IRPTC to the development of formats for data input. Careful attention is being paid to this ongoing activity because it will determine the efficiency of the retrieval capacities of the Register data bank. As

they are indispensable tools in the hands of contributing partners, these formats will be the subjects of future IRPTC publications as soon as they have been completed. In the course of 1981 IRPTC will publish its Register Index which contains names of chemicals for which data profiles exist, and the data fields on which information has been collected and extracted. Plans are being made for an annual microfiche edition of all data profiles stored in the central Register.

Improved Hazard Assessment and Priority Setting Through International Cooperation

Misuse of chemicals can greatly potentiate their hazards and insufficient knowledge of chemical/physical properties and biological activity may blur their noxious potential. Because of the mass of data to be considered for the assessment and control of hazards from chemicals, a condensed presentation of relevant data seems of value. The abbreviated data presentation proposed by IRPTC allows *rapid* scanning of the information available on the most significant fields (attributes) pertinent to potential hazards. Once the files will be systematically filled and updated by IRPTC and its Network Partners, and the number of chemicals has become sufficiently large, the Register will automatically start to function as an easy-to-handle priority setting instrument.

Moreover, it helps to identify gaps in existing knowledge concerning the harmfulness of chemicals. In this way, the Register functions, although indirectly, as a suggestion tool for further work. Participation by worldwide Network Partners would ensure global data coverage while at the same time unnecessary duplication of work is avoided. IRPTC is ready to start. It looks forward to working relationships with new Network Partners; their participation is vital to the functioning of the system. We invite all scientific institutions with expertise in the fields of chemical data handling to discuss with us modalities for cooperation depending on national priorities and existing methods of work. Finally, participation in a worldwide network with unequivocal and relatively uncomplicated arrangements for data selection and transfer will be of considerable benefit to all partners who, needless to say, will all have optimal access to the central files compiled by the entire network according to national needs and requirements.

Theodore Mill

Minimum Data Needed to Estimate Environmental Fate and Effects for Hazard Classification of Synthetic Chemicals

Abstract

Information on the several thousand synthetic chemicals often includes only the chemical structure, production level, and (possibly) uses. Initial hazard ranking of these chemicals will have to rely on this minimum information and the intelligent application of structure-activity relations for properties, transformations, and effects.

We indicate how systematic, integrated application of quantitative relationships between structure and properties (SPR), activities (SAR), and toxicity or effects (SER) can be used to develop a hazard classification methodology. First, simple equilibrium distribution and fate assessment models are developed using SPR and SAR; an effects model is developed in a similar manner from SER. Second, we show how information on fate and uptake coupled with information on production and use can be used to estimate the environmental concentration of a chemical (EC). Third, we describe how concentration and effects can be combined to provide a crude but useful hazard classification scheme that focuses attention on the few persistent, widely distributed and toxic chemicals. These chemicals will require laboratory testing.

Methodology for establishing a hazard classification is still very crude and imprecise. The probable reliability and limitations of this methodology are discussed along with the important gaps that now exist in our understanding of the relationships between structure and properties, activities, or effects. Selected chemicals are cited as examples of the application of the structure-activity methodology.

Introduction

Our present knowledge of how most synthetic chemicals are distributed and transformed in the environment and how they affect organisms in or on water or soil is too inadequate to develop exact estimates of the hazards * and risks † of their manufacture and use. In almost all cases the quantitative data needed to estimate reliably the hazard of using a specific chemical are simply not available, and to obtain such data would, in most cases, be expensive and time-consuming. With possibly forty- to fifty-thousand chemicals in current inventories, the cost of generating the data would quickly exhaust the resources of most regulatory agencies.

In this paper we indicate how well certain key data elements for hazard estimates can be developed using only chemical structure, production and use data, and structure-activity and structure-effects relations (SAR, SER); we briefly evaluate how reliable such data are and what gaps exist in SAR and SER methodology. Other complex issues related to this scheme include exposure assessment, mutagenesis versus carcinogenesis, and acute versus chronic toxicity effects, but these issues must be dealt with separately by experts in these field.

Methodology for Hazard Classification

Two key data elements are needed to formulate a hazard classification scheme:

- Environmental concentration of a chemical (EC).
- Lethal concentration or the concentration of a chemical needed to effect irreversible or genetic damage to an organism (LC).

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* Hazard refers to the harmful effect of a chemical on a specific organism that is exposed at some concentration.

† Risk refers to the probability that a certain number of organisms or humans will be exposed to a specific chemical at a specific concentration.

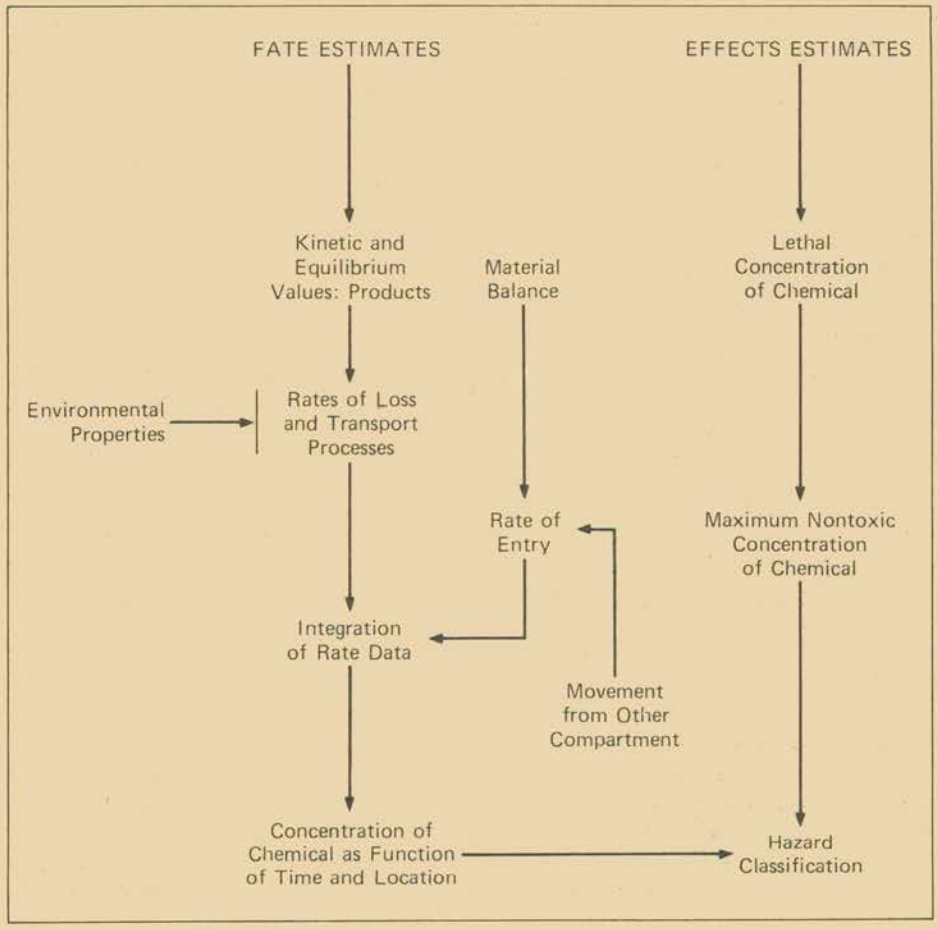

Figure 1. Hazard Classification: Relation of Chemical Fate and Effects

This simple conceptual model of chemical hazard is useful for exploring the most effective ways of coupling fate and effects information for hazard classification. Figure 1 shows how data on fate and effects can be used in a predictive way for hazard assessment in a specific environmental location: Fate data can be used to predict how rapidly and where a chemical will move in the environment, how rapidly and to what it will be transformed, and – coupled with information on the amount entering the environment – how long the chemical will persist and at what concentrations. Effects data can be used to predict whether, at the concentrations predicted, organisms at risk will be affected and how and whether the chemical will move up the food chain. If both data elements, EC and LC, were available for most chemicals, we could readily fashion a simple three-part classification scheme based on the value of the ratio EC/LC:

Black: >0.1
Gray: 0.01–0.1
White: <0.01

The exact values shown here are somewhat arbitrary, but obviously if a chemical were present in the environment at one-tenth or more of the LC value, it would be considered a great potential hazard and would have a high hazard ranking.

We emphasize that this simple hazard classification based on SAR serves only to focus attention and resources on the relatively few chemicals might be found at high concentrations (high EC) and have high toxicity (low LC); these chemicals would be subject to actual testing for transformation, distribution, and toxicity, from which we could make a more quantitative and reliable estimate of hazard ranking. In no case would structure-activity relations alone be used to make a regulatory decision.

Estimation of Environmental Concentration (FC)

Methodologies for estimating environmental concentrations of a specific chemical depend on a knowledge of how rapidly a chemical is discharged to a specific compartment in the environment and how rapidly the chemical is transformed or removed

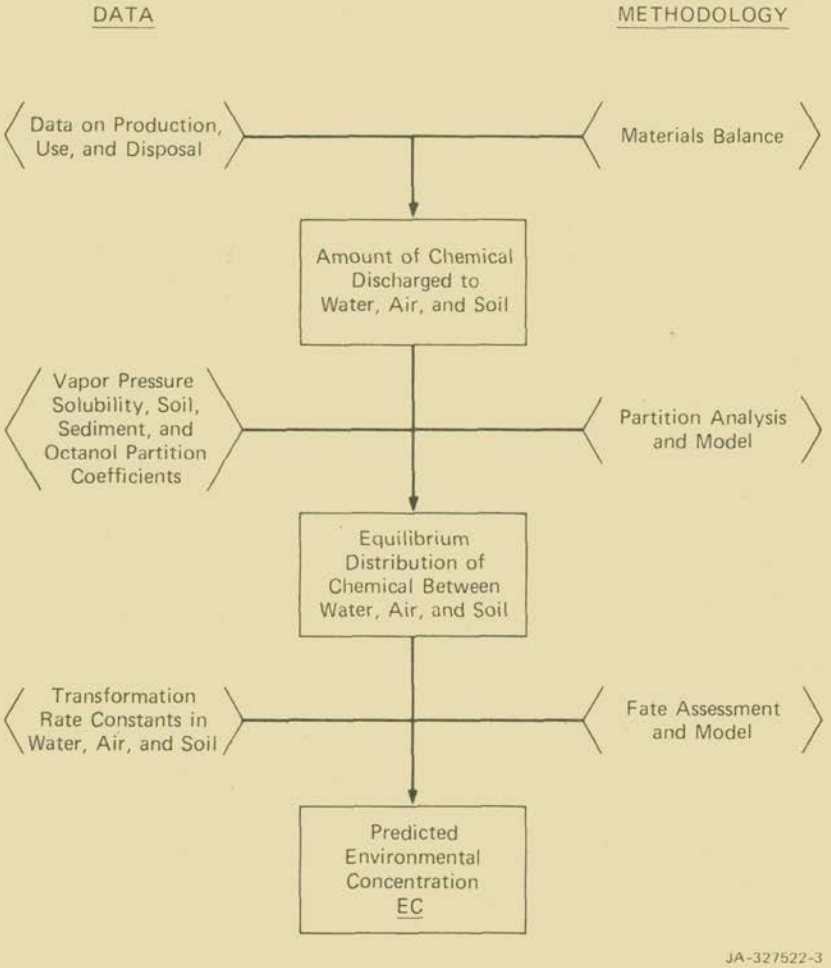

Figure 2. Data and Methodologies used to Estimate EC

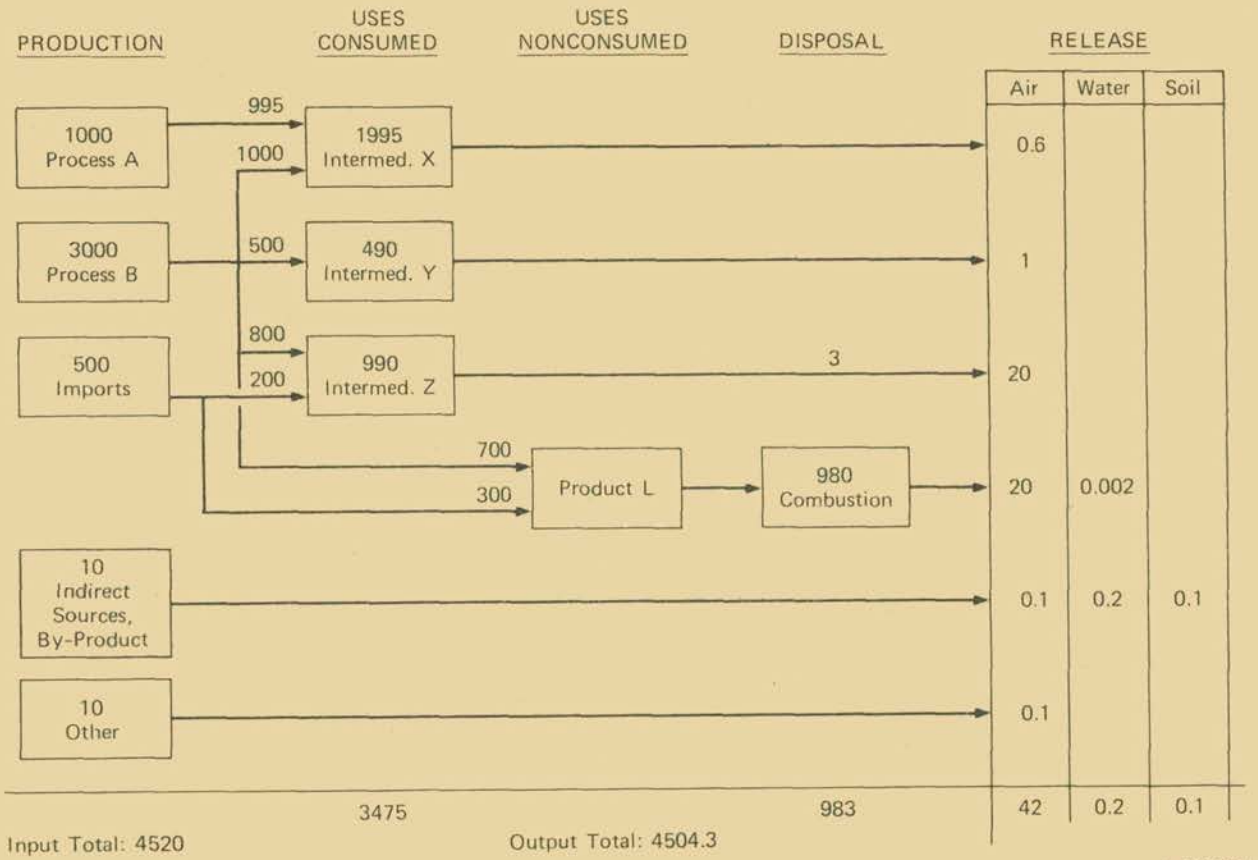

Figure 3. General Material Balance Scheme for Volatile Organic Chemicals

from the compartment by physical, chemical, and biological processes. EC is thus estimated from the relation

$$EC = R_I/\Sigma k_L \quad (1)$$

where R_I is the rate of input to the compartment and Σk_L is the sum of rate constants for all loss processes in that compartment. Figure 2 shows the U.S. Environmental Protection Agency's (EPA's) approach to estimating EC using material balance, equilibrium partitioning, and fate assessment methodologies (Wood, 1980). The key data elements in the scheme are

- A material balance on production, use, and disposal for input (Slimak and Durrel, 1980)
- Equilibrium constants for distribution of a chemical in air, water, soil, and biota (Mac Kay, 1980)
- Kinetic constants for transformation processes in air, water, and soil (Mill, 1980a)

Material Balances

Figure 3 shows a typical materials balance scheme (Slimak and Durrel, 1980) based on production use and disposal data. Although this material balance appears to account for all but 0.4 % of the chemical, in fact the estimates usually have standard errors of about ± 10 % and often are much larger; a small error in one of the disposal estimates would significantly affect the release data. For example, if combustion of product L is only 96 % efficient instead of 98 %, then the air discharge rate would be doubled. Moreover, release rates fluctuate daily and seasonally; smoothed production and release rates usually are used for material balances because no better estimates are possible. However, short-term values could easily be double or half the smoothed values. Production data for individual plants are rarely known, adding additional uncertainty to these estimates.

Equilibrium Distribution

In this approach the chemical is assumed to partition rapidly between air, water and soil in ratios that are governed only by the equilibrium partition coefficients for air/water and soil/water; transformation rates are assumed to be zero (MacKay, 1980). For equilibrium distribution estimates, several properties and equilibrium constants must be estimated from the chemical structure:

- Water/octanol partition constant (K_{ow}).
- Water/soil or sediment partition constants (K_{oc})
- Water/biota partition constant (K_{Bio}),
- Solubility in water (S)
- Vapor pressure (P)
- Henry's law constant (H_c)

The key datum is K_{ow}. From this value, S, K_{Bio}), and K_{oc} can be estimated directly from several linear regressions listed in Table 1. K_{ow} is also a key datum for estimating toxicity values (LC) (see below).

The equilibrium distribution helps to focus attention on the compartments in the environment with the highest *potential* concentrations. If the receiving compartment is also the one with the highest equilibrium distribution, one can safely assume that the chemical will not be redistributed. If the receiving compartment is different from

the principal equilibrium compartment, the equilibrium method is less useful. In either case the equilibrium distribution does not provide an estimate of EC because it does *not* take into account loss processes.

Estimation of K_{ow}

Estimation methods for K_{ow} based on structure have received considerable attention. The best methods currently available are the computerized FRAGMENT (additivity) scheme of Leo and Hansch (1979) and a statistical-thermodynamic method of Hopfinger (1976). Of the two, the additivity method is more widely used and is generally believed to provide values of log K_{ow} (log P) with an error bound of ± 0.5 log units, for most structures within the range of log K_{ow} values of – 2 to + 5. For values above + 5, measurements of K_{ow} become so difficult that verification of calculated values is unreliable (Leo, 1980). Some structures do not give reliable estimates; these include many heterocycles and very polar or bifunctional structures where intramolecular interactions become important.

Estimates of Solubilty and Sorption Constants for Soil and Biota K_{oc} and K_{Bio})

Solubility (S) can be reliably estimated from K_{ow}. Figure 4 illustrates the excellent correlation found by Chiou et al. (1979). Several regressions have been developed, but MacKay et al. (1980) provide one that corrects for solid-liquid entropy effects by using melting temperatures for solids (where T_m, the melting point, is greater than T).

$$\ln S(mol/m^3) = 7.494 - \ln K_{ow} + 6.8(1 - T_m/T) \qquad (2)$$

The mean deviation in log S is a factor of 0.2.

Sorption of organic molecules by soil, sediment, and biota follows closely the pattern found for distribution of chemicals between water and octanol (K_{ow}); thus sorption

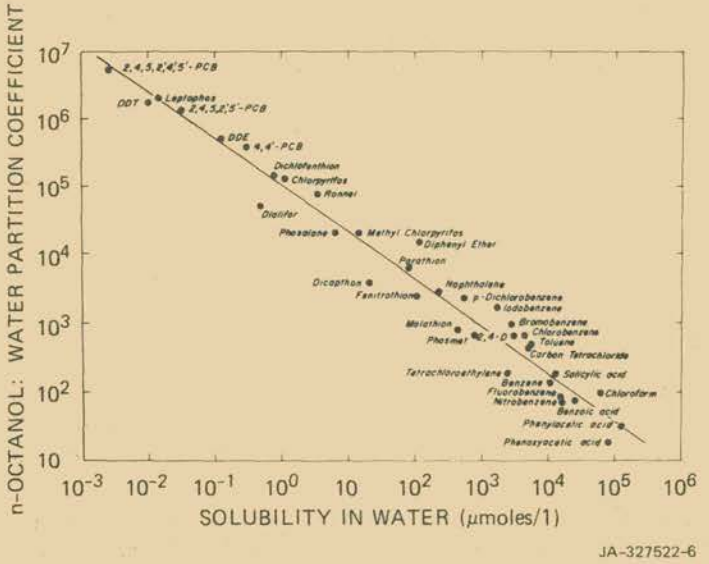

Figure 4. Partition Coefficients and Aqueous Solubilities of Various Organic Chemicals at Room Temperature (Chiou et al., 1977)

Table 1. Correlation Equations for K_{ow}, K_{oc}, and K_{Bio}[a]

Correlation	Equation	n	r
$K_{oc} - K_{ow}$	$\log K_{oc} = 0.524 \log K_{ow} + 0.381$	30	0.917
$K_{oc} - K_{ow}$	$\log K_{oc} = 1.00 \log K_{ow} - 0.21$	10	1.00
$K_{Bio} - K_{ow}$	$\log K_{Bio} = 0.542 \log K_{ow} + 0.124$	8	0.948
$K_{oc} - S$[b]	$\log K_{oc} = -0.782 \log S - 0.27$	97	-
$S - K_{ow}$[c]	$\ln S = 7.494 \ln K_{ow} + 6.8 \left(1 - \frac{T_M}{T}\right)$	45	0.988

[a] Kenaga and Goring (1978).
[b] Mill (1979).
[c] MacKay et al. (1980).

appears to be a distribution process rather than a classical interaction with a surface. In these cases distribution occurs between water and the organic or lipid fraction of the soil, sediment, or biota. It follows that one can estimate these distribution constants from a knowledge of K_{ow} or solubility in water (S) and the proportion of organic carbon in soil or lipid in the organism. Regression equations linking S, K_{ow}, K_{Bio}, and K_{oc} are summarized in Table 1. Their reliability appears to be high and is certainly adequate for screening for the likelihood that a chemical will partition significantly to soil or biota.

A useful generalization is that as water solubility decreases by a factor of 10^6, K_{oc} and K_{Bio} will increase by a factor of 2000 and by a factor of 500 (Kenaga and Goring, 1979).

K_{Bio} is usually estimated using aquatic vertebrates or invertebrates. The data for one organism can be correlated with those for another within an order of magnitude as for daphnia and fish

$$\log K_{Bio}\,(\text{fish}) = 1.001 \log K_{Bio}\,(\text{daphnia}) + 0.0431$$
$$r = 0.825 \quad n = 17$$

Volatilization and Henry's Law Constant

Kinetic models for diffusion of a chemical from water to air remain incomplete (Smith et al. 1981). Nonetheless estimates are possible of the rate constant, k_v, for volatilization of a chemical using a so-called two-film model for mass transfer and molecular properties. The relation is

$$k_v = \frac{1}{L}\left(\frac{1}{k_l} + \frac{RT}{H_c k_g}\right)^{-1} \tag{3}$$

where L is the depth, k_l and k_g the liquid- and gas-film mass transfer coefficients, and H_c is Henry's law constant; in this relation, H_c, k_l, and k_g are all functions of molecular structure. Smith et al. (1980, 1981) have shown how estimates of k_v may be made using molecular properties and have estimated k_v as a function of H_c for ponds, lakes, and rivers. Figure 5 illustrates the case for rivers. In general, if $H_c > 40$ torr M^{-1}, the halflife of the chemical in the river will be less than 10 days.

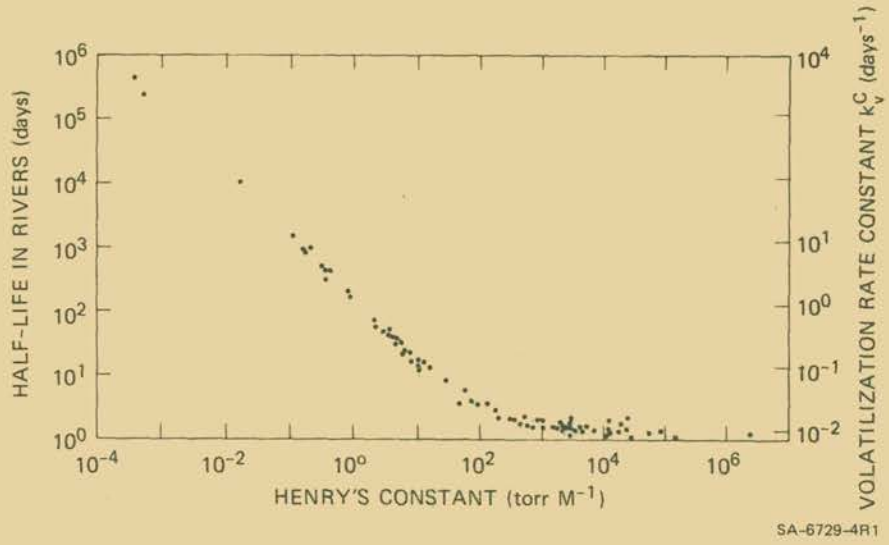

Figure 5. Estimated Half-Lives Versus Henry's Law Constant for Chemicals in Rivers (Smith et al., 1981)

Estimates of H_c

Mac Kay et al. (1980) and MacKay and Shiu (1981) have ably summarized current theory and methods for estimating H_c from structure. If we define H_c as

$$H_c = P/S \tag{4}$$

where P is the saturation vapor pressure and S the saturation concentration or solubility at a fixed temperature, it is evident that estimating H_c reduces to estimating P and S from structure.

MacKay et al. have shown that P may be expressed as a function of normal boiling point (T_B) and melting point (T_m) of the chemical by

$$\ln P\,(atm) = 10.6(1 - T_B) + 6.8(1 - T_m/T) \tag{5}$$

where T is $< T_B$ or T_m and is usually 298 K. Figure 6 shows the correlation of ln P with boiling point. In this correlation P ranges from 0.125 to 1×10^{-6} atm. Interestingly, calculated values were invariably higher than measured values by 10 to 100%.

Since

$$H_c = P/S \tag{6}$$

$$\ln H_c = \ln P - \ln S \tag{7}$$

Combining equations (2) and (5) and converting from mol/m^3 to mol/liters,

$$\ln H_c(atm\ M^{-1}) = 10.6(1 - T_B/T) - 12.104 + \ln K_{ow} \tag{8}$$

Figure 7 shows the interrelations among the physical properties.

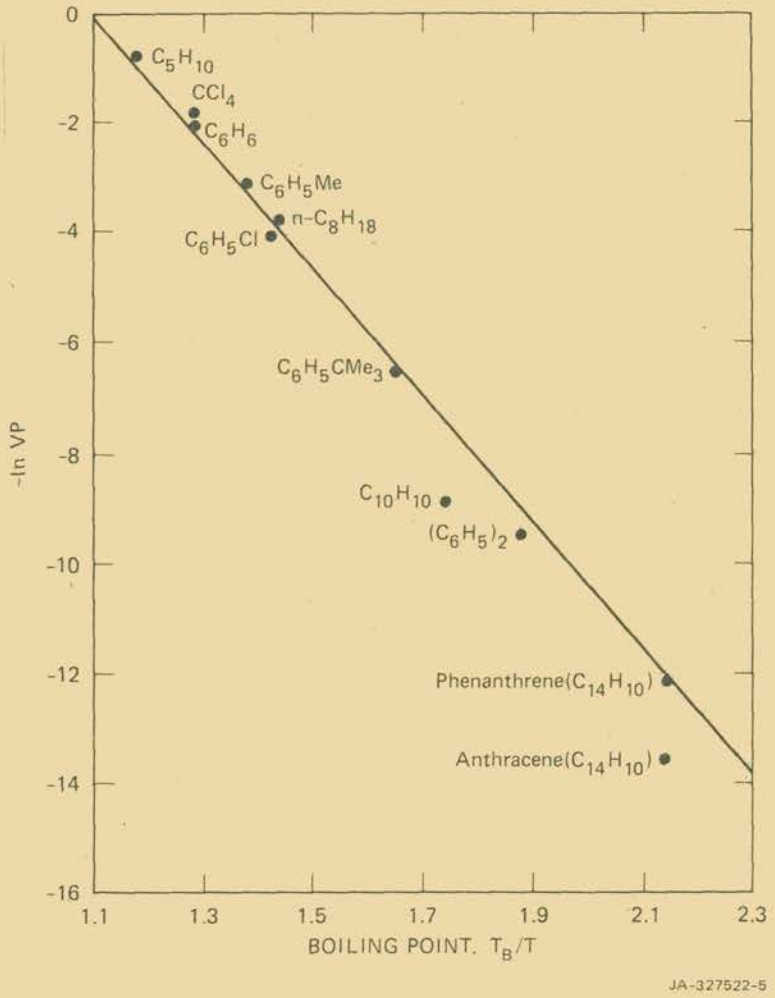

Figure 6. Relationship between Vapor Pressure and Boiling Point for Selected Solutes (MacKay, 1980)

Predictive Methodology for Kinetic Parameters and EC

Chemical fate assessment is generally used to mean a description of all major pathways for movement or transformation * of a chemical in a selected environmental setting. This description should include concentration as a function of time and location and all major products produced by all major transformation processes. The important environmental processes controlling movement and transformation have been reviewed recently (Mill, 1980), as have the structure-activity relations (SAR) needed to predict

* Transformation is the term preferred to describe any process in which a change takes place in molecular structure. Terms such as photolysis, degradation or oxidation refer to specific transformation processes and are used as appropriate.

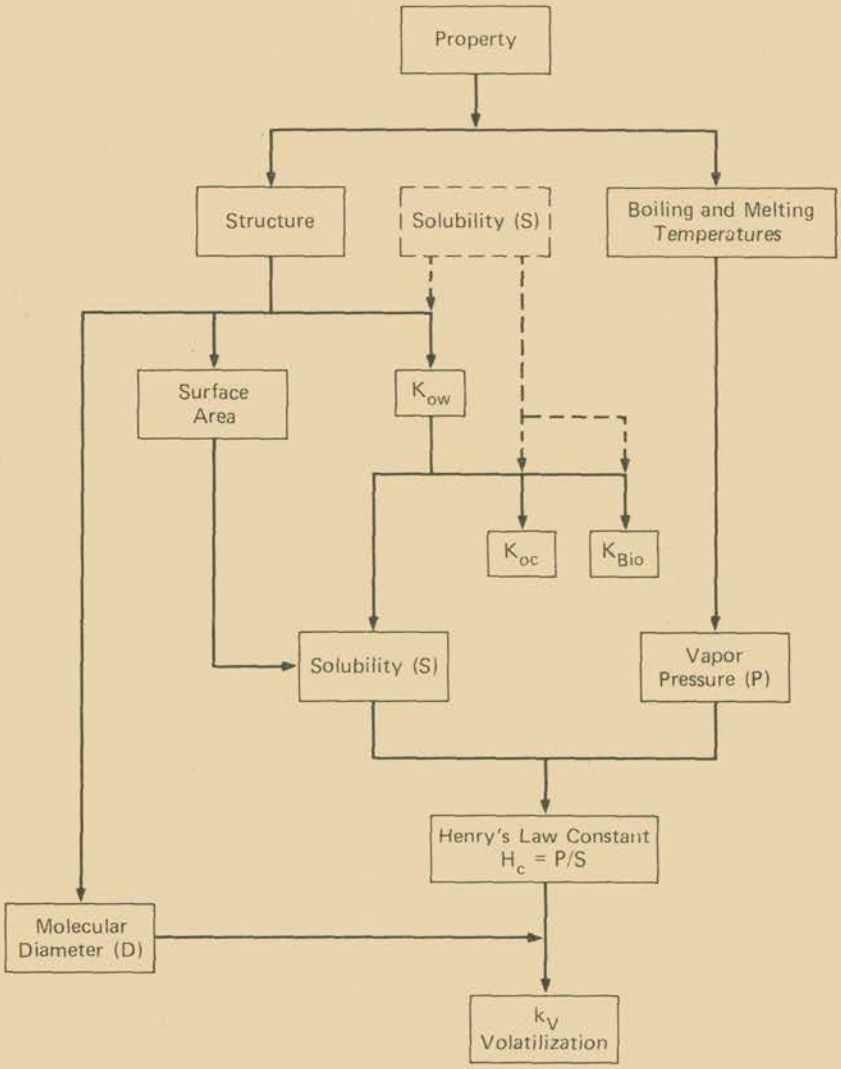

Figure 7. Relation of Molecular Properties and Physical Transport Constants

these kinetic parameters (Mill, 1979). Table 2 lists the major processes in each environmental compartment; Table 3 lists the environmental property associated with each process. In most cases the actual value of the property (e.g., solar irradiance, pH) will vary over a range both in time and space.

Kinetic constants for environmental processes couple the reactivity of a specific chemical structure to the specific process. For example, oxidation by a free radical may be represented by the relation

$$\text{Rate of loss} = \frac{d[C]}{DT} = k_{OX}[RO_n^{\cdot}][C] \qquad (9)$$

where C is the chemical, $RO_n^{\cdot}$ the radical, and k_{OX} the rate constant. The value of k_{OX} will usually increase with temperature for any C and $RO_n^{\cdot}$. SAR may be quantitative, providing a specific value for a rate constant (k) (Chapman and Shorter, 1972) or qualitative providing only an upper or lower limiting value for k. Both kinds of SAR can be equally valuable for fate assessment purposes. Whereas the quantitative estimate of k gives the investigator a basis for estimating the range of values of the rate process, the qualitative estimate often is a limiting value that allows the investigator to either eliminate the process from further consideration (because it is too slow).

A kinetic model for fate processes assumes that the net rate of loss of a chemical (R_T) is equal to the sum of all loss processes and that each loss process can be described by a simple first order process.

$$R_T = d[C]/dt = \Sigma k'_L [C] [E]$$

$$k'_L [E] = k_L$$

$$R_T = \Sigma k_L [C]$$

$$t_{1/2} = \ln 2/\Sigma k_L$$

Where k'_L and k_L are 2nd- and 1st-order rate constants, [E] is the environmental parameter in compatible units of concentration.

Many chemicals are introduced into air or water continuously. Under this circumstance, the persistence is better defined as the concentration resulting from equal rates of input (R_I) and loss (R_L) or the steady-state concentration, $[C]_{ss}$, rather than in terms of a half life.

$$0 = d[C]/dt = R_I - R_L$$

$$R_I = \Sigma k_L [C]$$

$$[C]_{ss} = R_I/\Sigma k_L$$

Table 2. Environmental Processes

Air	**Water**
Meteorological transport	Sorption
Photolysis	Bio-uptake
Oxidation	Volatilization
Fallout	Photolysis
	Hydrolysis
	Oxidation
	Biodegradation

Soil/Sediment

Sorption
Bio-uptake
Run-off
Volatilization
Leaching
Transformations
Biodegradation
- Hydrolysis
- Oxidation
- Photolysis
- Reduction

Table 3. Environmental Processes and Properties

Process	Property[a]
Physical Transport	
Meteorological transport	Wind velocity
Bio-uptake	Biomass
Sorption	Organic content of soil or sediments, mass loading of aquatic systems
Volatilization	Turbulence, evaporation rate, reaeration coefficients, soil organic content
Run-off	Precipitation rate
Leaching	Adsorption coefficient
Fallout	Particulate concentration, wind velocity
Chemical Transformation	
Photolysis	Solar irradiance, transmissivity of water or air
Oxidation	Concentrations of oxidants and retarders
Hydrolysis	pH, Sediment or soil basicity or acidity
Reduction	Oxygen concentration, ferrous ion concentration, and complexation state
Biological	
Biotransformation	Microorganism population and acclimation level

[a] At constant temperature.

or to conclude that no other process is important (because this process is much faster). Figure 8 illustrates the application of these two kinds of SAR. The following sections indicate how one can estimate many of the rate constants from structure alone using SAR.

Hydrolysis

Mabey and Mill (1978) reviewed hydrolysis reactions in water and reviewed kinetic constants for hydrolysis of most of the important classes of hydrolyzable chemical structures. SAR for hydrolysis are available for many kinds of acid, base, and neutral reactions. Quantitative SAR generally takes the form of a linear free-energy relationship (LFER) such as the Hammett and Taft

$$\log k_x/k_o = \rho\sigma \tag{10}$$

or Brönsted

$$\log k_x/k_o = mpK_a + C \tag{11}$$

where σ and ρ have their usual significance (Chapman and Shorter, 1973), k_o and k_x are the rate constants for the unsubstituted and substituted structures, respectively, and pK_a refers specifically to the acidity of the leaving group OR in the following reactions:

$$HO^- + RO-Y = RO^- + HO-Y \quad [Y \text{ is } \rangle C(O) \text{ or } -\rangle P(O)]$$

$$RO^- + H_3O^+ = ROH + H_2O$$

Wolfe et al. (1978, 1980) has reviewed and developed SAR for carbamates and phosphates. We have evaluated the validity of SAR for hydrolysis of several classes of

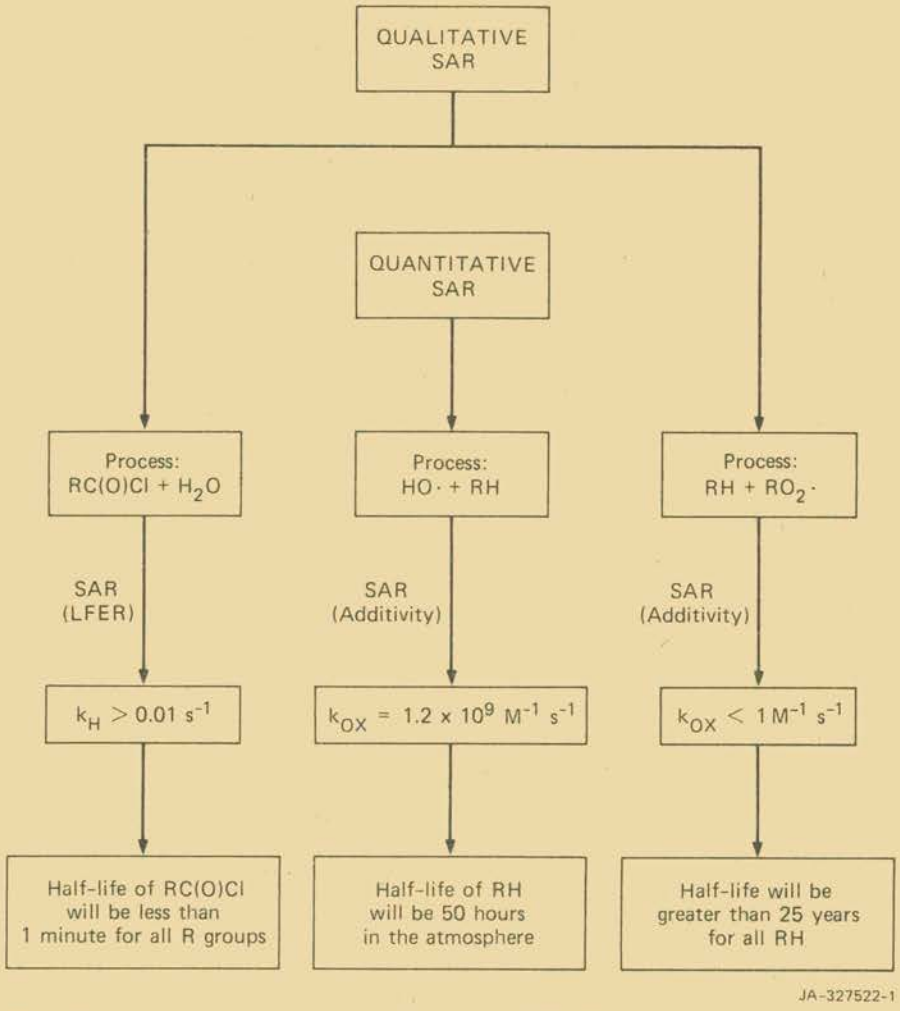

Figure 8. Application of Qualitative and Quantitative SAR to Environmental Processes

chemicals, including esters, phosphates, alkyl halides, and carbamates (Mabey et al., 1981). We believe that for reactive chemicals LFER provide estimates of log k_n for a specific structure with an error bound of 0.5 log units.

For very unreactive or reactive chemicals, qualitative SAR estimates are often quite adequate and reliable. Mill (1979) listed several classes of chemicals for which limiting values are readily available; these data are summarized in Table 4.

A variety of hydrolysis reactions have been observed on soils and sediments (Saltzman et al., 1974). In some cases, rates were markedly accelerated compared to bulk solution, but detailed understanding of mechanisms is limited and structure-reactivity relationships appear to be available for only a few compounds.

Table 4. Sar for Hydrolysis

Quantitative [a]	Qualitative [b]
esters	amides
carbamates	nitriles
phosphates	polyhaloalkanes
epoxides	acyl halides
alkyl halides	anhydrides

[a] LFER available.
[b] Limiting values available.

Photolysis

Direct photolysis results from absorption of photons by the chemical in the solar region above 290 nm. The kinetic relation for photolysis in water or air in sunlight is given by

$$k_{pE} = 2.3\,\phi \Sigma L_\lambda \epsilon_\lambda \qquad (12)$$

where ϕ is the quantum yield, ϵ_λ is the absorptivity of the chemical at wavelength λ, and L_λ is the solar irradiance at λ. Figure 9 gives typical absorption spectra, ϕ values, and solar irradiance curves. Generalizations about the relation of structure to ϵ_λ are

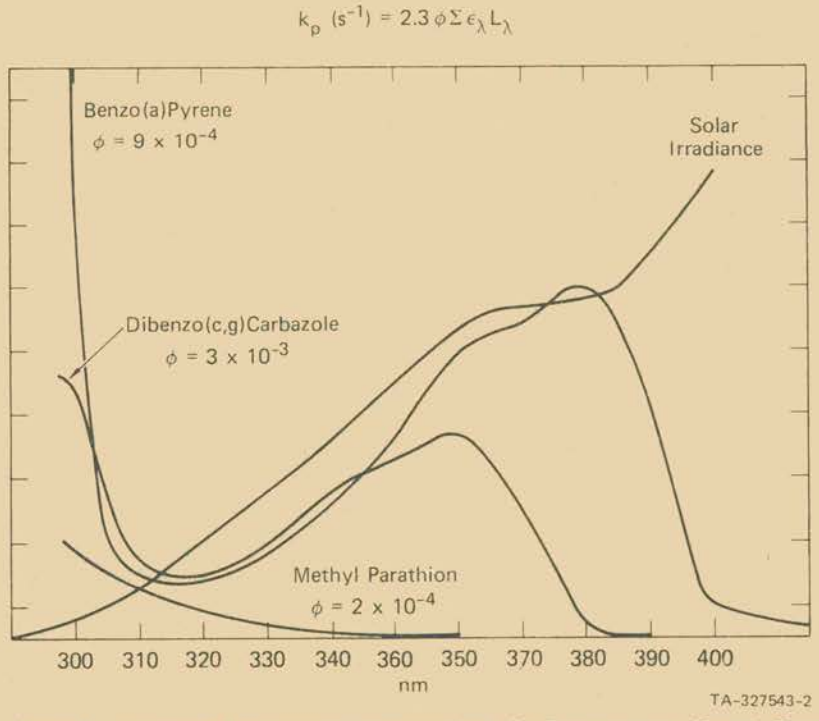

Figure 9. Absorption Spectra and Quantum Yields for Representative Organic Chemicals Plotted on the Same Coordinate with Solar Irradiance

found in Calvert and Pitts (1967), Hendry and Kenley (1980), and Mill (1979). No simple SAR are available to predict either ϵ_λ or ϕ, but a limiting value of k_{pE} may be estimated from equation (12) if the values of ϵ_λ are known (from the uv spectrum) by assuming that $\phi = 1$; L_λ values are available from tables as a function of latitude and season (Mabey et al., 1980). If k_{pE} estimated in this way is much smaller than values of rate constants for other processes, then one can ignore direct photolysis as an important process in air or water. Photolysis on soil is so poorly understood that neither kinetic relations nor SAR are available at this time.

Indirect photolysis may occur if a natural humic material can absorb solar photons and transfer part of the energy to a chemical. Thus chemicals that do not absorb light directly can still undergo photolysis and chemicals that photolyze directly may photolyze in natural waters much more rapidly by this process. For example, dienes photolyze in sunlight only by the indirect process (Zepp, 1981; Winterle et al., 1981), whereas nitroaromatics photolyze up to 70 times as fast in natural waters as in pure water (Mabey et al., 1981).

In summary, our ability to predict the rates of photolysis of many chemicals in water or air is severely limited by lack of SAR for ϵ_λ and ϕ and by lack of detailed understanding of the indirect process. Photolyses on soils remain largely unexplored.

Oxidation

Oxidizing agents are formed in air, water, and soil by action of sunlight on natural or pollutant chemicals (Mill, 1980b). Recent studies by several workers have shown that $RO_2^{\cdot}$ radical and singlet oxygen ($^1O_2$) are formed in natural water (Mill et al., 1980; Zepp et al., 1978) and HO· radical and ozone are important in urban air (Niki et al., 1972). Average concentrations of these species in these media are listed in Table 5.

SAR for oxidation by each of these species are available (Mill, 1980b; Hendry and Kenley, 1979) and can be used to estimate rate constants and half-lives for specific chemicals and for developing generalizations about the importance of oxidation as a loss process in water or air. Table 6 summarizes the reactivity of different classes of organic structures toward each oxidant (Mill, 1979). Here again we find that for many chemicals we need only qualitative SAR to establish the relative importance of these processes compared with others.

Table 5. Oxidant Concentrations in Water and Air

Oxidant	Concentration (M)
Water [a]	
$RO_2^{\cdot}$	1×10^{-9}
$^1O_2$	1×10^{-12}
Air [b]	
HO·	3.4×10^{-15} (8.2×10^{-18} ppm)
O_3	1.7×10^{-9} (4.1×10^{-2} ppm)

[a] From Mill (1979).
[b] From Hendry and Kenley (1979).

Table 6. Rates of Oxidation in Air and Water at 25 °C [a]

Class or Structure	Half-Life
Air: HO· Radical	
n-, iso-, Cycloalkanes	1–9 days
Olefins	0.05–1 day
Halomethanes	0.2–100 years
Alcohols, ethers	1–3 days
Ketones	0.2–6 days
Aromatics	0.1–3 days
Water: $RO_2^{\cdot}$ Radical	
Alkanes, olefines	220–2000 years
Alkyl derivatives	220–2000 years
Phenols, arylamines	1 day
Hydroperoxides	150 min
Polyaromatics	10 days
Water: $^1O_2$	
Aliphatic compounds	100 years
Substituted or cyclic olefins	8–40 days
Alkyl sulfides	1 day
Diene	19 hours
Eneamines	15 min
Furans	1 hour

[a] From Mill (1979).

Chemical structures most susceptible to oxidation in water by $RO_2^{\cdot}$ and $^1O_2$ include phenols, aromatic amines, electron-rich olefins and dienes, alkyl sulfides, and eneamines.

Most chemical are oxidized rapidly in air by HO· radical, but only substituted olefins, vinyl ethers, and eneamines are reactive toward ozone. Hendry and Kenley (1979) developed an additivity SAR for estimating values of k_{OX} for HO radicals. We are currently evaluating the validity of SAR for oxidations by RO_2, $^1O_2$, and HO by comparing values of k_{OX} estimated from appropriate SAR and those measured in the laboratory. Probably the error bounds on most estimates are $< \pm 0.7 \log k_{OX}$. It is important to realize that although oxidations are a subclass of indirect photolysis reactions, they are relatively well understood and are amenable to quantitative kinetic analysis including prediction of both rate constants and products, features not shared by other photolysis reactions.

Microbiological Processes

We prefer the term biotransformation to biodegradation as more accurate and general because many chemicals are not transformed at all or are transformed to products of comparable molecular complexity. Biotransformations in water and soil include hydrolysis, oxidation cleavage, and reduction, even in aerobic systems. Kinetics of biotransformation usually are based on the Monod model (Stumm-Zollinger and Harris, 1971) in which the rate of loss of the chemical is coupled to growth of the organisms. In the environment, however, growth is usually controlled by natural nutrients present in fairly constant amounts and the kinetic expression for biotransformation simplifies to a second- or first-order process

$$\text{Rate} = d(C)/dt = k_{bt}[C][B] = k'_{bt}[C]$$

where [B] is the number of organisms per unit volume and k_{bt} is the secondorder rate constant for biotransformation.

Well-informed microbiologists disagree among themselves as to whether broad generalizations and structure-activity relationships can be developed for biotransformation of organic structures in the same way as chemists have done for abiotic chemical processes. Dagley (1975) has discussed the problem in a limited way with respect to selected pesticides pointing out how structures common to otherwise diverse molecules, in this case carboxy esters, confer biodegradability on these compounds.

However, Alexander (1973) has long argued that some structures are inherently recalcitrant toward biotransformation, and it seems likely that insofar as oxidative biotransformation is concerned highly halogenated compounds have thermochemically limited rates.

Recently Wolfe et al. (1980) have shown that good correlations exist between rates of enzyme mediated- and HO^-promoted hydrolysis for diverse groups of chemical structures:

$$\log k_{bt} = 0.50 \log k_{OH} - 11.4 \qquad (13)$$

$$r^2 = 0.973 \text{ (general esters)}$$

$$\log k_{bt} = 2.1 \log k_{OH} - 6 \qquad (14)$$

$$r^2 = 0.933 \text{ (Phthalate esters)}$$

These relations may provide a valuable basis for estimating rate constants for biotransformation of esters. Correlations of this kind for other classes of hydrolyzable compounds are needed to begin to develop some useful SAR for this important group of loss processes.

Two examples are shown of the application of SAR for estimation of rate constants for (1) base-promoted hydrolysis of a carbamate and (2) $HO\cdot$ radical oxidation of a haloalkane in the gas phase.

SAR Estimation Scheme

1. Carbamate: Hydrolysis of $CH_3N(H)C(O)OC_6H_4CH_3$

   SAR: $\log k_B = -\rho \log K_a + C$ (Wolfe et al., 1978)

   $\rho = -0.91$; $C = 9.3$ for $CH_3N(H)-$ series

   $\log K_a$ of $HOC_6H_4CH_3$ is = 10.14 (CRC Handbook)

   $\log k_B = 0.1$

   Estimated value of $k_B = 1.3\ M^{-1}\ s^{-1}$

   Measured value of $k_B = 0.61\ M^{-1}\ s^{-1}$

2. Haloalkane: Oxidation of CH_3CHCl_2

   SAR: $\log k_{OX} = \Sigma n_i \alpha_{Hi} \beta_{Hi} k_{Hi} + \Sigma \alpha_{Ej} k_{Ej}$
   (See Hendry and Kenley 1979 for explanation)

   Estimated value of $k_{OX} = 0.40 \pm 0.27\ M^{-1}\ s^{-1}$

   Measured value of $k_{OX} = 0.26\ M^{-1}\ s^{-1}$

Estimation of Lethal Concentration (LC)

Biological Effects and Lethal Concentration (LC)

Toxicologists have long sought some relationships between chemical structure and biological effects in a variety of organisms and especially man (Leo et al., 1971). That they have succeeded even in small ways is remarkable considering the enormous complexity of even the most primitive species. Many toxicologists believe that acute and perhaps chronic toxicity of most chemicals results from one of three distinct types of chemical interactions with biological structures (Dagani, 1981):

- Nonspecific interactions with biological membranes
- Interactions with protein-active groups
- Interaction with specific receptor sites.

Thus effects might be catalogued by structural parameters such as K_{ow}, molecular reactivity toward a thiol or amino function or through a biochemical analogy such as binding of serine by phosphorus alkylating groups (anticholinesterase).

The membrane interaction mechanism is supported by correlations found between indices of toxicity (LC_{50}) and log K_{ow} for a variety of chemical groups and their effects on aquatic organisms. Table 7 lists a series of these correlations for several classes of chemicals taken from Konemann (1980). These structure-effects relations (SER) * are largely limited to acute effects, such as those observed in the 96-hour tests with the fat-head minnow. Probably SER for the 96-hour test can also be correlated reasonably well with 24- or 48-hour tests. The relatively good correlation observed using K_{ow} suggests that within a series of homologous compounds, the more hydrophobic members will be more toxic because of a larger accumulation in the membrane bilayer. However, this effect could be offset by more rapid elimination because of other structural effects; moreover, among a group of chemicals that can ionize in the pH range of interest, such as phenols, the more acidic species will experience less uptake by this passive distribution mechanism and thus exert a lesser effect (higher LC_{50}).

The effect of individual chemicals in a mixture is an important practical matter in an environment containing trace quantities of many different chemicals. Konemann's

Table 7. Correlation of LC_{50} with K_{ow}

Class	Correlation Equation	n	r
Chlorobenzenes	$\log(1/LC_{50}) = 0.845 \log K_{ow} - 4.63$	12	0.98
Chlorobenzenes and other chemicals	$\log(1/LC_{50}) = 0.970 \log K_{ow} - 4.94$	21	0.988
Chlorobenzenes, Chloroalkanes Alcohols, glycols Ethers, ketones	$\log(1/LC_{50}) = 0.871 \log K_{ow} - 4.87$	50	0.988
Chlorophenols [b]	$\log(1/LC_{50}) = 0.71 \log K_{ow} - 0.03\ pK_a - 3.20$	10	0.992

[a] From Konemann (1980)
[b] At pH 6.1.

* Various abbreviations are used to describe chemical-biological interactions, QSAR being the most common. We use SER here to distinguish it from the purely chemical phenomenon referred to as SAR.

(1980) recent studies of mixtures of chemicals having similar and dissimilar modes of actions, as judged by the similarity of their SER, suggest that in mixtures, chemicals having very similar actions will contribute additively to the total toxicity; the more dissimilar their action, the less additive their effects.

Extrapolation of Toxicity Data

Most successful SER are based on data for aquatic vertebrates and invertebrates. There is an understandable desire to use such data to judge the effects of very low concentrations of chemicals, particularly in man when exposed over long periods. However, the consensus is that such extrapolations are unwarranted at this time. The even more limited extrapolation of LC_{50} values from invertebrate to vertebrates and from class to class also are held to be unsafe. However, evidence is accumulating that extrapolations from species to species are acceptable; according to Kenaga and Goring (1979), LC_{50} values are within a factor of 100 more than 90% of the time when comparing effects of chemicals in two species of fish.

The concept of application factor defined as

$$AF = \text{No Observ. Effect Conc/96 hr } LC_{50}$$

has been used recently to relate acute toxicity to chronic toxicity for several species of fish. The AF is claimed to correct for differing LC_{50} values in different species. Apparently AFs do not correlate well among fish, mammals, and invertebrates.

Skurnick (1980) recently completed a detailed statistical study of the EPA data base on aquatic toxicity, including studies of acute and chronic toxicity and the relationships, if any, between them. The data base consists of toxicity values for 216 chemicals toward one or more of the 42 saltwater fish, 93 freshwater fish, 63 saltwater invertebrates, and 127 freshwater invertebrates. The analysis attempted to answer, among other questions, whether there is any basis for the simple relation of acute (A) and chronic (C) toxicity expressed as

$$C = mA$$

The data show wide variability, and, in particular, the scarcity of chronic test data effectively prevented Skurnick from reaching any satisfactory conclusion on this issue. Javitz (1981) has done a simple distribution analysis of these same data for the ratio of mean chronic to mean acute values; his analysis suggests that a median value is 0.06 and that about 80 percent of such ratios lie within a factor of ten of the median value. Thus for a very crude estimate of chronic toxicity in aquatic species one could use the relation

$$C = 0.06A$$

In summary, there appear to be a variety of simple SER available for estimating LC_{50} for several classes of chemicals based on K_{ow}; only limited extrapolation from species to species may be warranted, however, and for aquatic organisms at least, very crude estimations of chronic toxicity are available.

Reliability of Estimation Methods for Hazard Classification

The foregoing discussion shows how we can develop a hazard classification for chemicals based on their molecular structure, production data and only a few properties. An important question is how reliable are such estimates? A hazard assessment is based on

a chain of estimates of SAR, SPR and SER, each of which has a reliability limit and will contribute to the overall reliability in a way that is governed by the detailed estimation method for the hazard classification scheme. Thus we can give no single answer that applies to all chemicals. Bawol (1981) has approached the problem by setting a reliability limit on the value of H and then estimated what reliability each of the components must have to satisfy this initial condition.

Thus if a reliability factor of ten * is placed on the value of H, then the reliabilities of the components of H must be a combination such as the following:

Component	Reliability
EC	5.1
LC	5.1
Σk_L	4
R_I	2

It should be evident from the previous discussions that most of the existing estimation methods do not have the needed reliability; therefore for now we must accept less certainty in the hazard classification, work to improve the reliability of existing methods and, where SAR or SER do not exist for important processes, develop them as quickly as possible.

Acknowledgments

I wish to thank several colleagues at SRI for helpful comments and suggestions on this paper and for specific contributions to its content: Drs. Howard Johnson, William Mabey, Howard Bailey and Harold Javitz. Dr. Richard Bawol, Berkeley, CA made the statistical calculations for the reliability estimate. Dr. F. Schmidt-Bleek and A. Klein of Umweltbundesamt very kindly provided me with many OECD reports. Ms. Maria Buyco prepared the manuscript.

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* This means the true value of H lies between 0.1 H and 10 H with high confidence; if H = 0.01 there is very little chance that the true value is > 0.1.

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Uwe Wölcke

Selecting Existing Chemicals Under the Aspect of Occupational Hazards

Abstract

As an introductory remark the importance of the control of existing chemicals for occupational health purposes is emphasized.

The achievements of the Interagency Testing Committee under TSCA in the field of selecting existing chemicals for in depth review are referred to and the necessity of reconsidering the screening process in light of the different conditions of a supranational effort is indicated.

The demands resulting from occupational health aspects on the estimation of occupational exposure as an important part of the selection process are defined and illustrated by examples.

Possible consequences of such demands for the design of the selection process are discussed.

I am pleased to have been given the opportunity at this OECD workshop to illuminate the problem of selecting existing chemicals emphasizing the aspect of occupational hazards and to elaborate briefly on the possible consequences for the selection process when occupational aspects are to be incorporated.

In fact, as has been shown for asbestos, one of to-day's best understood hazardous chemicals, the working community belongs to those sections of the population which are most severely jeopardized by chemical substances capable of causing adverse health effects. Not infrequently workers are the sole target for chemical risks. It is therefore a moral and by the way well accepted obligation that the concept for the control of existing chemicals also meets the demands of occupational safety and health.

A more intense study of the selecting problem automatically leads one to the interesting work already achieved in this field by the Interagency Testing Committee installed in the United States under the Toxic Substances Control Act. The committee's work proves as an extremely fruitful basis for further discussion. (Unfortunately up to this afternoon I had no access to the Japanese undertakings in this field). Having followed the committee's efforts with great interest, I would characterize them with the term "integrated approach". Using this term I want to emphasize the fact that the ITC took into consideration the exposure probability of the environment, the public at large and the working population at the same time. The same holds true for the health effects side, where several effects were considered simultaneously. Furthermore it is obvious and has been stressed by the committee members themselves, that the ITC-exercises were strongly influenced by the short time schedule the committee had been granted to come up with lists of existing chemicals to be tested under TSCA.

Turning to the envisaged coordinated action of the OECD member countries it appears obligatory to evaluate the experiences already accumulated in the United States (and Japan) conceiving in a way their selection exercises as pilot studies and to transfer their experiences to the different premises of a joint venture. In this context the increase of resources for the selection of chemicals for detailed review and for their laboratory testing including the following hazard assessment and the absence of strict regulatory deadlines for the supranational undertaking are of primary importance permitting or even enforcing a reconsideration of the screening process itself for OECD purposes.

In a concerted approach of all OECD member countries it appears both desirable and feasible to start out from inventory lists of existing chemicals such as the TSCA Chemical Substances Inventory, the MITI-Inventory and the impending EEC-Inventory of

Substances on the Community market by 18th of September 1981 which form the basis of national or supranational regulations. Such an approach has been postulated before during the workshop. The tremendous overlappings to be expected between the various lists would have to be eliminated resulting in a merged inventory. The merged inventory would give us then a fairly good assurance not to have omitted important chemical substances even before selection criteria have been applied.

As a contribution to the reconsideration "how to select priority existing chemicals" I would like to concentrate now on the impact of occupational health aspects on the design of the process. Basically this impact is possible both on the definition of selecting criteria and on their sequence of application as filters to identify chemicals seriously suspected to be hazardous at the workplace.

As is true for other purposes there are two types of criteria: those indicative for exposure probability on the one hand and those indicative for adverse health effect probability on the other, simply because it is always the probability of hazard which determines the whole effort.

As part of an exposure probability criterion for the workplace the volume of production however appears not to be sufficiently reliable contrary to environmental exposure. This is for example shown by a chemical like dichlordimethylether which has always been produced at a rather small scale commercially and by small cohorts of workers, a compound which therefore would easily be missed in the screening process during the exposure scoring and ranking.

Using this example, I am of course aware of the fact that no matter how screening processes for large numbers of chemicals are designed one can always cite chemicals which are not properly identified. However dichlordimethylether, I am convinced, would be just a typical representative of a number of compounds not adequately evaluated for occupational exposure probability using production volumes. It is rather the handling of a chemical substance which in combination with certain physico-chemical parameters determines decisively exposure intensity, frequency and duration at the workplace. Consequently typified modes of handling divided by experience into classes of exposure should be used unless workplace exposure data are available for the compound in question or comparable chemicals together with the number of workers exposed. Compounds added in small quantities to cooling liquids which in turn are intensively inhaled as aerosoles in metal processing are another example to illustrate my point.

It is obvious that the application of a criterion as defined above increases the information need and the effort per substance and may therefore have its bearing on when such a criterion is being used with respect to other criteria within the screening process. The increased effort necessary probably caused the ITC under its special circumstances of operation to define the occupational exposure index differently.

With respect to the size of the initial listing it is certainly desirable for economic reasons to use those filters in the early stage of the process yielding valid results whilst requiring the smallest effort compared to other filters for assembling and evaluating the necessary data. In light of what I have said about the proper definition of an occupational exposure criterion however it becomes difficult to decide whether the exposure screening should be performed ahead of the biological screening or vice versa.

Perhaps it would be wise to decide the question of sequence from another point of view. To improve the aspect not to have overlooked any important chemical it may be appropriate as a true supplementation to the work already done by the ITC to in fact reverse the sequence that means to put the application of the effect probability

criteria ahead of the criteria for exposure probability. Following along this line the effort for the biological screening could possibly be kept within reasonable limits by concentrating single exercise on particular adverse health effects or effect-groups according to an established priority list for biological effects and by subdividing the biological screening into steps with increasingly demanding criteria.

Setting out from a merged inventory I am sure that many elements of the ITC approach would be maintained such as the use of formal criteria in the beginning to eliminate for example compounds which are sufficiently regulated or which have already been selected in the United States or Japan for detailed review or testing. Also compounds well characterized or considered inert like most of the polymers would be put aside.

The suggested reversal of part of the screening process would, because of the reduced list of candidate chemicals after the biological screening, allow independent exposure evaluations for occupational settings, the public at large and for the environment each of which sufficing the needs of the individual aspect. The chemicals obtained through these separate runs with hazard probabilities for workers, the general public and the environment would possibly have to be pooled and ranked for detailed reviews and laboratory testing.

I have submitted the specific needs of the occupational helath aspect with respect to the selection of existing chemicals discussing possible consequences for the screening process itself. In this context it appears of equal importance to me to consider both the already existing experience in the United States and Japan and the extended possibilities of a supranationally coordinated enterprise.

Bernhard Broecker

Contribution of CEFIC on the Problem of Selecting Priority Chemicals

Background

As far as we know today, there are somewhat more than 50,000 chemicals for commercial purposes on the market. However, only a limited number of these – perhaps 100 to max. 500 – are produced in large quantities of 50,000 t/a and more. The overwhelming majority of the commercially-available chemicals are produced in quantities of only a few tons per year.

The present level of knowledge concerning the toxicological and ecological effects of these chemicals differs extremely. In the case of many of the so-called "commodity chemicals" – that is, chemicals that are used in considerable quantities by a large number of consumers – we already have an adequate knowledge of the toxicological and ecological effects, although there are however gaps in our knowledge concerning a number of fields in isolated cases. On the other hand, we have comparatively little knowledge about some other chemicals, particularly some of those that are only produced in limited quantities for special purposes.

How many substances still have to be investigated?

According to findings from the inventory of the existing substances of the US EPA, one can assume that a large number of the substances that are available on the market belong to product classes that can be regarded as relatively innocuous. According to the findings, about one-third of the registered substances belong to the polymers, this means to substances which as such are in general not toxic or hazardous to the environment. About 20% are so-called UVCB (substances of *u*nknown or *v*ariable *c*omposition and *b*iological materials) substances; that is, substances that cannot be represented by a definite structural formula, because their consistents either change or are not known. Many of these substances are derivates of natural occurring products which are also in general not toxic.

The conclusion that the majority can be regarded as innocuous is also supported by the fact that many of these chemicals have already been on the market for some years without harmful effects of any kind having become known.

On the other hand, there can be no doubts that there are still considerable gaps in our knowledge, particularly as regards the long-term effects of chemicals; that is, the chronic, teratogenic and carcinogenic effects of certain product groups.

Also largely unknown is the ecotoxicological behaviour of many substances, in particular, their long-term effects on ecological systems. It is very difficult to make any statements concerning the gravity of the possible risks for man and the environment, as it is practically impossible to make even fairly accurate estimates of the number of substances that could possibly lead to harmful effects and what concrete risk actually results when the substances are used.

The responsibility of industry

The main responsibility for the safe handling of chemical substances lies with the manufacturers who, as producers, must make certain that information is available about the substances that they market so that they can be used for their proper pur-

pose by customers without endangering man and the environment. As a result, one frequently hears the opinion that the fact that one must expect an incalculable risk in the case of old substances because of a lack of knowledge of the effects chemical substances can be attributed to incorrect behaviour by the industry, so that the responsibility for recognizing the risk by carrying out the necessary tests lies solely with the industry itself. This approach is however wrong, for two reasons:

1. The fact that numerous old substances have not been adequately investigated to determine chronic effects is not due to the industry having been unaware of its responsibility; the reasons must be sought in the rapid progress that has been achieved in the field of toxicology but also in ecotoxicology over the past decades.

   Our knowledge, particularly concerning chronic effects has increased considerably over this period. This increase has come about due predominantly to an increased realisation of the foreseeable hazards from products but unfortunately in part also due to cases of damage as a result of the chronic effects which, up to that time, had remained unrecognized. Looking back from the year 1981, it is therefore completely unfair to accuse the manufacturers of having failed to meet their obligation to test their products in the past. It was absolutely impossible to foresee the hazards from the knowledge that existed at that time. A consciousness of such dangers only began to develop – also in industry – as further scientific progress was made. One must also remember that industry made important contributions towards these achievements.
2. The extent to which human health and the environment are actually endangered by industrially-manufactured chemicals is an extremely hotly-contested matter. It is however now generally accepted that most of the cases of cancer which can be attributed to the effects of chemical substances are not due to industrially-produced chemicals but are caused by cultural, behavioral and diet factors. Especially with respect to the third factor chemicals that occur in nature are of much more importance: one need only think of the nitrosamines, aflatoxins and benzypyrenes. To really eliminate the corresponding risks, one would not only have to determine the long-term effects of industrially-produced chemicals but also those of many chemicals that are found in nature.

Economic limits

Even when one assumes that only a small percentage of the substances that are available on the market still have to be investigated to determine their long-term effects, as we have done, the number involved is still so large that testing these chemicals would be beyond all existent financial resources and also impossible in view of the present numbers of scientists and analytical laboratories. The only choice that remains open to us is therefore to limit the number of chemicals to be examined and then to set priorities for the evaluation of old substances and first concern ourselves with only those substances of which one can say that a considerable risk cannot be excluded without further tests.

What is already being done?

At present, numerous governmental agencies and university departments but also the industry are engaged in the testing of old substances. I need only refer to the efforts in the USA, where old substances are being investigated to determine their long-term effects, particularly their carcinogenic and teratogenic effects, as part of the National Toxicology Programme. The Japanese government is also having old substances investi-

gated to determine what ecological risks they represent. An increasing number of countries has introduced legislation by which the manufacturers of certain substances can be obliged to test old substances in individual cases, when justification exists. The industry has voluntarily established numerous project groups, some of which are even international, to confirm or refute suspicions concerning certain chemicals by suitable tests.

What can OECD do?

In spite of the numerous efforts that are already being made, OECD attempts to achieve a certain division of labour in the testing of old substances can only be desirable from the industry's view-point. One should, however, be aware of the limits to which such an undertaking within OECD is necessarily subject.

The legal situation with regard to the testing of old substances differs greatly from country to country within OECD. I need only mention that the testing of old substances is a matter for the state in Japan, whilst the USA, France and the Federal Republic of Germany prefer to have the manufacturers arrange for the necessary testing at their own expense. There are also differences in the conditions under which governmental agencies in the various countries can order the performance of such tests. As there is no reason to expect that OECD member states will be able to achieve a uniform legal basis for the treatment of old substances within the foreseeable future, CEFIC's opinion is that OECD should not make any attempts to establish a general control mechanism for testing of existing chemicals.

On this reason CEFIC believes that OECD in no way should try to elaborate a further priority list. Besides the fact that already too many of these lists exist the responsibility for testing chemicals can only be with the national governments. CEFIC recommends therefore to confine OECD's rule to three main aspects:

1. Discussion of criteria for the selection of priority substances.
2. Co-ordinating function to avoid duplicative testing.
3. Agreement concerning which effects are to be investigated, elaboration of commonly accepted study plans, mutual acceptance of the results and, as far as possible, agreement on time schedules for the tests.

The decision as to how many old substances are to be tested each year and who is to bear the costs thereof can only be reached on a national basis. CEFIC believes that the industry should also take part in such testing. In view of the enormous costs that these investigations can give rise to, one must strictly reject a general obligation to investigate old substances unlimitedly. Each country must be left to decide what costs its industry can be expected to bear.

If, however, the OECD member states believe that OECD should also take over direct responsibility for testing the only possible solution which in CEFIC's opinion could be realized would be to set up a test programme to be financed by the member states.

From the viewpoint of CEFIC, I would now like to make a number of proposals concerning the selection criteria for old substances and possible approaches that could be taken in the individual countries.

Criteria for the selection of priority substances

The risk that is caused by a chemical substance depends on its effects and the probability of being exposed to them. These must therefore be the prime factors in making

selections. There is however a further fundamental question: the order in which they should be applied in selecting substances. There have been many proposals that one should first concentrate on those substances with which many people come into contact or which are emitted into the environment in large quantities. Such a selection procedure that is exclusively orientated to the probability of exposure, however, makes no allowance for the fact that an entire series of serious cases of damage involving chemicals were due to substances that are only manufactured in small quantities and only handled by a few people. Examples are dichlorodimethyl ether, propane sultone and hexamethylphosphoric triamide.

From the CEFIC's viewpoint, it appears more adviseable to take the effects of chemical substances as the first criterion and the probability of exposure as the second. At first, as already indicated, one should concentrate mainly on those long-term effects that can lead to irreversible damage, that is, the mutagenic, teratogenic and carcinogenic effects. Other effects, particularly the ecological effects, are of lesser importance in comparison with these. During the first phase, one should therefore limit the investigations to those substances that are seriously suspected of having irreversible long-term effects on the basis of the results of existent studies.

The CEFIC, however, assumes that studies have already been carried out, are in progress or are at least planned for most of these substances.

The next and far more difficult phase in the programme must therefore be the investigation of those substances for which we can only suppose a possibility of irreversible long-term effects in the light of present knowledge. The chemical structure should be taken as an indicator for carcinogenic and mutagenic effects (not for teratogens); that is, it appears advisable to concentrate on carefully defined classes of substances whose structural elements give reasons for suspicion insofar as compounds with similar structural elements have already proved to be carcinogenic or mutagenic.

The CEFIC is well aware of the fact that this approach based on structural analogy must be applied with extreme care. Above all, one must avoid the definition of unacceptably large risk categories that include a large number of chemically-related substances although many of them are completely innoccuous.

With the assistance of qualified experts some classes of substances should be defined, which are considered to have first priority.

The substances belonging to these classes must then be evaluated on this basis of further parameters. The pertinent criteria and their sequence of application is as follows:

- relevance of the respective structural elements
- exposure data (level of production, fields of application, physico-chemical properties);
- in the case of substances that could be emitted into the environment, details of their ultimate fate (that is, mainly their persistency and data concerning possible bio-accumulation);
- present knowledge of the toxicological effects of the substance.

At the present juncture, it is not possible to predict the extent to which fixed values can be allocated to the previously-mentioned criteria. The allocation of a certain number of points to the individual criteria and selection by means of a scoring system does however seem to be feasible in principle. A large number of proposals in this direction have already been made. CEFIC would be pleased if an OECD working party that has yet to be formed could concern itself with this question.

Possibilities of testing priority substances

As already stated, CEFIC does not believe that the OECD should set up its own priority list, using the given criteria. This must remain a task for the member states. The member states must also be left to decide who is to test the selected substances and who is to bear the costs thereof unless the OECD member states will finance themselves a testing programme within OECD. In view of all previous experience, CEFIC does however believe that only two models could prove to be feasible:

1. Testing carried out and also financed by the state (Japanese model). A similar approach could be used by member states for an OECD testing programme.
2. Testing carried out by the chemical industry on a more or less voluntary basis, (of course, if possible in agreement with the government), whereby the distribution of costs should be the subject of agreements within the industry, which of course, would ultimately be funded by the consumer.

All other approaches, in particular, the ordering of tests by the state for certain manufacturers will scarcely be feasible, because no sensible solution to the problem of the distribution of costs can be found.

OECD's task should be to ensure that only one state carries out the tests when various member states list one and the same substance, in order to optimalise use of the existent capacities. For the same reason, it will be essential to reach agreement on what is to be studied and the methods which are to be employed. If this is not done, there will be a danger of one and the same substance being tested a number of times, simply because some countries refuse to accept the results of testing or certain states regard other effects than those which have been investigated to be far more important.

Conclusion

CEFIC recognizes the fact that there are gaps in our knowledge concerning substances that are already available on the market, particularly concerning their long-term effects, and that these gaps must be closed. The state and industry must cooperate closely and do all they can to close these gaps.

CEFIC is in favour of industry participating in the corresponding programmes, but rejects the idea of imposing unlimited obligations on the industry. In view of the enormous costs, clear agreements must be reached concerning the volume of funds that will have to be provided to finance these investigations.

This decision must be reached on a national level, by the various member states, and cannot be a task for the OECD, unless the OECD member states will finance themselves a testing programme within OECD.

OECD should concern itself with the definition of suitable criteria for the selection of substances, with the elaboration of general accepted study plans, with the mutual acceptance of test results and should aim to prevent the testing of one and the same substance by different states. CEFIC is very happy to contribute to this work and is prepared to take active part in further discussion to achieve this objective.

STATEMENTS BY DELEGATES ON CHAPTER III

Willem Hans Könemann (Netherlands)

When preparing the dutch answers to the questions on selection procedures for existing chemicals, one very essential question arose. That question is whether it is necessary and useful to subject all about 60,000 chemicals to the same selection procedure.

It is obvious that we have very little information about most of these chemicals. Only for a few of them we know from experience or from extensive toxicological testing that they are principally harmless. A few other compounds are known to be harmful but for the majority of the chemicals we do not know whether they pose any hazard to man or the environment or not.

However, when we want to assess the hazard potential for all these chemicals, within a reasonably short period of time let us say 10 years, several problems arise. We think that it is necessary to consider for the hazard assessment of a chemical *a number of criteria in combination.* Of course a combination of *effects and exposure parameters* will be needed. The use of only one criterion seems to us not appropriate.

A certain minimum of information has to be available. Even in a large, internationally coordinated effort, it is not possible to collect enough information to enable an acceptable first assessment for such a large amount of chemicals. Extensive searching in literature, which is very time-consuming,is a first need, but even this will only reveal sufficient information for a small part of these chemicals. When, because of efficiency reasons, a more limited search procedure is used, even less information will be found.

In our experience, even for wellknown chemicals the available data bases give only part of the information on effects and on exposure which is necessary for a first assessment. This means that *much of the information, has to be generated by testing.* For so many chemicals, however, it will only be possible to perform a few screening tests and even then the capacity to perform all the necessary tests will not be available.

Another problem is that *screening* should not be directed toward the acute effects, but only *toward long term effects.* High acute toxicity will generally have been identified during the normal use of a substance unless it has a very low exposure potential. However, only very few screening tests are available, predicting long term effects.

In view of this lack of information about the vast majority of the chemicals and the limited possibilities to obtain the necessary information within a reasonable timeframe, our conclusion can only be that it is not possible to make an assessment of the hazard potential for all 60,000 existing chemicals. An approach using too little information will give rise to too many wrong hazard evaluations.

If not all 60,000 chemicals can be considered for the evaluation exercise the question remains, *how to select a smaller number* for which a more detailed hazard assessment is possible. Such a preselection of chemicals deserving special attention must reveal those which are more likely to cause any hazard than the others.

Such a procedure has not yet been worked out very well in the Netherlands, but I can give some indication of our approach: We think that, as a good start, those chemicals can be selected which *have been found with a certain frequency in the environment or* which have drawn some attention because *of adverse effects on man or the environment.*

Several lists of such chemicals exist e.g. for water and air pollutants. I can give some other examples. Particulary useful may be the Emission Inventory made in the Netherlands. This list gives the names of chemicals, or groups of chemicals, which are emitted into air or water in substantial quantities. The information for this list has been provided by industry under guarantee of confidentiality of the source of emission. Also the MAC list gives useful information on exposure potential since only for chemicals with a fairly high exposure potential these MAC values have been established. Moreover, for chemicals on the MAC list also a fair amount of information on mammalian toxicity exists. Quite useful are several lists of substances which are made in other countries for several purposes e.g. the OSHA list of potential industrial carcinogens and mutagens etc. From a series of lists of this type, which will of course show an overlap in the chemicals mentioned, we want to make a preselection of a few hundred chemicals. These chemicals will be subjected to a more detailed assessment.

We realize that inevitably a number of compounds, which are hazardous will be omitted when following this preselection procedure. Such chemicals may not have been recognized as such or may not have been found in the environment for instance because of analytical difficulties and may therefore fail on any list.

However, with a procedure which starts with a very large number of chemicals in our opinion probably still more hazardous chemicals will be omitted because of the lack of information or the superficiality of this information.

There is one additional reason for dealing first with chemicals which already have drawn some attention. For these chemicals there will be probably more social support for regulatory measures to be taken than for chemicals which have been mentioned as hazardous before. We must realize that the possibility and speed of regulatory reasons will probably be the rate-determining step in our effort to protect man and the environment against existing chemicals.

Helmut Kainer, Verband der Chemischen Industrie e.V. (Federal Republic of Germany)

It has been estimated that more than 50,000 chemicals are presently on the market. Most of them are manufactured, distributed and used in rather small quantities. Many of these chemicals have been known for many years and have not caused any major concern. It has to be recognized, however that there are gaps in our present knowledge which ought to be filled within a reasonable time. VCI, therefore, supports the idea that selected existing chemicals should be tested.

Risks emanating from a given chemical depend on various factors such as its *toxicological and ecotoxicological effects and also on exposure.* The latter itself is greatly influenced by several factors such as *production quantities, number of persons exposed, use patterns and existing regulations.* Some of these factors may vary considerably from country to country. Consequently, each country must be responsible for its own risk assessment and in the case of existing chemicals should have the freedom to decide which chemicals have to be tested with priority. This approach fits into already existing programs in some of the member states which provide for testing of existing chemicals either under the authority of the state or by industry or other institutions. Examples of such programs are Japan where selected chemicals are tested by the state itself. In the Federal Republic of Germany, the Berufsgenossenschaften (employers' accident insurance association) have, under their health programs, begun examining existing chemicals. These activities will form the topic of a separate state-

ment to be made by the Berufsgenossenschaft der chemischen Industrie. VCI is of the opinion that these activities of the Berufsgenossenschaft should be further developed and expanded to make a useful instrument for examining the health effects of existing chemicals in the Federal Republic of Germany.

It would be possible, without any great difficulties to supplement these activities by an additional program dealing with the environmental effects of existing chemicals, the latter programs being under the charge of the Umweltbundesamt, the German environmental protection agency.

We think that testing programs should be conducted by industry or other institutions on a national basis in the member states. What can and what should OECD do? OECD should focus and limit its activities on the following two important aspects:

1. Development of sound and scientifically based criteria for the selection of existing chemicals for testing;
2. Coordination of existing and future testing programs of the member states.

Scientifically based selection criteria could offer valuable assistance to national governments and industry, making selection of chemicals more specific and thus more productive. Such selection criteria may in the future also assist in monitoring long-term health effects not yet discovered, thereby stimulating adequate prevention measures. Rather than setting up priorities of its own OECD should list current test programs in the member states and keep a record of plans to undertake such programs. It would then be up to the member states to decide whether to participate in such programs or to start new programs for chemicals not yet tested. Thus, OECD could effectively help to avoid duplication of testing.

Joachim Oberhansberg, Berufsgenossenschaft * der Chemischen Industrie (Federal Republic of Germany)

Within the scope of its "Program for Preventing Health Hazards from Substances used in Industry", the Berufsgenossenschaft is concerned with drawing up a list of substances, in which "existing chemicals" are recorded which are suspected of posing a chronic health hazard to the employees.

For this purpose, substances are recommended for addition to the substance list on the basis of observations by the technical inspectors of our Berufsgenossenschaft as well as on the basis of proposals from elsewhere.

Addition to this list is done in accordance with the following criteria:

1. Only substances which are not on the Maximum Concentration Values-List (MAK-Werte–liste)
2. Only substances which are handled beyond the laboratory level
3. Only substances for which warnings of long-term effects are given

On the basis of these criteria, 45 substances have so far been entered into the substance list of the Berufsgenossenschaft of the Chemical Industry.

When deciding which substances to add to the list as well as when making the final evaluation, the Berufsgenossenschaft is advised by a consultant body which includes occupational physicians, toxicologists and chemists.

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* Employment Accident Insurance Fund

After a substance has been added to the list, it is checked by means of a data catalogue whose comprehensive details, e.g. physical-chemical properties, toxic properties, toxicological criteria, mode of action, occupational-medical experiences allow to characterize the substance with respect to the properties which are hazardous to health. In this matter, the following steps are taken:

- Literature research by a toxicological institute in order to determine how much data is available on the specific substances about their acute or chronic toxicity, but also, if applicable, references to mutagenic or carcinogenic properties as established in short-term tests.
- Evaluation of the results of this literature research by toxicologists.
- Decision about how to proceed, made by the honorary organs of the Berufsgenossenschaft of the Chemical Industry as recommended by the consultant body.

Depending on the result of this literature research the following steps are taken:

- If the tested substance is not hazardous, no further measures are necessary.
- If there is a strong indication of acute but above all chronic toxicity or else a confirmed suspicion of mutagenity or carcinogenity, these results are published and made accessible to the Deutsche Forschungsgemeinschaft's* Senate Commission for Testing Substances Hazardous to Health. At the same time, in the plants which work with these substances, the protective measures are checked and, if necessary, improved.
- If no confirmed statements on toxicity, mutagenity or carcinogenity ensue, then one must decide from case to case how to proceed in evaluating the substances, whether and which experimental studies are to be carried out in each individual case.

The Berufsgenossenschaft of the Chemical Industry and, beyond that, all industrial Employment Accident Insurance Funds are convinced of the importance of testing existing chemicals, since this is the basis for improving health protection on the job when handling substances used in industry.

The Berufsgenossenschaft of the Chemical Industry thus repeats its offer to share its experience and findings as well as its present and future activities in order to contribute to the testing of existing chemicals.

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* German Research Association

List of SUBSTANCES of the BERUFSGENOSSENSCHAFT DER CHEMISCHEN INDUSTRIE

Substance Nr.	Denomination	Name of Substance (IUPAC)	Synonyms	Trivial- and trade names
1	Ethylenthioharnstoff (ETU)	2-Imidazolidinthion	2-Imidazolidin-2-thiol, ETU	ETU
2	Aminoazotoluol (AAT)	4-Amino-2', 3-dimethyl-azobenzol	o-AAT, o-Toluolazo-o-toluidin, 4-(o-tolylazo)-o-Toluidin (CAS)	teilweise als Buttergelb bezeichnet
3	Aminogu: 'inbicarbonat	Aminoguanidinbicarbonat	Aminoguanidiumbicarbonat	
4	Ammoniumpersulfat	Ammoniumperoxydisulfat	p-o-Disulfosäurediamoniumsalz (CAS)	
5	Benzotrichlorid	α, α, α-Trichlortoluol	Phenylchloroform, Trichlormethylbenzol	Trichlormethylbenzol
6	p-t-Butylphenol	p-(tert.-Butyl)-phenol	1-Hydroxy-4-tert.-Butylbenzol	
7	γ-Butyrolacton	Dihydro-2(3H)-furanon	γ-BL	Butyrolacton, BL
8	Chloracetamid	2-Chloracetamid	2-Chlorethanamid	Chloressigsäureamid
9	p-Chloranilin	p-Chloranilin	1-Amino-4-chlorbenzol, 4-Chloranilin, 4-Chlorphenylamin	
10	5-Chlor-2-aminotoluol	5-Chlor-o-toluidin	2-Amino-4-chlortoluol, 1-Amino-3-chlor-6-methylbenzol, 3-Chlor-6-methylanilin	5-CAT
11	Diethylenglykol	Diethylenglykol	Bis-(2-hydroxyethyl)-ether, 2,2'-Oxydiethanol, Diglykol	DEG, Dicol
12	Di-t.-butylzinnchlorid	Di-tert.-butylzinnchlorid	tert.-Butylzinndichlorid	
13	3,4-Dichloranilin	3,4-Dichloranilin	1-Amino-3,4-dichlorbenzol, DCA	DCA
14	1,4-Dichlorbuten-2	1,4-Dichlorbuten-2	2-Butylendichlorid, trans-1,4-Dichlorbuten, 1,4-Dichlor-2-buten (CAS)	
15	Dicykan	4,4'-Diaminodicyclohexylmethan		Dicykan

Substance Nr.	Denomination	Name of Substance (IUPAC)	Synonyms	Trivial- and trade names
16	Dicyclohexylcarbodiimid	N,N′-Dicyclohexylcarbodiimid	Carbodicyclohexylimid, DCC, DCCI	
17	Dimethylaminosulfochlorid	Dimethylaminosulfochlorid		
18	Diphenyl	Biphenyl	Phenylbenzol, PHPH	
19	Hydrazobenzol	Hydrazobenzol	1,2-Diphenylhydrazin, N,N′-Bianilin	
20	Kerobit	N,N′-Di-sek.-butyl-p-phenylen-diamin		Kerobit
21	Maleinsäuredimethylester	2-Butendionsäuredimethylester	Dimethylmaleinat, DMM	DMM
22	N-Methyl-bis(2-chlor-ethyl)-amin	N-Methyl-bis(2-chlorethyl)-amin	2,2-Dichlor-N-methyldiethyl-amin (CAS), N-Lost, N-Mustard	
23	Monochloressigsäure	Monochloressigsäure	Chloressigsäure, MCA	
24	1,5-Naphthylendiamin	1,5-Diaminonaphthalin	1,5-Naphthyldiamin	1,5-Naphthylen-diamin
25	4-Nitro-2-aminotoluol	4-Nitro-2-aminotoluol	4-Nitro-o-toluidin, p-Nitro-o-toluidin	
26	5-Nitro-2-aminotoluol	5-Nitro-2-aminotoluol	5-Nitro-o-toluidin, 5-Nitro-2-amino-methylbenzol	
27	p-Nitrosophenol	p-Nitrosophenol		
28	o-Phthalodinitril	o-Phthalodinitril	1,2-Dicyanbenzol, 1,2-Benzodicarbonnitril	o-PDN
29	Tetrahydrothiophen	Tetrahydrothiophen	THT, Tetrahydrothiofuran, Thiophan, Thiolan	
30	Toluidinbase	3,3′-Dimethyl-4,4′-diaminodi-phenylmethan	4,4′-Methylen-bis(2-methylanilin), 4,4′-Methylen-di-o-toluidin	Toluidinbase

Substance Nr.	Denomination	Name of Substance (IUPAC)	Synonyms	Trivial- and trade names
31	2,4-Toluylendiamin	2,4-Diaminotoluol	Diaminotoluol, 4-Methyl-1,3,-benzoldiamin	m-Toluylendiamin
32	2,3,4-Trichlorbuten-1	2,3,4-Trichlorbuten-1	2,3,4-TCB	
33	Tris(2-chlorethyl)-phosphat	Tris(2-chlorethyl)-phosphat	2-Chlorethanol-phosphat(3:1), Phosphorsäure-tris-(2-chlorethyl)ester	
34	Vinylfluorid	Vinylfluorid	Fluorethen, Fluorethylen	VF, MVF (FVM)
35	Vinylidenfluorid	Vinylidenfluorid	1,1-Difluorethen, 1,1-Difluorethylen (CAS), VDF	VDF
36	Chlorameisensäuremethylester	Chlorameisensäuremethylester		
37	Dimethylaminopropionitril	3-(Dimethylamino)-propionitril	β-Dimethylaminopropionitril	
38	2-Chloracrylnitril	2-Chloracrylnitril		CACN
39	4,4'-Methylen-bis-(2,6-di-tert. butylphenol)	4,4'-Methylen-bis-(2,6-di-tert. butylphenol)	4,4'-Methylen-bis-(di-tert. butylphenol)	
40	Dioctyldiphenylamin	4,4'-Dioctyl-diphenylamin	4,4'-Dioctyl-N-Phenylanilin	
41	Dinonyldiphenylamin	4,4'-Dinonyl-diphenylamin	4,4'-Dinonyl-N-Phenylanilin	
42	Gallium	Gallium		Galliummetall
43	1-Chlor-2,4-dinitrobenzol	1-Chlor-2,4-dinitrobenzol	2,4-Dinitro-1-chlorbenzol (CAS) 2,4-Dinitrochlorbenzol	
44	3-Chloranilin	m-Chloranilin	1-Amino-3-chlorbenzol, 3-Chloranilin, 3-Chlorphenylamin	Orange GC Base
45	1,4-Naphthochinon	1,4-Naphthochinon		

Gerd Albracht, Deutscher Gewerkschaftsbund – IG Chemie-Papier-Keramik (Federal Republic of Germany)

As the only representative of the trade unions amongst a lot of representatives of the chemical industry I want to remind you that trade unions have always tried to strengthen the efforts in review and control of existing chemicals – recently within the framework of the European Communities Directive (79/831) and the German legislation on chemicals.

Summarizing our experiences – and I must say: harmful experiences – we must state that the use of certain substances at the workplace over a long period of years does not at all automatically mean that we have achieved a sufficient level of safety in this field.

Vinyl chloride, asbestos and many other substances which are cancerous or mutagenic are good examples of this kind of harmful experiences. The Deutsche Forschungsgemeinschaft has pointed out in a new study the risks of cancer for the workers in the industries which produce or use chemicals. The results of this study are alarming because they indicate that the risk of cancer is multiple higher for employees of the chemical industry than for the normal population.

The study refers to "existing chemicals":

- According to it 25 % of all cancer diseases, which happen to employees, originate from occupational factors.
- In an investigation comparing the death reasons of chemical workers with the death reasons of male population in same age, was the share of death by cancer in male population in the range of 20 %, but the share of employees of the reviewed chemical trust near 33 %.

But only less than 1 % of cancer cases are officially recognized as being caused by occupational factors.

The results and experiences of substances which have been used in industry for many years and are then found to be carcinogenic or mutagenic must be considered in contrast to the rather optimistic prognosis of the representative of CEFIC – Mr Broecker – about the "experiences with existing chemicals". The "Programme for Preventing Health Hazards from Substances Used in Industry" of the Berufsgenossenschaft was initiated by the pressure – and it was I recall strong pressure – of the trade unions reacting to the case of vinyl chloride and asbestos. But this programme does not cover environmental protection.

Furthermore, we know that many data on toxicology, medicine and epidemiology results are available in the chemical industry – but they are not available for government, authorities for the protection of health and environment, the workers and their unions.

The priority position which the question of confidentiality has over health and environmental protection does not allow any discussions and prevents exchange and coordination of the available data on existing chemicals which pose a problem.

A systematic review of these substances, which are especially relevant to practice, has to be the basis for an investigation about "problematic existing chemicals".

This review has to be carried out under an international sharing of costs and work considering the "principle of involvement".

Obviously it never caused either financial or 'sharing of effort' – problems to the international operating industry to carry through – in international co-operation – toxicologic and epidemiological studies on substances, especially of high economic relevance – e.g. ethylene oxide.

The trade unions support every effort towards an international co-operation to reveal and to minimize the risks of chemicals products posed to man *and* the environment.

The Environmental Programme of the Deutsche Gewerkschaftsbund supports these efforts on environmental risks to the same extent as those on health risks. But we feel that a good start can be made by reviewing the substances which may be harmful at the workplace.

The proposal of the Berufsgenossenschaft is in the opinion of the trade union at present not ratifiable. The Deutsche Gewerkschaftsbund considers this offer to be a short national step – but not as means of a systematic, methodical review of "existing chemicals", hazardous for men and environment.

Michael van den Heuvel (United Kingdom)

It is important to realize as Dr Somogyi pointed out, that toxic effects in man are unfortunately largely unpredictable. This presents problems in deriving criteria for setting up lists of chemicals for priority testing. Not generally in favour of lists – UK experience of such lists is that priorities change rapidly in an international context where inevitably things take longer to agree. I suspect that by the time a list was agreed it would already be out of date.

E. W. Langley (United Kingdom)

The United Kingdom believes that after selecting an existing chemical, but before further testing, a critical review of all available information should be made.

The UK Government and industry have been strongly opposed to the drawing up of arbitrary lists, which are often unscientific; UK industry has also declared its opposition to an international programme of testing without any clear indication of the need and final implications of actual risk and cost.

We heard much about factors influencing selection of chemicals but little or nothing about criteria for human health. The one common aspect of all schemes which has emerged is that at the end of the exercise the greatest reliance is placed on personal professional judgment. This is in line with the pragmatic approach used in the United Kingdom.

Michael J. Flux (United Kingdom)

The following points arise in relation to points made during this session but I was unable to make them in the time available.

Dr Brydon's case for an international (OECD) priority list contains an internal inconsistency. He accepts that because of local political and cultural considerations the final assessment of acceptable risk must be carried out at national level. However, those very same political and cultural views are the reason for different national priorities in the assessment of the chemicals themselves. Indeed, I would suggest that views on the priority for testing and the judgements about acceptable risk are very closely connected. If then you argue that you cannot get international agreement about risk

analysis then you must accept that no one international list will be universally acceptable.

Industry has been asked to say something about cost. This is so far difficult because we have not yet been told the cost of what (perhaps there may be more to be said under Topic IV).

However, one can say that it costs about £ 3 million to carry out a toxicological and ecological evaluation of a pesticide. It is extremely difficult to believe that much by the way of a worthwhile study on a "chemical about which nothing is known" for less than £ 1/2 million to £ 1 million.

On this basis the suggestion by Dr Nösler that OECD should carry out the testing against a priority list with a proposed budget of DM 5 million can be seen to be as a very limited programme which would allow the test of, at best, two substances per year.

Robert L. Bohon (United States of America)

I would like to call the conference attention to the very useful classification scheme derived by the U.S. National Academy of Science in its publication "Principles of Evaluating Chemicals in the Environment", page 227 (see Fig. 1).

This concise, long-to-understand-and-apply scheme emphasizes the interaction of

- chemical dispersal
- biological impact.

It also recognizes the increasing seriousness (and time need for more information) for effects on entire ecosystem functioning

vs

chronic effects at the level of the individual

vs

acute effects at the level of the individual.

This rating system (from 1 to 12) provides a possible "handle" on existing chemical screening for future international and/or national consideration for further testing or monitoring or both.

Jacques Exsteyl (Belgium)

Following to what I have said in the morning as Inspector of Labour in the field of industrial hygiene, may I enforce strongly what have presented Mr Roderick and Mr Somogyi in this context.

We need a model for managing the identification of risks. This model needs a conceptual approach (means) and an objective for identification of dangerous situations.

1. The conceptual means is a genial theory on the effects on health and environment caused by substances,
2. the model itself (operationally) must give the scientific and social men the possibility to detect effects on men and environment of new or not known substances in regard of known effects or results after short or long exposure to the action of known substances

Scheme for Classification of Chemicals According to Biological Impact and Dispersal

Chemical Dispersal	Biological Impact		
	High (1)	Medium (2)	Low (3)
(1) Widespread, high release	1	2	3
(2) Widespread, low release	2	4	6
(3) Localized, high release	3	6	9
(4) Localized, low release	4	8	12

NOTE: Low number indicates high priority.

the environment would have high priority and required extensive testing for biological effects.

The elements of biological impact listed in Table 11 are not meant to be all-inclusive, but they are indicative of the complexity of environmental problems. Table 10 reflects national or regional problems and priorities. In dealing with highly localized release of chemicals, several other factors might be considered:

- What receptors are close to the source?
- Which are the most sensitive?
- How important are they as a group?

Short-Term Tests on Individuals

Experiments of relatively short duration—from a few hours to perhaps 1 or 2 weeks—using high concentrations of the test chemical would be undertaken at this stage to determine the acute toxicity of a chemical

Factors Contributing to Biological Impact

Factor	Level of Importance		
	(1)	(2)	(3)
Toxicity	high	medium	low
Receptor importance	high	medium	low
Type of effect	Interference with ecosystem functioning	Chronic effects at the level of the individual	Acute effects at the level of the individual
Availability to organism	high	low	
Potential for biomagnification	high	low	
Stability and persistence	high	low	

NOTE: Low number indicates high significance.

Fig. 1

by identification a priori, this is the experimental approach with animal experiences

by identification a posteriori research of changes, lethal results on users by systematic control or on all the population living in a known environment.

So, this second means will be very useful and must always be used to describe a state – in the philosophical meaning of the word – of risks for men's health and for disturbance or change to the environment.

Heinz G. Nösler (Federal Republic of Germany)

There are a number of common elements in the contributions of almost all the speakers of the past two days:

1. It is very difficult to set up priority criteria for selecting chemicals for a priority list.
2. This work should be done together by authorities and chemical industry because industry has a lot of information and experiences about its chemicals.
3. Before setting up a priority list, all available information – published and unpublished – should be scrutinized.
4. The financial as well as the experimental resources are limited.

So far we are more or less in agreement. In spite of all the agreement I am, however, missing a long-term international concept to solve the real problem, and that real problem is the question: how will we get – internationally harmonized – the missing toxicological and ecological experimental data of suspicious chemicals? These data must be acquired and that costs a tremendous amount of money. The answer may be very easy for many people: industry has to pay; but the same suspicious chemical is produced by a lot of different companies in different countries.

There is, in my opinion, just one possibility to solve this problem: the OECD must not only concern itself with the establishment of priority criteria, the OECD itself has also to compile the priority list. But such a list wouldn't help anything, it would be the 10th or 15th priority list in the world. The decisive point is, the OECD also has to finance the investigations it deems necessary. Each OECD member country would have to contribute proportionately to its membership fee. This would constitute neither for the economically poor nor for the strong member countries an intolerable burden.

Let me demonstrate this with an example: Suppose it is decided to spend five million DM on such investigations every year. A small OECD member country would have to pay 1 %, equal to 50 000,– DM, in this case, the USA about 20 % = one million DM and the Federal Republic of Germany about 12 % = 600 000,– DM. Each member country may now pay this fee out of public funds or may try for a financial participation of its industry. In is my personal feeling that the latter should present no problem in most countries.

Each member country would receive the full data set after the conclusion of the investigation and would conduct a hazard assessment in its own national responsibility. The hazard assessment is a question of national political responsibility. The OECD can only work out Guidelines for hazard assessment, as it is done now by OECD.

Such an internationally harmonized effort would not only solve the financial problem but also that of the mutual acceptance of data.

This proposal may easily be misunderstood in the sense that industry tries to shed its responsibilities. However, I would like to emphasize that, in my opinion, industry

would be willing to finance the project. I am convinced that such an international effort constitutes the only means to provide a harmonized and long-term solution to the problem of existing chemicals.

Walter Niemitz (Federal Republic of Germany)

The Catalogue of Hazardous Substances in Water as an Auxiliary Means for Prescreening Existing Chemicals

The Federal Ministry of the Interior has recently published a so-called "Catalogue of hazardous substances in water" (Gemeinsames Ministerialblatt 1980, Nr. 26, S. 430–452). At present, this catalogue comprises only about 200 substances, but it may easily be enlarged. The catalogue serves as an aid to determine safety measures for accident prevention, above all in connection with storage and transportation, and classifies the chemicals by 4 classes, that is:

Class 0 – generally non-hazardous in water;
Class 1 – slighly hazardous;
Class 2 – hazardous; and
Class 3 – highly hazardous.

The evaluation for this classification was based primarily on the results of tests, namely acute toxicity for the rat, for fish, and for bacteria, plus biodegradability. The methods for determining these values are exactly prescribed and comparable, as far as possible, to the corresponding methods in the OECD Guidelines.

In principle, everybody is able to test and classify a substance as a precaution in accordance with the prescribed evaluation, but for the generalization of such individual classification a Commission has been authorized, consisting of chemists, biologists and toxicologists, nominated by the Federal Government, the "Länder" and the Industry, too. The Commission will classify the substances finally, considering all aspects described in literature and experiences as well as other dangerous properties such as chronic toxicity, carcinogenicity, mutagenicity, bioaccumulation, etc. In difficult cases, the Commission may suggest additional investigations before taking its decision.

In actual cases of decisions by Water Authorities, the first step will be the submission of the test results by the manufacturer concerned and their examination by the Water Authority. If the case is worth generalization or if the results are doubtful or if the Authority has the impression that such a simple evaluation may be imperfect, the Authority will appeal to the Commission for final decision.

All decisions of the Commission will be published sooner or later in new editions of the above-mentioned catalogue.

In this way it may be possible that within some years a lot of chemicals will have been roughly evaluated at rather small expense. Perhaps this will be a little contribution to the prescreening of existing chemicals.

Digby F. Gascoine (Australia)

The topic we have been discussing – that of the appropriate selection criteria for existing chemicals – is already a complex one, and further complication by introduction of an additional aspect may not be welcomed. Nevertheless, it is important that the economic aspect of selection criteria be taken up.

I am not referring here to the important question of the costs of obtaining further information necessary to a proper evaluation of existing chemicals, on to the overall resource constraint imposed by the finite availability of necessary facilities and expertise. Those are matters which have already been touched upon by industry representatives, and which Mr Welinder will address us on tomorrow. Rather, the concern here to the inclusion of an economic element amongst the selection criteria themselves.

Why is it appropriate to take account of economic factors alongside hazard and risk (which is a function of hazard and exposure)? The reason is that, from the point of view of the Community, we are not merely attempting to apply our additional testing and evaluation effort on existing chemicals in a way which would bring about the greatest reduction in the risk being borne by the Community. After all, as Peter Menke-Glückert told us yesterday, in our industrial societies risk-taking is built into our value systems. We take those risks willingly because they are outweighed by the benefits which we expect to receive. So, if we concentrate only on the reduction of risk, we may end up making decisions whereby risk is reduced, but it can be concluded that when we are making our first judgement on which chemicals we should make the subject of investigation, (a judgement inevitably based on inadequate information) then we should be taking into account also the importance of the chemicals from an economic point of view.

Indeed, it is more important that we look at this economic aspect in relation to existing chemicals than it is in the case of new chemicals, because a change in the regulatory regime applying to an existing chemical may lead to certain dislocation costs if as a result some reallocation of economic resources is necessary.

What economic factors are important? It may seem rather paradoxical, but what we are looking for, other things being equal, are the least important existing chemicals in economic terms (we are also looking for those chemicals for which the gap between the perceived risk associated with any chemical and the actual risk – which we would hope to determine by a new evaluation – is widest). Not surprisingly, there is no methodology ready to hand which will give us a quick, prior indication of the economic worth of any particular chemical. Such parameters as profitability and employment come to mind, but for various reasons it is not very likely that these characteristics could readily be obtained in respect of industrial chemicals.

There may, however, be some relevant indications. Other things being equal, we should prefer to investigate those chemicals for which we know there are close substitutes rather than those which are unique. Similarly, it may be preferable to give less attention (again, other things being equal) to basic chemicals which are inputs into many other productive processes than to other chemicals. These are, however, only very early thoughts.

Where does this line of thinking lead us? I do not believe it is possible at this stage to confidently predict what conclusions might emerge from further consideration of the economic parameter in selection criteria. Nevertheless, I do believe it important that we give this issue further thought.

F. Sherwood Rowland (United States of America)

Public opinion polls taken in the United States by the chemical industry in the last few years have uniformly shown that the chemical industry is viewed negatively by a

substantial fraction of the population. I speek frequently in public on some of the scientific aspects of environmental chemistry and am therefore regularly exposed to the question of anyone who chooses to come. From this point of view, let me make four one-sentence comments:

1. An important part of the public concern is directed toward the obvious current inadequacies of chemical waste disposal, a subject which is surely a part of the existing chemicals problem, but which has been barely mentioned in this workshop.
2. People believe that the effects on the general public have been omitted from the economic calculations which imply that testing on animals in the laboratory is more expensive than currently accepted procedure of testing on man.
3. People react that the EEC 30% production decrease for only one of the multiple uses of chlorofluorocarbons is a force, intended to give the impression of action where none exists.
4. People are not impressed by the depth of the commitment involved in a special CMA programme which has spent only 16,000,000 dollars since 1972, expecially when it includes "politically oriented activities". After all the $ 7,000,000 spent by CMA on research on chlorofluorocarbons since 1972 is approximately the value of the chlorofluorocarbons sold since this conference began 2 days ago.

It is my opinion that the current low public impressions of the chemical industry have many valid bases. Nothing I have yet heard at this conference leads me to expect a more favorable public impression of the chemical industry for at least a decade, probably two or longer.

Etcyl H. Blair (United States of America)

A Framework of Consideration for Setting Priorities for the Testing of Chemical Substances

Introduction

The magnitude of the number of commercial chemical substances and the limited testing resources pose a problem akin to the man who was asked how one could eat an elephant. He responded, "Simply, one bite at a time". We need to prioritize our testing efforts by focusing on those materials where the potential risk and hazard uncertainty are the greatest. In this presentation I will describe the problems that face us and an approach which will allow us to direct our efforts to those areas where the greatest benefit can be achieved.

Policy Considerations

A. The universe of substances to be considered:

Before attempting to discuss the need for testing or the importance of setting priorities, we need to understand the universe of chemicals we are considering. I tried to obtain such understanding by examining the U.S. Environmental Protection Agency (EPA) Toxic Substances Control Act (TSCA) inventory information which has been made available to the public. The data included in this collection include those materials submitted early in the reporting period and omits, of course, confidential information. The data used in this discussion was that made available by the EPA from the TSCA inventory. This data collection does not include all the materials on the inven-

tory and does not have production volume information when that information was claimed confidential. Since the production volume was reported in ranges, in this exercise an appropriate midpoint was used for each range – except that 1,000 pounds was used for materials reported as produced in quantities less than 1,000 pounds, and one billion pounds was used for those reported as being produced in quantities larger than one billion pounds. Nevertheless, it is adequate to provide a good picture of the universe of commercial chemicals.

As would be expected, we find that a small number of materials account for the bulk of the production volume. In this case, those materials produced in excess of 100 million pounds per year represent only 1.8% of the total number of substances reported and account for 98.9% of the total pounds produced. Lowering the limit to 10 million pounds adds 2.7% of the chemicals, so we now have 4.5% of all the substances and we increase the total volume represented to 99.7%. Going further to one million, we find that only 9.5% of the materials account for 99.9% of the total production reported (Table I).

To better understand these high-volume materials, we divided all those substances reported as produced in quantities of one million pounds per year or more into several categories such as organics, inorganics, polymers, etc. This exercise was most revealing. We found that those materials which can be classified as petroleum derivatives (gasoline, kerosine, distillation cuts, etc.) represent 10% of the total number of entries in the inventory, but account for 55% of the total production. The inorganics represented 12% of the materials and 12% of the production. Another 7% of the production is due to materials which are residues from the processing of ferrous metals. The saturated hydrocarbons (methane, ethane, hexane, etc.) were responsible for 7%.

We found that structurally well-defined organic substances, the materials we are most concerned about in testing, were the most numerous as they represented 34% of the inventory sample, but they account for only 6% of the total production. Polymers and plastics represent 24% of the number of materials and 3% of the total production (Table II).

Some institutions are giving some type of attention to the petroleum refining, metal or metallurgical substances. However, it appears that the U.S. EPA has either consciously or unconsciously leapfrogged those materials and began by focusing attention on organics and some of the inorganics. Thus, attention is being centered on some 1,307 substances which represent about 6% of the U.S. total production volume.

Table I. Volume Distribution. Entire EPA Inventory

Production Range (Lbs/Yr)	Number of Materials	%	Total Production (Million Lbs/Yr)	%	Cummulative Production %
$>10^{11}$	1	<0.1	102,000	2.5	2.5
$10^{10}-10^{11}$	95	0.2	3,119,000	76.5	79.0
$10^{9}-10^{10}$	216	0.5	656,000	16.1	95.1
$10^{8}-10^{9}$	436	1.1	155,000	3.8	98.9
$10^{7}-10^{8}$	1,065	2.7	33,800	0.8	99.7
$10^{6}-10^{7}$	1,983	5.0	8,140	0.2	99.9
$10^{5}-10^{6}$	3,798	9.7	1,720	0.04	99.98
$10^{4}-10^{5}$	4,689	11.9	225	0.01	99.99
$<10^{4}$	27,010	68.7	28	<0.01	100.00

Table II. Volume Distribution by Type of Substance (Produced in Excess of 1,000,000 Lbs Annually)

Type of Substance	Count	% Count	Production Volume Millions	% Volume
Petroleum, Primary Derivatives	380	10.0	2,258,000	55.4
Inorganics	452	11.9	503,000	12.4
Metals, Refining Residues (Ferrous)	20	0.5	281,000	6.9
Alkanes	21	0.5	272,000	6.7
Organics	1,307	34.4	246,000	6.0
Polymers & Plastics	893	23.5	122,000	3.0
Other	18	0.5	95,000	2.3
Coal, Primary Derivatives	30	0.8	90,500	2.2
Natural Products & Derivatives	254	6.7	84,200	2.1
Metals, Refining Residues (Non-Ferrous)	52	1.4	59,700	1.5
Organics, Variable Composition	287	7.6	27,000	0.7
Metals	24	0.6	19,600	0.5
Minerals	29	0.8	14,300	0.3
Alloys	13	0.3	1,600	0.04
Dyes & Pigments	15	0.40	133	<0.01
Living Organisms	1	0.03	1	<0.01
Total	3,796	100,00	4,074,000	100.00

The organic grouping exhibits the same volume pattern of production as the inventory as a whole. There were 3.3% of the organics produced in quantities in excess of a billion pounds, and this group represents 77% of the total organic production (34% of total). The 100-million to one-billion range represents 9.2% of the number and an additional 17.2% of the volume (Table III).

Obviously, testing decisions cannot be made on the basis of volume alone, but certainly the higher-volume materials deserve early scrutiny and consideration.

B. Current state of knowledge of health and ecological effects:

Most of the commodity organic chemicals have rather complete data bases, although knowledge of certain effects may be missing. For the small-volume organic chemicals, health and environmental data bases are sometimes non-existent or limited to a knowledge of a few physical properties that may impact health and environmental effects.

Table III. Volume Distribution of Organic Substances (Production Volume >1,000,000 Lbs/Yr)

Production Range (Lbs/Yr)	Number of Substances	%	Total Production (Million Lbs/Yr)	%
$>10^{10}$	7	0.5	97,830	39.8
10^{9}–10^{10}	36	2.8	91,141	37.1
10^{8}–10^{9}	120	9.2	42,273	17.2
10^{7}–10^{8}	383	29.3	11,249	4.6
10^{6}–10^{7}	761	58.3	3,086	1.3
Total	1,307		245,580	

Since many of the commercial chemicals have been in use for decades, it is apparent that major health and ecological effects should have been observed and reported in the literature if such effects occur under historical conditions of manufacturing and use.

Generally there appears to be concensus that testing to determine the health and ecological effects of many commercial chemicals should continue. However, the resources available for such testing are limited. In addressing this challenge of testing needs vs resource limits, it seems obvious that priorities for testing programs will have to be established.

C. The need and purpose of testing:

Testing is intended to provide knowledge of the health or environmental effects of chemicals in terms of both the nature of the effects and the dose-response relationship. With this knowledge and an estimate of exposures, one can establish means to manage risk in manufacture, process, use and disposal of chemicals.

The main purpose of testing is to *reduce the uncertainties* about effects for our assessment of the risks in manufacturing and using chemicals. Thus, priorities for testing must focus on gaps in the data base of the group of chemicals under consideration and judgment of the degree to which the uncertainty may be reduced by filling each of these gaps.

An important distinction needs to be drawn. Risk management is usually based on knowledge of health and ecological effects or presumptions about these effects – plus a value system that acknowledges some acceptable level of risk. In contrast, testing and research is aimed at expanding the data base. Setting priorities for testing is a process distinct from management of risk. This discussion deals only with the setting of testing priorities.

It is important to define terms in addressing testing priorities:

Risk is a two-component term and can be defined as the probability of an *adverse effect*(s) occurring under a condition of *exposure* or a set of exposures.

Hazard is the description of the adverse effect (e.g., cancer, neurological disorder) and the dose-relationship. It is frequently expressed as the potential for injury either in qualitative terms or in a quantitative sense with qualifications on the uncertainties.

Testing yields information to characterize the hazard component of risk. Exposure can be estimated by the use of monitoring data, environmental release data and modeling systems.

Table IV. Volume Distribution of Inorganic Substances
(Production Volume >1,000,000 Lbs/Yr)

Production Range (Lbs/Yr)	Number of Substances	%	Total Production (Million Lbs/Yr)	%
$>10^{10}$	17	3.8	348,731	69.3
10^9–10^{10}	35	7.8	112,934	22.4
10^8–10^9	89	19.7	36,443	7.2
10^7–10^8	133	29.5	4,375	0.9
10^6–10^7	178	39.2	775	0.2
Total	451		503,258	

Table V. Volume Distribution of Polymers and Plastics
(Production Volume >1,000,000 Lbs/Yr)

Production Range (Lbs/Yr)	Number of Materials	%	Total Production (Million Lbs/Yr)	%
$>10^{10}$	1	0.1	78,593	64.3
$10^{9}-10^{10}$	9	1.0	22,400	18.3
$10^{8}-10^{9}$	40	4.5	13,251	10.8
$10^{7}-10^{8}$	204	22.8	5,476	4.5
$10^{6}-10^{7}$	693	71.6	2,462	2.1
Total	893		122,182	

D. The need to set priorities:

Global limitations on toxicological and ecological testing capacities, coupled with increasing demands for statutorily-prescribed testing of new substances, make it possible for only a very few existing chemicals to be investigated each year. It is therefore necessary for a selection process to be established to prioritize substances to be tested. By one process or another, every institution with a testing program establishes priorities. Frequently the processes are informal.

Prioritization of which chemicals to test, careful assessment of the extent of testing on a chemical and avoidance of duplicative testing are essential in order to obtain the most effective use of limited and valuable resources. Because many chemicals are produced in more than one country, it may be desirable to appraise the division of testing among nations and to determine the extent of duplication.

The Role of the Organization for Economic Co-operation and Development (OECD)

A. OECD should not establish priorities:

Mandatory priorities should not be imposed by supernational governments or organizations on manufacturers or users of chemicals in the foreseeable future. Such action would disrupt existing approaches and be very difficult to manage effectively. In addition, many national governments lack statutory authority to implement this activity.

Table VI. Volume Distribution of Primary Derivatives of Petroleum
(Production Volume >1,000,000 Lbs/Yr)

Production Range (Lbs/Yr)	Number of Materials	%	Total Production (Million Lbs/Yr)	%
$>10^{11}$	1	0.3	102,171	4.5
$10^{10}-10^{11}$	51	13.4	1,847,835	81.8
$10^{9}-10^{10}$	85	22.4	266,906	11.8
$10^{8}-10^{9}$	91	23.9	36,241	1.6
$10^{7}-10^{8}$	96	25.3	4,376	0.2
$10^{6}-10^{7}$	56	14.7	272	<0.1
Total	380		2,257,799	

Existing institutions should carefully define their present roles and determine what their role might be in relation to related priority-setting bodies. Their efforts could be greatly enhanced by the existence of a consensus framework for priority-setting and the existence of a reliable clearinghouse of information on current testing and established priorities. Let me expand on these points.

B. Institutions already establishing priorities:

It is important to recognize the important role played by several types of institutions in establishing testing priorities. In a sense, the actual programs of institutions involved in testing represent the current priorities of important segments of society. Mr McCollister has described the current testing efforts by a number of organizations, and that information need not be repeated here.

While none of these institutional approaches may span the entire universe of chemicals, each represents important segments of industrial and societal interest. Any international efforts on prioritization should enhance, not undermine, the existing institu-

Table VII. Major Substances. Production Volume (Million Lbs/Yr)

Organics		Inorganics	
20,046	Propylene	49,174	Sulfuric Acid
19,021	Ethylene	31,723	Calcium Oxide
13,837	Benzene	30,618	Ammonia
13,203	Urea	29,565	Sodium Hydroxide
11,306	Butylene	29,413	Carbon Dioxide
10,383	Toluene	19,169	Hydrogen
10,036	Ethylene Dichloride	18,498	Chlorine
8,603	Xylene	18,125	Sodium Carbonate
6,716	Ethyl Benzene	17,073	Phosphoric Acids
6,500	Vinyl Chloride	16,311	Nitirc Acid
5,944	Methanol	15,127	Ammonium Nitrate
4,928	Styrene	13,519	Sulfur
3,881	1,3-Butadiene	13,136	Ammonium Phosphate (2 : 1)
3,838	Acetic Acid	13,068	Aluminum Oxide
3,793	Ethylene Glycol	12,326	Calcium Hydroxide
3,351	o-Xylene	11,583	Calcium Carbonate
3,045	Cumene	10,304	Carbon Monoxide
3,006	Ethylene Oxide		
2,961	Formaldehyde		

Polymers and Plastics		Primary Derivatives of Petroleum	
78,593	Cellulose Pulp	102,171	Gas Oil (Middle)
5,191	Polyvinyl Chloride	99,525	Atmospheric Tower Residuum
4,963	Polyethylene	93,700	Vacuum Residuum
3,622	Butadiene/Styrene Copolymer	82,381	Kerosine
2,107	Poly (Ethylene Terephthalate)	80,856	Gas Oils, Heavy Vacuum
1,915	Polystyrene	78,582	Naphtha, Heavy Straight Run
1,245	Polypropylene	76,400	Gas Oils, Straight Run
1,161	Urea-Formaldehyde Polymer	73,960	Naphtha, Light Straight Run
1,113	Phenol-Formaldehyde Polymer	71,230	Naphtha, Light Catalytic Reformed
1,082	Polybutadiene	69,140	Naphtha, Light Catalytic Cracked
		68,135	Naphtha, Heavy Catalytic Reformed
		66,310	Naphtha, Sweetened
		65,875	Naphtha, Heavy Catalytic Cracked

tional approaches to prioritizing and testing of chemicals. Stated another way, any international efforts, if needed, should recognize the need to continue existing efforts. Further, as a matter of general principle, any international effort should start from the premise that considerable knowledge is already available on the effects of some existing chemicals.

C. The unfilled needs in setting priorities:

1. Lack of understanding of prioritizing process

There is a lack of understanding and consensus of the process of setting priorities and the factors to be considered in setting these priorities.

Varied approaches are used by different groups in setting priorities. In some cases, panels of highly-qualified, interdisciplinary experts drawing upon experience and peer discussion make the final selection of priorities. Assemblage of the available data base for consideration is varied. In some instances rather complete service dossiers may have been assembled. In other approaches, considerable reliance may be placed upon scoring or screening systems which attempt to display readiliy-available information. (For example, ranking of production volumes as a surrogate for exposure.)

Although there is general agreement that both the hazard potential and the exposure potential need to be considered, many approaches to priority-setting seem to lack desired objectivity. It can also be said that existing institutional approaches not only have areas of overlap but also sometimes fail to prioritize testing needs on a broad international basis. It is possible that the OECD could provide a framework for establishing priorities for testing. National and institutional priority-setting bodies could then use this framework to set their course of action in a more objective and coordinated manner.

2. A clearinghouse to communicate established priorities

Those setting priorities for testing spend considerable time assessing whether the work they propose would be duplicative of work already in progress. Furthermore, fact collections and dossiers prepared by one institution may be of considerable value to another body which is setting priorities.

A clearinghouse would minimize duplicative efforts in preparation of fact collections and dossiers and in testing programs.

It would be logical, then, that an international body should undertake the function of serving as a clearinghouse of information on health and ecological testing currently being done as well as planned. Such a clearinghouse could also collect the established priorities for testing of the various institutions conducting testing. The availability of this information would allow institutions to establish their own priorities, taking into consideration the efforts of others and avoid unnecessary duplication.

The Process of Setting Priorities

In setting testing priorities, there are a number of factors which must be considered in order to arrive at meaningful conclusions. These factors will be discussed individually.

A. A screening process:

Any prioritizing body must define its interest sphere in terms of chemicals of interest. For example, a manufacturer may well confine his interest to those materials he

produces or uses as raw materials. A national government may want to consider all the chemical substances manufactured, processed or used within its territory. However, the prioritizing body must first understand the nature of the universe of substances it is considering, as this understanding will have a significant influence on the process and criteria for setting priorities.

Once a universe of chemical substances has been identified and characterized, a selection or elimination process must be applied to focus on those materials which should be considered for priority testing. The U.S. EPA Interagency Testing Committee developed a methodology which has been used by the committee to identify candidates for recommendation for priority testing under TSCA. Industry has reviewed this process and has offered modifications which are the basis of a general screening process for commercial chemicals, which is summarized here and described in detail elsewhere.

A generalized screening process would consist of a series of steps which would successively reduce the number of materials under consideration to a rather small and manageable group. These steps are:

1. Identification of the starting universe of chemicals.
2. *Volume Considerations* – All those materials which are produced over a given threshold are included for further consideration. Those which fall outside the threshold are eliminated.
3. *Current Status* – The remaining materials are reviewed, and those materials which are currently under test are scheduled for testing, or those which have been adequately characterized or controlled are eliminated from further consideration.
4. *Biological Scoring* – On the basis of readily-available information, the materials remaining are scored by a panel of experts on the basis of lack of data and reasonable suspicion of causing a health or environmental effect.
5. *Exposure Scoring* – Those materials which were scored in Step 4 as probably needing testing are then scored on the basis of their potential of general and occupational exposure. Those materials which were deemed to present a significant exposure potential would be retained.
6. *Comprehensive Data Acquisition* – As the previous steps are taken, the need for additional information becomes apparent. The screening has now eliminated enough materials that an extensive effort to obtain and analyze all the available information about this selected group is feasible. This step would produce detailed dossiers on each of the substances.
7. *Refined Scoring* – The biological and exposure scoring described earlier would be repeated using the complete information obtained in Step 6. The substances which emerge from this step would then be the candidates for consideration for priority testing.

B. Priority setting:

Typically, the dossier of a chemical will show gaps in data. These gaps can be considered as voids that may need to be filled by testing. Simplistically, among the groups of chemicals under consideration, the chemicals with the greatest number of gaps and the greatest exposure potential would receive priority consideration.

Realistically, however, priority-setting is more complex. Expert judgment, utilizing analogy and experience, is necessary to assess qualitatively the most sensitive toxicological or ecological effect likely to be of concern, and for this effect(s) it is necessary

to estimate the amount of uncertainty in risk on the basis of existing data and on the anticipated results of further testing.

A panel of experts would be expected to take into consideration the accumulation of experience with a given substance, including past exposure as well as current steps being taken, to control the exposure to the substance. A substance which has been produced in significant quantities over a long period of time with no known adverse effects would be of less concern than a substance whose production is rising rapidly and for which there is little experience. If the exposure to a substance has been reduced through changes in production or use patterns, that substance should also receive less attention than one over which no control is exercised. When available, epidemiological data should be considered along with animal data.

The expert panel can bridge the information gaps of concern for a given chemical and provide a qualitative ranking of those risk uncertainties which are to be clarified by testing. This case-by-case approach will be directed by the basic interests and mission of the institution conducting the prioritizing of the substances. Thus, we see here an approach for selection of substances based on a well-defined procedure for narrowing the overall universe followed by case-by-case consideration by appropriate experts.

In the U.S. it has become apparent that the number of materials which need to be considered for priority testing is such that, even after the screening approach described is applied and case-by-case selections are made, it will require our combined resources the next five to ten years to adequately fill the data gaps so identified.

Such prioritization is needed to assure that scarce testing resources are focused on those materials of greatest concern.

Summary

The magnitude of the number of commercial chemical substances and the limited testing resources available require that testing be done in such a way that it is focused on those materials where the potential risk and hazard uncertainty is the greatest. The OECD can best serve its member countries by developing a framework for the determination of priorities for testing to be used by those institutions which will be responsible for the testing and by establishing a clearinghouse of information about current and planned testing and existing testing priorities. It would be inappropriate and counterproductive for the OECD to impose mandatory priorities in the foreseeable future. There are many institutions who are actively pursuing the testing of commercial chemicals according to priorities dictated by their policies and objectives. An impressive amount of work has been done. Any international efforts on prioritization should enhance, not undermine, the existing institutional approaches.

CHAPTER IV

Identification of Resource Needs for Testing and Evaluating Existing Chemicals

Albert Sabroe Welinder

A Survey of Resource Needs for Testing and Evaluating Existing Chemicals, Based, in Part, upon the Results of the Questionnaire Circulated by the Host Country.

Introduction

The question which this presentation tries to answer is the following: What are the resources needed to test and evaluate existing chemicals in one thorough process, which for each chemical gives the information required to estimate the health and environmental hazards connected with the chemicals' use and, where necessary, to serve as technical documentation for regulating existing or planned use of the chemical.

In principle, this evaluation of resource needs for testing and evaluation of chemicals should be quite simple, since the figure asked for obviously is obtained by multiplication of the cost of testing and evaluating one chemical by the number of chemicals to be tested and evaluated.

And since the questionnaire circulated by the host country asked each participating country to estimate

- the number of chemicals considered to be dangerous to health and to the environment and
- the average costs and the range of costs as well as the time period required for the laboratory investigations necessary to verfy or dispel the dangerous nature of each chemical,

this multiplication should be relatively simple to perform.

The replies to the questionnaire indicated the number of dangerous chemicals to be:

1.000– 5.000 dangerous to the environment and
500–10.000 dangerous to man.

Average figures would be approximately 3.000 and 1.000 respectively.

The costs of testing are estimated to fall in the range of 10,000 to 2,000,000 DM, with testing times ranging from a few days to several years. The average cost comes to approximately 650,000 DM. Consequently, the total cost for testing seems to end up around 4,000 x 650,000 DM, which equals 2.5 billion DM. Add to this the cost of evaluation and reporting, which by conservative estimates add at least 25 % to the test cost figure, and the total cost ends up at approximately 3 billion DM.

This figure is, however, of a rather uncertain nature. This is so partly because few estimates are available – only around one-third of the questionnaires contain cost or number estimates, and only some of their replies contain both – and partly because most of the replies cover very wide ranges of cost and manpower figures. On this background, it becomes of interest to consider alternative estimates of resource needs. One such estimate developed from more basic principles and using other sources of information, mainly in the form of reports from government agencies and institutions and from international organizations, including much of the work presently going on in the OECD Chemicals Programme.

I should like to stress the fact that this alternative estimate is *my* best guess. The fact that it is based on cost figures, of which many are reasonably accurate, does not necessarily mean that the synthesis of these figures is closer to the truth than the average given above. Consequently, the main advantage of this model may well be

that the assumptions behind the calculations can be presented in a way which will make it possible to repeat the calculations, using different figures as appropriate.

The presentation falls in two parts:

First, a test flow diagram is developed, and secondly cost estimates are developed and combined with the flow diagram to give the total cost estimate.

The following prerequisites should be kept in mind:

- the presentation deals with industrial chemicals only (e.g. drugs and pesticides are excluded),
- the test flow diagram is based on principles of tiered testing, as developed in particular in parts of the OECD Chemicals Testing programme and in the EEC 6th amendment;
- decisions to stop or continue testing are made on the basis of exposure and effects in combination;
- the final product of the testing and evaluation should be a document, which, in combination with national exposure information and legislative practice, can be used for regulatory purposes.

2. The test flow scheme

The test flow scheme, chosen for this presentation, as shown in figure 2, falls in four parts:

- screening and selection of chemicals for evaluation;
- base testing and review;
- level one testing and review, and
- level two testing and review.

This test flow scheme means that some of the chemicals selected will be tested only through the base level, others will go through level one, while a third group will go through level two as well.

Assuming that the total number of existing chemicals is fixed at the starting point – new chemicals being tested and evaluated under some notification system – the test flow scheme can be considered as respresenting a fixed amount of work. This, however, holds true only to the extent that a level one or two testing requirement does not lead to withdrawal of a chemical and retraction of the testing requirement, or, that the exposure to chemicals tested through the base level or level one does not change, since increasing exposure may necessitate further testing.

In this flow scheme, the difference between chemicals presenting health hazards and environmental hazards – the so called category A and B chemicals – is apparent mainly in level two testing. Category I chemicals – the sufficiently well known chemicals – leave the test scheme after level one or level two testing.

a. Screening and selection of chemicals

The first part of the test flow scheme comprises the screening of all existing industrial chemicals and selection of possibly dangerous candidates.

The possibly dangerous chemicals are selected from a list of chemicals in commercial production at around 1980 (EPA or EEC inventories similar lists), i.e. from among 45–50,000 chemicals, according to principles discussed yesterday:

Criteria for selection are

- exposure data (e.g. quantity produced, use pattern),

– toxic effects criteria (e.g. acute toxicity, ecotoxicity),
– persistence criteria.

Toxic effects and persistence may be evaluated from structure/activity data.

Assuming a selection method can be developed from the methods described yesterday and presently used in i.a. Canada, Japan, USA, it is estimated that 5–10% of the chemicals are selected.

(For comparison: In Japan, 2140 priority chemicals have been selected from the list of 24,000 existing chemicals; in USA, approximately 2500 chemicals have *so far* been selected; in Switzerland, approximately 10,000 substances are considered dangerous).

Consequently, 2500–5000 chemicals are selected for testing and evaluation. The chemicals selected may represent a health hazard and/or an environmental hazard.

The fact that a number of existing chemicals are presently included in one or more priority lists and testing and review of these is underway does probably not affect this estimate, since the number of chemicals on existing lists is relatively small, compared to the number of existing chemicals.

b. Basic testing and review

This phase consists for each chemical of the following parts:

– readily available information is collected,
– base level testing is performed, and
– the chemical is evaluated.

It is assumed, that

– an evaluation requires testing equivalent to MPD and additional toxicity and ecotoxicity, as an example corresponding to the mandatory parts of annex VIII, stage 1, of the 6th amendment notification system (including a 90-day toxicity study): The testing required at this stage will in principle be fixed, but should not duplicate earlier studies or existing knowledge of obviously good quality. This may lead to "overtesting" of a few chemicals; a disadvantage which is probably offset by the advantage of not having to discuss the necessity for one or two of the tests in the package for each and every chemical, and will probably also make the review process easier; also, one should always bear in mind that it may – especially at this level – be cheaper to repeat a test, using adequate, modern test guidelines, than to use scarce resources e.g. in the form of expert reviews, to find out if existing data are "good enough". On this, quality criteria for existing test data would seem to be desirable;
– for each chemical, the information available before testing and of sufficiently high quality on the average is limited, covering part of the physical chemistry, one of the acute toxicity studies and a fish toxicity (this assumption is based on very limited evidence from notifications received in my agency, on experience from the working party on dangerous substances within EEC, and, to a limited extent, on information reportedly submitted with PMN's to US EPA). This point of view is not in agreement with earlier speakers; a better knowledge seems desirable;
– a hazard assessment, taking into consideration the information obtained and the exposure, gives as a result that 10% of the chemicals needs no further testing. (This assumption is difficult to qualify; it is expected, that the percentage stopped here will be quite small, e.g. because limited testing on bio-degradation and -accumulation is included on this level).

The consideration of the amount of information available does cover the fact that for some chemicals, all the information required to write the final chemicals report is actually available. It is estimated that the number of such chemicals – the class I chemicals – is small.

Based i.a. on the IARC summaries of carcinogenicity evaluations – which is actually only one of several possible health hazards – it is assumed that class I contains no more than 200 chemicals representing a health hazard and probably no more than 100 chemicals representing an environmental hazard. This again means that category I chemicals do not present significant savings in the total cost estimates.

c. Level one testing and review

On this level, all remaining (2,200–4,500) chemicals are taken through a battery of ecotoxicity and toxicity tests, consisting for each type of a mandatory set of tests and a set of additional tests to be chosen from a larger number of tests. This level should include screening tests for health hazards of a more specialized nature, e.g. neurotoxicity, as well as a chronic toxicity study. Similarly, long-time exotoxicity as well as accumulation – degradation studies will be included.

It is assumed that it will be necessary to take all chemicals through both types of tests to give sufficient information for evaluation.

It can be argued that this approach may lead to overtesting of a large number of chemicals. But it can also be argued that this approach will actually prevent overtesting, in the form of unnecessary repetition of work already done.

If testing and evaluation of existing chemicals is to be carried out by some sort of international mechanism, it is to be expected that various interest groups will have very valid reasons to follow the work closely, and the whole exercise will suffer seriously, if these groups can show that essential chemicals have not been tested, that doubtful test methods have been used, or that reasonable suspicions, which could have been resolved by one more test, have in fact been left unresolved.

Consequently, the test flow scheme suggested here should select a relatively large number of chemicals for testing and reject relatively few of these before they have been tested through level 1.

Another consequence of this, from my point of view, is that it is of paramount importance to the success of a project of this nature that the whole process is carried out with full public access to the information developed.

It is assumed that 25–50% of the chemicals are found to require no further testing, and that of the remaining, 1/3 represents a health hazard, 1/3 represents an environmental hazard and 1/3 represents both types of hazard. This assumption cannot be qualified, except possibly by studying the experience from the testing of pesticides.

d. Level two testing and review

On this level, the testing required will depend to a large extent on results obtained from the level one testing. It is assumed that the chemicals representing a health hazard will have to be taken through at least a second lifetime rodent study, and that chemicals representing an environmental hazard will be tested for bioaccumulation, biodegradation and possibly for effects in simulation studies.

As a result, the flow scheme means that:

50,000 chemicals are screened,
2,500–5,000 are tested on the base level,

2,000–4,500 are tested on level one and
1,500–3,500 are tested on level two; of these,
500–1 200 are tested for health effects,
500–1 200 are tested for environmental effects and
500–1 200 are tested for both.

3. Cost estimates

The costs for testing and evaluating a chemical on each level are determined as follows:

A. Screening and selection of chemicals

Based on the assumption that the collection and evaluation of volume, health and environmental effects data by manual or database search takes the equivalent of 1/2 man-month per chemical, a cost of 5,000 DM is estimated.

By comparison to the time actually spent, in our experience, for collecting and evaluating data on potentially dangerous substances, this figure seems low. It is expected, however, that this phase can be performed, using computer search and evaluation procedures to a relatively large extent, and it is assumed that this will keep costs relatively low.

B. Basic testing and review

The costs of MPD (or the base set of the 6th amendment) is estimated at app. 100,000 DM (corresponding estimates are available from Germany, from European industry and from EPA, whereas UK estimates are somewhat higher). The information available does not on the average reduce this figure significantly.

Based on cost estimates for the tests included in the 6th amendment, it is expected that the additional testing will add approximately 150,000 DM to this.

It is estimated that the evaluation of tests takes as a minimum one man-month or the equivalent of 10,000 DM. This figure is supported e.g. by experience within this agency.

Consequently, the phase B cost per chemical is estimated at approximately 260,000 DM.

C. Level one testing

This level can be estimated on the basis of cost figures from European industry for annex VIII tests and US EPA estimates for chronic health effects testing.

On the basis of this information, the cost for testing on this level is estimated at a minimum of 700.000 DM and an average of 900.000 DM. For the calculations, the average figure is used.

It is estimated that the review on this level takes at least 3 man-months per chemical, adding another 30.000 DM to the costs.

D. Level two testing and review

On a similar basis, it is estimated that health effect testing costs average around 1.000.000 DM, and environmental effect testing costs average around 100.000 DM. The average testing cost figure for this phase, consequently comes to approximately 750.000 DM.

Again, the review phase adds another 30.000 DM to costs.

4. Total cost estimates

On the basis of the figures given above, the total cost can be calculated as shown in figure 3:

Phase	No of chemicals tested	Cost per chemical, testing/review	Total cost mio DM
A	50.000	5.000	250
B	2.500–5.000	250.000/10.000	650–1.300
C	2.000–4.500	900.000/30.000	1.600–4.100
D	1.500–3.600	750.000/30.000	1.000–2.800
			3.500–8.500

It should be mentioned, that the total cost figures have been calculated by the assumption that type I chemicals, numbering between 100 and 300, carry review costs only in phases C and D. It should be mentioned, that the type I chemicals are included in the range calculations to give the type II chemicals range as 1.700–4.100 and 1.300–3.500.

On the basis of these figures, a total cost estimate in the range of 3.5–8.5 billion DM is found.

This figure should be qualified in two respects:

Firstly, the lower limit, 3.5 billion DM, is certainly a very low limit, mainly because the number of chemicals selected in the initial screening process is low, comparable to what is already in many countries selected as potentially dangerous, existing chemicals.

Secondly, the upper limit, 8.5 billion DM, may not be the upper limit, e.g. because the cost of testing on the highest level may go considerably beyond the average figure of 750.000 DM.

In addition, two features should be mentioned:

Firstly, the initial screening process is not of major importance to the total resource need; consequently, a more detailed screening, which reduces the number of substances carried forward, may result in significant cost reductions.

Secondly, what weighs heavily, is – besides the level II uncertainty – the number of substances taken through chronic toxicity testing. Consequently, the development of screening tests and decision criteria, which reduce the need for chronic testing, would be of major importance.

On this basis, and with reference to the 3 billion DM figure obtained from the questionnaire, I would suggest that the resource needs be estimated as follows:

The total cost of testing and evaluating existing chemicals will fall in the range of 3–10 billion (3.000–10.000 million) DM.

Whether the total cost ends at 3 or 10 billion depends, among other factors, on

- the uncertainty accepted in a hazard assessment (since this determines the number of chemicals selected in the screening phase and the extent of testing);
- the harmonization and cooperation obtainable (since this will determine the amount of double testing), and
- the general acceptability of the project.

Consequently, better estimates require the making of assumptions which are considered beyond the scope of this presentation, but certainly need to be studied more closely.

It is not possible to estimate the needs for laboratory facilities, for test animals and for manpower.

The timescale will, since the testing of one chemical through all levels may take 5–6 years, probably not be less than 10 years from the start of the screening phase.

It is at this point interesting to compare the results presented here to the conclusions of a study, carried out for the OECD Chemicals Secretariat by a consultant, and made available to me by the Secretariat. I should like to stress that what is presented in the following is not in all cases the actual data of the study, but figures calculated there from and, consequently, is presented on my responsibility.

This study, from slightly different presumptions, ends up with a total cost figure for the testing of existing chemicals, which is equivalent to 2.000 million DM.

The main reason for the difference between this figure and the range given above is, that a smaller number of chemicals are tested above MPD level.

What is much more interesting is the comparison to the volume of testing being performed already. The study estimates that the chemicals industry and the contract research organizations in Europe in 1980 undertook a total of approximately 600 million DM of testing work for the European chemicals industry, while the testing capacity is estimated to be close to 800 mio DM/year. This corresponds to 3.5 % of the estimated R and D costs of the European chemical industry.

85 % was work concerned with pharmaceuticals, pesticides and food additives, while 15 % was concerned with industrial chemicals.

The study concludes, that the increasing industrial chemicals testing, which results from the MPD concept and from the existing chemicals programme as described, in other words increasing from the present day level of 90 mio DM to 175 mio DM in 1986 means that the existing capacity will be exceeded in 1984 and then will have to grow by 11 % over a two-year period. In the same period, the annual growth of business volume will vary between 6.5 and 3 %.

In other words: Because the testing industry is occupied to a limited extent only with industrial chemicals, it can accomodate rapid growth in the testing of existing chemicals. Consequently, the testing resources to carry out an existing chemicals project over a 10 to 15-year time scale seem available.

To this, I should like to add two final comments.

One is that it is interesting to note, that if the level of testing given above, using a figure of 3 billion DM, is distributed between OECD member countries, according to the usual scale of contributions, and carried out over a period of say 15 years, the annual cost to a relatively small, chemicals importing country like the one which I come from, does not seem unreasonable in comparison to the benefits from a really thorough testing and evaluation of existing chemicals.

The other is that a project of this type cannot be seen in isolation. To our way of thinking, it would not be acceptable to have too many well-described, dangerous chemicals in unregulated use. In other words, as soon as the testing and evaluation project gets started it will be necessary to start the work needed to ensure, that the knowledge gained actually results in reduced hazards to health and to the environment from society's use of chemicals.

Donald D. McCollister

Resource Needs for Selection, Evaluating and Testing Existing Chemicals as Illustrated by Present National and International Institution Programs

Introduction

The Business and Industry Advisory Committee to OECD appreciates the invitation by the government of the Federal Republic of Germany to attend this workshop dealing with the legal, administrative and scientific issues important to the control of existing chemicals. Also, we appreciate the opportunity to present a statement on behalf of the international chemical industry as represented through the BIAC Chemicals Committee.

Background

The Business Industry Advisory Committee was designated as one of several non-governmental international organizations having „consultative status" when OECD was created in 1961. Thus, BIAC is the officially-recognized instrument for communication of the management sector of international business and industry to OECD programs. Since 1961 various trade and economic-oriented groups and committees have maintained an effective interface for BIAC with OECD with mutually beneficial results. Beginning in 1974 OECD consolidated its environmental policy and mandated its current Environment Committee from which followed the OECD Chemicals Division. The Chemicals Testing Program followed by activities under the Part II program inspired and resulted in the formation of the BIAC Chemicals Committee.

BIAC Chemical Committee membership is open to all OECD member nations and currently includes representatives from 14 OECD countries. It functions primarily to assist OECD and working groups involved with the chemical group and management committee programs. It endeavors to study all relevant documents concerning the program (and progress of said programs) and to produce proposals, comments or opinions on matters which it considers to be of importance to the chemical industry.

Selection and Testing Programs for Existing Chemicals

Any statement implying that the chemical industry knows little or nothing about the existing products it currently markets constitutes a myth, not the real situation. "State-of-the-art" testing programs have been carried out for many years. These programs began with the determination of oral, inhalation and dermal toxicological properties needed for precautionary labeling as to safe handling, use and medical attention in case of exposure, and for classification for packaging and shipment according to transportation codes.

Both industry and the authorities have generated satisfactory information that was considered adequate at the time about acute and subacute toxic properties. Much experience also has accumulated on long-term risks and exposure effects including, for many chemicals, no effects observable in spite of long-term exposure. Such experience, when adequately observed, should not be discharged lightly, in spite of the fact that many industrial chemicals have not been tested, or not adequately tested, according to present-day scientific standards. The science of experimental toxicology and ecotoxicology has developed substantially in the last decade. As a result of this development, we are faced with a large backlog of work. However, progress has been made.

Presently, many national and international institutions (including the chemical industry) are testing "existing" chemicals largely on a voluntary basis. These organizations have programs which also have resulted in lists, or priorities, for evaluation and testing. The BIAC Chemicals Committee has concluded that a brief review and some specific examples will provide important illustration of this fact, and will provide background information helpful to this workshop's discussion and decisions.

National Science Foundation (NSF)

As early as 1974 the NSF began investigating "the establishment of priorities which will hopefully guide future environmental and human health research on manufactured organic chemicals". A workshop was held and attended by prominent chemistry and toxicology scientists who reviewed data on the production, use, disposal, properties and toxicity of candidate chemicals assembled on the basis of a list ranked according to the annual amount of the chemical lost during manufacture, plus the quantity entering non-intermediate dispersive use patterns. A supplementary list was formed as judged by panel members to be of present or future concern because of a known or suspected hazard potential. The total list numbered 340 chemicals. After an indepth analysis, a final group of 80 compounds were placed in a dual listing of priority chemicals: 1) on the basis of environmental impact (biotic) and, 2) on the basis of human health hazards. Of the "top ten" chemicals in each ranking list, only benzene, carbon tetrachloride, chloroform and polychlorinated biphenyls appeared as priorities based on *both* environmental and human health hazards (Annex I).

USA Toxic Substances Control Act of 1976 (TSCA)

Section 5 of TSCA provides the US Environmental Protection Agency with substantial authority to require testing of existing chemicals based either on judgment that: 1) the substance *may* present an "unreasonable" risk of injury or 2) that exposure conditions are such that there is a substantial potential for human exposure, either by quantities which will enter the environment or that production volumes are substantial.

The Interagency Testing Committee (ITC) established by Section 4(e) of TSCA has recommended 42 substances or categories of chemicals for priority consideration. The procedures utilized by ITC include priority factors as follows: 1) quantitiy manufactured, 2) quantity which will enter the environment, 3) number of exposed persons and duration of exposure, 4) exposure level for exposed persons, 5) relation of chemical structure to known toxicants, 6) any data on effects on health or environment, 7) whether testing will develop useful data and, 8) availability of facilities and personnel for testing.

The TSCA inventory of existing substances numbering some 55,000 chemicals was used to produce an initial list of 1877 chemicals by selecting only those of high production volume (greater than 2 million pounds, or 1000 tonnes, per year). Then, a three-step process of preliminary screening, exposure scoring and ranking, and biological scoring and ranking reduced the list to the current number of 107. This exercise was carried out by groups of technical experts using numerical scoring for a large number of exposure and biological effect indices. Each of the current 107 chemicals have been assigned to a contractor for development of indepth literature and gathering of other available information. A document will be produced entitled "Hazard Information Review" on each candidate (Annex II).

International Program on Chemical Safety (IPCS)

A joint IPCS/CEC Task Force on Priority of Industrial Chemicals met in Ispra, Italy November 17–19, 1980. It is understood that the participants established criteria for selection of priority chemicals from a list prepared by the IPCS Secretariat. A qualitative evaluation based on potential for actual exposure and judgment of adverse effects posed to human health and/or the environment was utilized by the expert working groups. For the purpose of the IPCS program, including criteria documents, non-human environmental reviews, etc., 19 chemicals were selected in addition to the 33 already programmed for the World Health Organization. It was noted by this task group that the priority chemical selections were usually based on mammalian toxic effects, physical chemical properties, accumulation/degradation and persistence in the environment, entry/dispersion/distribution within the environment, amounts manufactured, population affected, toxicity to terrestrial and aquatic organisms, damage to property and impact on climate and weather (Annex III).

European Chemical Industry Ecology and Toxicology Centre (ECETOC)

ECETOC (Brussels) has produced a short document on priorities for choosing which chemicals to test. This is intended mainly as a guideline for use by member companies making judgments for their own product chemicals. Briefly, this document recommends an initial screening based on consideration of chemical structure, physical-chemical properties and already publicized evidence causing suspicion. This would be followed by subsequent consideration of human and environmental exposure at manufacturing, use and customer sites, pattern of use, pattern of disposal, and review of the toxicity and ecotoxicity information available. Once it is determined that data are lacking, then ECETOC is in a position to initiate organization for joint sponsorship of testing. Emphasis is placed on the importance of carcinogenicity, mutagenicity and teratogenicity tests.

ECETOC is also initiating a scheme known as JACC (Joint Assessment of Commodity Chemicals). Under this scheme member firms will pool and exchange information on and assessments of the toxicity and ecotoxicity of chemicals. Again, they would attempt to identify major data gaps leading to priorities for filling these gaps by appropriate testing. The ECETOC Scientific Committee has chosen the following chemicals for a trial run: dioxane, methylene chloride, melamine, methyl ethyl ketone, hydrazine.

USA Chemical Manufacturers Association (CMA)

CMA's Special Program was started on a modest scale in 1972. When petitioned by one or more manufacturers, CMA can develop an appropriate charter for a testing program which would be conducted under the CMA "umbrella" with costs borne by companies with an interest in the chemical. Seventeen programs were underway by the end of 1978. There are now 20 chemicals or categories being covered. Project types are varied from research to more politically oriented activities involving interaction with regulatory agencies up to and including litigation in the courts. The latter, designated as "advocacy programs," have involved the benzene standard for worker exposure from the Occupational Safety and Health Administration, and the fluorocarbons use restrictions by the Environmental Protection Agency. Examples of chemicals in the testing program include allyl chloride, benzene, epichlorohydrin, ethylene dichloride, phosgene, phthalate esters, styrene, titanium dioxide and vinyl chloride (Annex IV).

USA Chemical Industry Institute of Toxicology (CIIT)

CIIT is an independent "not for profit" organization dedicated to the scientific, objective study of toxicological problems from the manufacture, handling, use and disposal of commodity chemicals. A large scientific testing facility is owned and maintained by CIIT at Research Triangle Park in North Carolina. CIIT's testing, research and training programs are supported by 36 member companies representing 85 % of the USA chemical industry's production. CIIT has a current list of 40 priority commodity chemicals. These were selected on the basis of their physical volume, physical and chemical properties, estimated human exposure, toxicological suspicion and opinion, public interest and significance to society. Eight chronic toxicity studies have been completed on the chemicals ethylene, toluene, aniline hydrochloride, dinitrotoluene, terephthalic acid, maleic anhydride, methyl chloride and formaldehyde (Annex V).

Chemical Industry Consortiums

Voluntary testings have been undertaken by groups of chemical companies who have perceived a need for the health and safety testing of specific chemicals judged important to their companies. Examples of these are studies of trifluoroethylene, acrylates and acrylyic acid, methacrylates, ethylene oxide (26 chemical companies participated) and propylene oxide (10 European-based chemical companies are cooperating).

The so-called "Berufsgenossenschaft Chemie" a body within the self government of the German Chemical Industry controlled 50 percent each by employers and employees – organization has established since 1977 a programme for the prevention of hazards for the health by chemicals used at the work place. In the frame of this programme existing chemicals which have shown some potential hazardous effects or are considered suspicious regarding their long-term effects will be evaluated. So far 38 chemicals have been selected which are not presently in the reviewing process with the aim to set up testing programmes.

It is anticipated that there will be a substantial increase in the voluntary cooperative efforts by groups of companies either as independent consortiums or under the banner of a recognized trade association, but the selection more and more will likely be influenced by governmentally-derived "lists" which spotlight the need for testing consideration (regulatory demand).

USA National Toxicology Program (NTP)

NTP was organized through the USA Department of Health, Education and Welfare and combines all the research and testing components of the Food and Drug Administration, National Cancer Institute, National Institute of Environmental Health Sciences and the National Institute of Occupational Safety and Health. It is undoubtedly the most grandiose government-sponsored (and financed) program of testing of chemicals of public health concern. The chemical selection process involved each government agency proposing testing initiatives with the principles of selection being: 1) estimated or known extent and intensity of human exposure, 2) estimated or known severity of toxic effects and, 3) scientific needs to compare testing methodologies and to study structure-activity relationships. A selection of a chemical commits the NTP to: 1) ascertain specific toxicologic and regulatory concerns, 2) evaluate adequacy of existing data (or current efforts) and, 3) propose and conduct specific tests that are needed. As of July 1979, chemicals have been selected for specific types of testing,

for example, teratology (12 materials), mutagenic assays (18), and lifetime bioassays (106 chemicals). Lifetime bioassays were in progress on 146 other chemicals. At the end of fiscal year 1980, NTP had 234 compounds in various stages of a two-year bioassay process.

The NTP program is viewed by the US government as relating to the responsibility of the private sector to bear the burden of chemical testing as mandated by specific federal requirements. Therefore, NTP has decided to develop and provide a set of principles (or guidelines) for assistance in selecting chemicals for testing, and has awarded a 2 million dollar contract to the Board of Toxicology and Environmental Health Hazards of the National Research Council. NRC has established a "Committee on Priority Mechanisms for Research on Agents Potentially Hazardous to Human Health" which will use the TSCA inventory list of 55,000 substances as a starting point. The charge to this committee is to estimate the number of chemicals in the marketplace of compounds for which toxicity data are needed, to rank compounds for which there is no biological data, plus an evaluation of all current priority ranking systems. All of these ranking systems are to be evaluated with the objective of developing one that is functional and broad in scope. Five major elements are to be used: 1) degree of exposure stability when influenced by such factors as environmental transport, bioaccumulation, secondary uses and production volume, 2) profile and size of population exposed, 3) toxicity, metabolic pathways and mechanism of action, 4) management and control technology including manufacture, transport, use and ultimate disposal and, 5) potential costs of correcting or reversing an error in terms of human health and welfare, environmental quality and economy (Annex VI).

Summary and Comparison of Existing Institutional Approaches

Nature of Prioritized Chemicals

Lists of chemicals prioritized for testing and/or currently under test from the national and international institution activities which have been summarized above are attached to the text of this paper prepared for publication in the Proceedings of this Workshop. We have not attempted an indepth review or summary comparing the chemicals by specific names. Obviously, however, there is much duplication and overlap. As a general impression it can be said that the aromatic organohalides comprise a large percentage, followed by the oxygen types (oxides, ethers, phenols, alcohols, acids, aldehydes, ketones) then the aromatic, the amines, and finally with lesser amounts of nitrogen-phosphate compounds and sulphur-containing compounds. Not only has a large amount of work been done to prioritize and test chemicals, but the number of materials scrutinized also is quite impressive.

Priority Selection Procedures and Criteria

The selection of priority chemicals for testing would appear to have been based upon a number of implicit criteria, varying somewhat according to the specific objectives intended. The more important criteria in use appear to have been a measure of exposure (either indirectly based upon volume of production or estimated environmental release), physical chemical properties and known (or suspected) toxicological properties. These were the major criteria used by the International Program on Chemical Safety, USA TSCA Interagency Testing Committee, USA National Toxicology Program and National Science Foundation. Trade association procedures, such as those of the Chemical Manufacturers Association and the Chemical Industry Institute of Toxicology, are influenced significantly by nominations of chemicals of interest from

member companies. These are most likely to be commodity (non-proprietary) materials of large tonnage which have been the subject of some public concern and are of social significance.

The use of production volume as an indirect estimate of exposure seems to have been useful particularly when reducing a large list of chemicals (55,000 TSCA inventory of existing substances). It is also apparent that the larger volume production materials are those of greatest economic importance, and those which will support with least financial strain the economic burden involved with the cost of testing. In any event, the likely exposure to man or the environment of a chemical, and its biological and toxicological effects, must be considered very early in the selection process.

Structure-activity relationships have been mentioned as an important aspect of a selection procedure, particularly by groups of scientific experts making predictive hazard evaluations or rankings and when the known toxicological properties of the specific chemical are somewhat limited. Some attempts have been made to include chemicals of low market volume which may be important in priority lists of chemicals. This has been most effective by the use of narrow, carefully defined structure-activity relationships, in delineating possible potential carcinogens. It should be recognized that advances in the toxicological "state-of-the-art" are not as yet adequate to provide substantive guidance by SAR to produce other toxic effects, e.g. teratogenesis.

Costs of Health and Safety Testing

Although costs have not been mentioned specifically up to this point, it would seem obvious that testing is extremely expensive. Presently, the cost of long-term chronic effects testing alone can range from five hundred thousand to one million dollars per chemical. Perhaps 15 to 20 years ago, before the advent of more recent high annual rates of inflation, the entire spectrum of mammalian toxicology tests believed appropriate by both industry *and* government could be acquired at the cost of approximately one million dollars. By 1975, testing for all toxicology, ecotoxicology and environmental fate effects (based upon requirements for chemicals used as pesticides) were estimated as costing 8–10 million dollars.

Available examples of costs involved with some of the testing programs which have been presented above include the fact that the National Toxicology Program in the USA for fiscal year 1979 had a budget allowance of 41 million dollars. The USA Chemical Manufacturers Association, which has now reached the level of 20 chemicals in its special projects program, has accumulated an expense of 16 million dollars. The Chemical Industry Institute of Toxicology has received total contributions by 36 companies of 27 million dollars. The annual budget for operating and research expenses now lies between 9 to 10 million dollars per year. Building of new facilities and training of scientific personnel are expensive and time-consuming.

In recognition of such costs and considering limitations imposed by the availability of trained personnel, facilities and test animals only a relatively small number of chemicals, whether new or existing, can be subject to testing programs each year. In such circumstances, these limited resources must be employed efficiently and every advantage realized from previous experience.

General Views of the BIAC Chemicals Committee

As yet, the international chemical industry through BIAC (or any other group) has not developed any position encompassing detailed principles and procedures for the selection, testing and/or control of existing chemicals. Pending further elaboration by the

OECD Chemicals Group as to the structure and objectives planned for their future programs on existing chemicals, we will make only a few general remarks at this time.

All responsible segments of the chemical industry accept the obligation that adequate health and safety testing be carried out on its products, and as we have pointed out a substantial amount of testing and other programs have been carried out to meet these obligations. Some countries have already started programs. In other countries programs should be expanded, or even begun. The chemical industry will continue to ensure that its products are tested. "Gaps" must be filled, but it is important that these be carried out in the most cost-effective manner. Any governmental mandated program must recognize the limitations which make it possible to test only a relatively small number of new and existing chemicals per year, and that these must be selected with the best information and expert knowledge available. With this in mind, therfore, it would seem advisable that primary attention be directed to the study of chronic, carcinogenic and reproductive effects.

For many chemicals of national or international importance, and those of non-proprietary nature which become of public concern and social significance, government may well have to bring this need to the attention of industry for their assessment. If necessary, government itself may have to invest in undertaking of testing sponsorship as its own obligation. At the least, such a concept would seem to warrant careful evaluation by individual national governments.

Role of an International Organization Such as OECD

The role of the OECD will become more certain depending upon the influence which the recommendations of this workshop, sponsored by the Federal Republic of Germany, may have on the future programs of the OECD Chemicals Group and Environment Committee. OECD involvement would have to be undertaken with the careful consideration of its relationship to national governments or agencies, the United Nations Organization (WHO/UNEP) and other institutions involved in setting priorities and/or testing of existing chemicals. Perhaps it should restrict itself to braod policy questions, and undertaking the establishment of "guidelines" for the selection of priorities from the universe of chemicals to be considered. The actual selection should be left to national governments and to institutional programs, some of which are already underway with chemical industry support. Also, chemical manufacturers must be free to decide on and carry out their own testing programs according to national laws and regulations.

Another possible role for OECD would be that of providing a mechanism functioning as a "clearing house" for consolidating and comparing lists of chemicals prioritized for testing by national governments, institutions and the private sector (the chemical industry). Communication of information about chemicals tested, under test and of highest priority for testing would assist both governments and the international chemical industry with efficient management of their own testing programs. Finally, the same type of information could be communicated by OECD to other international organizations such as the EEC, WHO/IPCS and IARC which are concerned with harmonization programs.

Interpretation and Use of Test Data

The number and quantity of chemicals manufactured or imported by OECD countries varies considerably. It is important therefore that decisions on how chemicals are to be regulated within a given jurisdiction be left to the competent authority within that country.

The assessment of test data for new chemicals is presently being investigated by the OECD Step Sequence Group and is not yet complete. Undoubtedly, the recommendations of this expert group will have some influence on the assessment of existing chemicals. Through these and other efforts, OECD should continue to ensure harmonization of test procedures and the mutual acceptance of data.

Depending on whether a chemical is produced domestically or is imported, the supplier of information to government will be either the domestic producer or the importer. It should be recognized that two classes of importers exist; those associated with established companies who are knowledgeable about the product being imported and brokers who are selling a product they know nothing about.

It is important to avoid damage to domestic producers that both the type and quantity of the information requested by government be the same in all cases. To safeguard commercially sensitive information we recommend that government obtain its information directly from the producer or the importer as the case may be. Failure to supply legally required information would mean forfeiting the right to market in that jurisdiction.

Conclusions

In view of the world-wide limitation on toxicology and ecotoxicology testing capacities which in addition are being increasingly blocked by the statutory prescribed testing of new substances, it is only possible for a very restricted number of existing chemicals to be investigated each year. Prioritization of what chemicals to test, careful assessment of the degree of testing on the chemical, and avoidance of duplicate testing are essential in order to obtain the greatest effectiveness for the limited resources.

Many institutions have already established priorities and actual program of testing. An impressive amount of work has been done. This experience provides strength upon which to build for the future. Any international efforts on prioritization should enhance, not undermine, the existing institutional approaches.

ANNEX I

National Science Foundation

Table I. Research Priority List of Organic Compounds Considered to be Hazardous to the Environment and Human Health

Compound	Priority rank		United States production * (millions of pounds)	Estimated annual release rate (millions of pounds)
	Environmental impact	Human health hazard		
Dichlorodifluoromethane	1	32	439.2	445.8
Trichlorofluoromethane	2	28	299.6	274.1
Polyhalogenated biphenyls (Aroclor 1254)	3	9	30.0	30.3
Carbon tetrachloride	4	5	967.7	60.0
Chloroform	5	7	234.7	38.7
Hexachlorobenzene	6	25	1.3	1.32
Ethylenedinitrilotetraacetic acid, tetrasodium salt	7	75	64.3	65.3
Hexachlorobutadiene	8	23	8.0	7.3
Benzene (chemical uses)	9	1	8,937.1	89.4
1,3-Dichloropropane, 1,2-dichloropropane mixture	10	43	60.0	60.6
Nitrilotriacetic acid, trisodium salt	11	72	85.0	14.3
Methylchloride	12	45	453.5	16.7
Zinc di(butylhexyl)phosphorodithioate	13	58	67.0	68.0
Ethylene dibromide	14	3	315.5	304.4
Benzidine	15	4	N.A. *	N.A.
Dodecylbenzenesulfonic acid, sodium salt	16	80	364.1	369.6
Nitrobenzene	17	27	551.2	19.3
N.N. Dimethyldodecylamine oxide	18	22	35.0	36.1
Vat blue dye # C(7.16-dichloroindanthrone)	19	63	2.9	3.0
Silicone fluids (dimethyl polysiloxane)	20	65	74.7	75.8
Tricresyl phosphate	21	6	50.2	43.4
Phenol	22	46	1,915.5	47.0
Ethylene dichloride	23	40	8,600.0	458.0
1.1.1.-Trichloroethane	24	21	440.7	284.5
Chlorinated parafins (35–64% chlorine)	25	48	48.8	50.3

Table I. – continued

Compound	Priority rank		United States production * (millions of pounds)	Estimated annual release rate (millions of pounds)
	Environmental impact	Human health hazard		
Dimethyl tephthalate	26	49	2,167.3	32.5
Dioxane	27	24	13.8	14.0
Tri(2 chloroethyl) phosphate	28	38	29.4	25.9
Ethylene	29	54	20,582.1	521.3
Benzolalpyrene	30	10	N.A.	N.A.
Tetraethyl lead	31	19	302.4	285.0
Di(2 ethylhexyl)phthalate	32	59	435.0	441.5
Methylene chloride	33	50	471.3	366.9
Ethylchloride	34	61	575.5	34.6
Dichlorobenzidine	35	17	4.6	0.01
Tris(2,3 dibromopropyl) phosphate	36	26	N.A.	N.A.
Xylenes mixed total (m xylene)	37	44	5,800.0	904.6
p Dichlorobenzene	38	60	77.3	70.8
2,2 Dithiobis(benzothiazole)	39	39	21.3	19.7
Polyvinyl chloride	40	67	4,258.0	4,238.8
Polyethylene glycols (MW, 400)	41	79	52.4	16.3
Bis(2 chloroethyl) and bis(2 chloroisopropyl)ether	42	33	N.A.	N.A.
Fluorescent brightening agents (# 28)	43	64	25.7	25.5
Perchloroethylene	44	14	734.2	562.0
o Dichlorobenzene	45	66	62.4	27.1
Acetonitrile	46	62	3.0	2.5
2 Merenplobenzothiazole	47	29	6.0	0.06
Vinylchloride	48	20	5,088.5	146.5
Nonylphenol, ethoxylated	49	71	177.9	162.8
Trichloroethylene	50	37	426.7	429.5
Allychloride	51	8	295.0	4.4
2 Methoxyethanol	52	41	119.1	95.2
p Nonylphenyl phosphite (mixed)	53	55	20.0	20.3

Compound	Priority rank: Environmental impact	Priority rank: Human health hazard	United States production * (millions of pounds)	Estimated annual release rate (millions of pounds)
Bis(hydrogenated tallow alkyl) dimethylammonium chloride	54	56	31.4	32.3
Vinyl toluene	55	35	40.0	12.6
Diarylarylenediamines, mixed (Wingstay 100)	56	53	20.0	18.6
Toluene diisocyanate (TDI)	57	12	419.4	6.3
Formaldehyde (37 % by weitht)	58	52	5,651.8	141.0
Ethylenimine	59	2	5.0	N.A.
Aniline	60	34	409.8	6.2
Methylbromide	61	57	24.6	22.4
Chloroprene	62	11	402.0	6.0
Ethylene oxide	63	15	3,961.8	98.7
N(1,4 dimethylpentyl)-*N'*-phenyl-*p*-phenylenediamine	64	47	20.0	16.8
Acyclic xanthic acid salts (sodium isopropylxanthate. Dow Z-11)	65	70	41.8	42.4
Sulfolane	66	68	35.0	35.5
Polyarethane and diisocyanate resins	67	42	99.4	102.4
Tetrabromoethane	68	16	N.A.	N.A.
Hexamethylenetetramine. ?	69	51	95.2	42.3
Naphthalene	70	77	640.7	20.1
Vinylidene chloride	71	31	60.0	0.9
Toluene	72	69	6,640.1	1,189.8
Dimethylamine	73	36	95.9	15.8
Di(2 ethylhexyl)adipate	74	74	44.9	39.5
4,4 Methylene (bis)-2-chloroaniline	75	13	6.7	0.1
Tetrakis (hydroxymethyl) phosphonium chloride	76	18	N.A.	N.A.
Ethylbenzene	77	76	6,920.0	203.5
Dodecylmercaptan	78	73	15.2	15.5
o Cresol	79	30	49.7	5.7
Acrylonitrile copolymers	80	78	630.0	607.6

* Based on 1972 U.S. Tariff Commission reports.
' N.A. denotes information not available.

ANNEX II

USA Interagency Testing Committee

Interagency Testing Committee (ITC) . . . Section 4(e)

Under Section 4(e), the ITC was established to recommend to EPA substances which should be tested for specified effects to determine the hazardous potential of the substances to human health or the environment. Committee members are: Council on Environmental Quality (CEQ), Department of Commerce (DOC), Environmental Protection Agency (EPA), National Cancer Institute (NCI), National Institute of Environmental Health Sciences (NIESH), National Institute for Occupational Safety & Health Administration (OSHA). The committee may list up to 50 chemicals or categories and is to consider revising or adding to its list every 6 months. The EPA must respond within one year to each recommendation by initiating rulemaking under Section 4 or stating its reasons for not doing so. Both ITC reports and EPA responses appear in the Federal Register.

On October 24, 1980, the ITC sent to EPA its seventh priority list of chemicals for consideration in promulgating 4(e) test rules. The report which added two chemicals and two chemical categories and removed one chemical from the list, was published on November 25, 1980 (45 FR 78432). The two added chemicals are benzyl butyl phthalate and butyl glycolyl butyl phthalate, the two new chemical categories are alkyltin compounds and fluoroalkenes. Because EPA had addressed all the ITC's concerns about chloromethane, that chemical was removed from the priority list. With the additions and the deletion the priority list now contains 42 entries.

The TSCA Section 4(e) Priority List

Entry	Date of Designation
1. Acetonitrile	April 1979
2. Acrylamide	April 1978(b) (d)
3. Alkylepoxides	October 1977(a)
4. Alkylphthalates	October 1977(a)
5. Alkyltin compounds	October 1980
6. Aniline and bromo, chloro and/or nitro anilines	April 1979
7. Antimony (metal)	April 1979
8. Antimony sulfide	April 1979
9. Antimony trioxide	April 1979
10. Aryl phosphates	April 1978(b)
11. Benzidine-based dyes	November 1979
12. Benzyl butyl phthalate	October 1980
13. Butyl glycolyl butyl phthalate	October 1980
14. Chlorinated benzenes, mono- and di-	October 1977(a),(c)
15. Chlorinated benzenes, tri-, tetra- and penta-	October 1978(c)
16. Chlorinated naphthalenes	April 1978(b)
17. Chlorinated paraffins	October 1977(a)
18. Cresols	October 1977(a)
19. Cyclohexanone	April 1979
20. o-Dianisidine-based dyes	November 1979
21. Dichloromethane	April 1978(b)
22. 1.2-Dichloropropane	October 1978
23. Fluoroalkenes	October 1980
24. Glycidol and its derivatives	October 1978

Entry	Date of Designation
25. Halogenated alkyl epoxides	April 1978(b)
26. Hexachloro-1.3-butadiene	October 1977(a)
27. Hexachlorocyclopentadiene	April 1977
28. Hydroquinone	November 1979
29. Isophorone	April 1979
30. Mesityl oxide	April 1979
31. 4.4-Methylenedianiline	April 1979
32. Methyl ehtyl ketone	April 1979
33. Methyl isobutyl ketone	April 1979
34. Nitrobenzene	October 1977(a)
35. Phenylenediamines	April 1980
36. Polychlorinated terphenyls	April 1978(b)
37. Pyridine	April 1978(b)
38. Quinone	November 1979
39. o-Tolidine-based dyes	November 1979
40. Toluene	October 1977(a)
41. 1.1.1-Trichloroethane	April 1978(b)
42. Xylene	October 1977(a)

(a) Responded to by EPA Administrator 43 FR 50134–50138
(b) Responded to by EPA Administrator 44 FR 28095–28097
(c) Responded to by EPA Administrator 45 FR 48524–48564
(d) Responded to by EPA Administrator 45 FR 48510–48512

Significant New Use . . . Section 5(a)(2)

Under 5(a)(2), EPA determines when certain uses of existing chemical substances are for significant new uses (SNUR). A determination is made by a rule promulgated after considering all relevant factors. The factors include the projected volume of manufacturing and processing of the substance, the extent to which the new use changes the type and form of exposure to humans or the environment, the extent to which the use of the substance increases the magnitude and the duration of exposure to humans or the environment and the anticipated manner and methods of manufacturing, processing, distributing in commerce and disposal of the substance. Under Section 5(a)(1)(B), persons must notify EPA at least 90 days before manufacturing process or import a chemical substance for a significant new use, as determined by EPA.

II. 1980 List of Chemicals Selected for Review by TSCA Interagency Testing Committee
(Ascending CAS No. Sequence)

CAS No.	Chemical Name	Formula
70553	Benzenesulfonamide, 4-methyl-	$C_7H_9NO_2S$
75343	Ethane, 1,1-dichloro-	$C_2H_4Cl_2$
75796	Silane, trichloromethyl-	CH_3Cl_3Si
75865	Propanenitrile, 2-hydroxy-2-methyl-	C_4H_7NO
75876	Acetaldehyde, trichloro-	C_2HCl_3O
76017	Ethane, pentachloro-	C_2HCl_5
76084	2-Propanol, 1,1,1-tribromo-2-methyl-	$C_4H_7Br_3O$
77736	4,7-Methano-lH-idene, 3A,4,7,7A-tetrahydro-	$C_{10}H_{12}$
78831	1-Propanol, 2-methyl-	$C_4H_{10}O$

CAS No.	Chemical Name	Formula
78897	1-Propanol, 2-chloro-	C_3H_7ClO
79027	Acetaldehyde, dichloro-	$C_2H_2Cl_2O$
79049	Acetyl chloride, chloro-	$C_2H_2Cl_2O$
79367	Acetyl chloride, dichloro-	C_2HCl_3O
85698	1,2-Benzenedicarboxylic acid, butyl 2-ethyl-hexyl ester	$C_{20}H_{30}O_4$
88197	Benzenesulfonamide, 2-methyl-	$C_7H_9NO_2S$
90437	[1,1'-Biphenyl]-2-ol	$C_{12}H_{10}O$
91087	Benzene, 1,3-diisocyanato-2-methyl-	$C_9H_6N_2O_2$
92524	1,1'-Biphenyl	$C_{12}H_{10}$
95498	Benzene, 1-chloro-2-methyl-	C_7H_7Cl
95636	Benzene, 1,2,4-trimethyl-	C_9H_{12}
98511	Benzene, 1-(1,1-dimethylethyl)-4-methyl-	$C_{11}H_{16}$
98566	Benzene, 1-chloro-4-(trifluoromethyl)-	$C_7H_4ClF_3$
98599	Benzenesulfonyl chloride, 4-methyl-	$C_7H_7ClO_2S$
98873	Benzene, (dichloromethyl)-	$C_7H_6Cl_2$
100185	Benzene, 1,4-bis(1-methylethyl)-	$C_{12}H_{18}$
103651	Benzene, propyl-	C_9H_{12}
104723	Benzene, decyl-	$C_{16}H_{26}$
105055	Benzene, 1,4-diethyl-	$C_{10}H_{14}$
107120	Propanenitrile	C_3H_5N
108805	1,3,5-Triazine-2,4,6(1H,3H,5H)-trione	$C_3H_3N_3O_3$
110009	Furan	C_4H_4O
110656	2-Butyne-1,4-diol	$C_4H_6O_2$
110883	1,3,5-Trioxane	$C_3H_6O_3$
111693	Hexanedinitrile	$C_6H_8N_2$
115286	Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid, 1,4,5,6,7,7-hexachloro-	$C_9H_4Cl_6O_4$
120127	Anthracene	$C_{14}H_{10}$
121142	Benzene, 1-methyl-2,4-dinitro-	$C_7H_6N_2O_4$
123013	Benzene, dodecyl-	$C_{18}H_{30}$
123024	Benzene, tridecyl-	$C_{19}H_{32}$
131113	1,2-Benzenedicarboxylic acid, dimethyl ester	$C_{10}H_{10}O_4$
137268	Thiperoxydicarbonic diamide, tetramethyl-	$C_6H_{12}N_2S_4$
140089	Ethanol, 2-chloro-, phosphite (3 : 1)	$C_6H_{12}Cl_3O_3P$
140669	Phenol, 4-(1,1,3,3-tetramethylbutyl)-	$C_{14}H_{22}O$
540498	Ethene, 1,2-dibromo-	$C_2H_2Br_2$
541888	Acetic acid, chloro-, anhydride	$C_4H_4Cl_2O_3$
542756	1-Propene, 1,3-dichloro-	$C_3H_4Cl_2$
563473	1-Propene, 3-chloro-2-methyl-	C_4H_7Cl
577117	Butanedioic acid, sulfo-, 1,4-bis(2-ethylhexyl) ester, sodium salt	$C_{20}H_{38}O_7S \cdot Na$
584849	Benzene, 2,4-diisocyanato-1-methyl-	$C_9H_6N_2O_2$
594423	Methanesulfenyl chloride, trichloro-	CCl_4S
606202	Benzene, 2-methyl-1,3-dinitro-	$C_7H_6N_2O_4$
719324	1,4-Benzenedicarbonyl dichloride, 2,3,5,6-tetrachloro-	$C_8Cl_6O_2$
760236	1-Butene, 3,4-dichloro-	$C_4H_6Cl_2$
764410	2-Butene, 1,4-dichloro-	$C_4H_6Cl_2$
1000824	Urea, (hydroxymethyl)-	$C_2H_6N_2O_2$
1119853	3-Hexenedinitrile	$C_6H_6N_2$
1241947	Phosphoric acid, 2-ethylhexyl diphenyl ester	$C_{20}H_{27}O_4P$
1313275	Molybdenum oxide	MoO_3
1459105	Benzene, tetradecyl-	$C_{20}H_{34}$
1476115	2-Butene, 1,4-dichloro-, (Z)-	$C_4H_6Cl_2$
1497683	Phosphorochloridothioic acid, ethyl-, O-ethyl ester	$C_4H_{10}ClOPS$
1772254	1,3,6-Hexanetricarbonitrile	$C_9H_{11}N_3$
2431507	1-Butene, 2,3,4-trichloro-	$C_4H_5Cl_3$
2524030	Phosphorochloridothioic acid, 0,0-dimethyl ester	$C_2H_6ClO_2PS$
2782572	1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3-dichloro	$C_3HCl_2N_3O_3$
2893789	1,3,5-Triazine,2,4,6(1H,3H,5H)-trione, 1,3-dichloro-, sodium salt	$C_3HCl_2N_3O_3 \cdot Na$

CAS No.	Chemical Name	Formula
2941642	Carbonochloridothioic acid, S-ethyl ester	C_3H_5ClOS
3268493	Propanal, 3-(methylthio)-	C_4H_8OS
4461523	Methanol, methoxy-	$C_2H_6O_2$
4553622	Pentanedinitrile, 2-methyl-	$C_6H_8N_2$
4635874	3-Pentenenitrile	C_5H_7N
5216251	Benzene, 1-chloro-4-(trichloromethyl)-	$C_7H_4Cl_4$
6742547	Benzene, undecyl-	$C_{17}H_{28}$
7327608	Acetonitrile, 2,2',2'',-nitrilotris-	$C_6H_6N_4$
8075749	Lignosulfonic acid, chromium iron salt	
9066506	Lignosulfonic acid, chromium salt	
10025782	Silane, trichloro-	Cl_3HSi
10026047	Silane, tetrachloro-	Cl_4Si
10039540	Hydroxylamine, sulfate (2 : 1)	$H_3NO \cdot 1/2H_2O_4S$
12200883	Vanadic acid, hexasodium salt	$H_6O_{28}V_{10} \cdot 6Na$
12656858	C.I. Pigment Red 104	
13042029	2-Hexenedinitrile	$C_6H_6N_2$
13414545	Benzene, 1-[(2-methyl-2-propenyl)oxy]-2-nitro	$C_{10}H_{11}NO_3$
13414556		
15547178	9,10-Anthracenedione, 6-ethyl-1,2,3,4-tetra-hydro-	$C_{16}H_{16}O_2$
15883597	Benzenesulfonic acid, 2,2'-(1,2-ethenediyl)bis [5-nitro-,] sodium salt	$C_{14}H_{10}N_2O_{10}S_2 \cdot xNa$
16529569	3-Butenenitrile, 2-methyl-	C_5H_7N
17773410	Butanenitrile, 2-hydroxy-4-(methylthio)-	C_5H_9NOS
19355692	Propanenitrile, 2-amino-2-methyl-	$C_4H_8N_2$
25155300	Benzenesulfonic acid, dodecyl-, sodium salt	$C_{18}H_{30}O_3S \cdot Na$
25321099	Benzene, bis(1-methylethyl)-	$C_{12}H_{18}$
25322207	Ethane, tetrachloro-	$C_2H_2Cl_4$
25340174	Benzene, diethyl-	$C_{10}H_{14}$
25340185	Benzene, triethyl-	$C_{12}H_{18}$
25550145	Benzene, ethylmethyl-	C_9H_{12}
26471625	Benzene, 1,3-diisocyanatomethyl-	$C_9H_6N_2O_2$
26545733		
27176870	Benzenesulfonic acid, dodecyl-	$C_{18}H_{30}O_3S$
30995654	Benzenesulfonic acid, ethyl-, sodium salt	$C_8H_{10}O_3S \cdot Na$
36452218	1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, disodium salt	$C_3H_3N_3O_3 \cdot 2Na$
38640629	Naphthalene, bis(1-methylethyl)-	$C_{16}H_{20}$
50854949	Benzenesulfonic acid, undecyl-	$C_{17}H_{28}O_3S$
61790134	Naphthenic acids, sodium salts	
63494597	Ethanesulfonamide, 2-[ethyl(3-methyl-4-nitrosophenyl)amino]-N-methyl	$C_{12}H_{19}N_3O_3S$
68081812	Benzenesulfonic acid, mono-ClO-16-alkyl derivs., sodium salts	
68279549	9,10-Anthracenediol, 6-ethyl-1,2,3,4-tetra-hydro-	$C_{16}H_{18}O_2$
68298464	7-Benzofuranamine, 2,3-dihydro-2,2-dimethyl-	$C_{10}H_{13}NO$

Billing Code 6 56 0-31-C

Chemicals in the secretariat list recommended for action

No.	Chemical	Working Env. (Man)	General Env. (Man)	General Env. (Non-Human)	Type of Document	Reasons	Remarks
1.	Acrylamide		*		Criteria Document	High exposure; possible water contaminant; delayed neuro-toxicity	-
2.	Alkyl epoxides		*		Preliminary class study	Possible wide community exposure; possible mutagen; carcinogen; teratogen	-
3.	Halogenated alkyl epoxides	*	*		Comprehensive review	Extensive exposure; possible carcinogen	-
4.	Aniline and derivatives		*		Preliminary class study	Exposure; toxicity	-
5.	Asbestos		*		Alert/warning	Carcinogen	Information on hazard and problem available but needs to be disseminated
6.	Benzene	*	*		Criteria document	High exposure carcinogen	1. Urgent need for document. 2. Important to evaluate long-term exposure to low levels
7.	Benzidine and benzidine based dyes	*	*		Criteria document	High exposure; widely used; well-known carcinogen	Consider short document too
8.	Dimethyl sulphate	*			Criteria document	High exposure; widely used; cancer risk; neurotoxicity	-

No.	Chemical	Working Env. (Man)	General Env. (Man)	General Env. (Non-Human)	Type of Document	Reasons	Remarks
9.	Chlorofluoro-carbons		*	*	Criteria document	Widely recognized problem; increased UV flux; skin cancer; some mutagenicity data	Data available
10.	Formaldehyde	*	*		Criteria document	Wide exposure; suspected carcinogen; local irritant; sensitizing effect	-
11.	Organochlorine solvents	*	*		Criteria document	Wide exposure; suspected carcinogen; neurotoxicity	1. Consider short document too 2. Include chloromethanes, ethanes, propanes, ethylenes etc.
12.	Pentachlorophenol and its salts	*	*		Criteria document	Wide exposure; possible carcinogen; (chlorance)	Commercial grades to be noted
13.	Phenols		*		Preliminary class study	-	Determine extent of problem and decide on chemicals to be included
14.	Phenylene diamines	*	*		Criteria document	High exposure; carcinogens and suspected carcinogens; suspected mutagens; sensitizers (dermatological effects)	-
15.	Phtalic acid and esters	*	*	*	Criteria document	Widespread use; local irritant and sensitizing agent in respiratory organs; possible environmental effects	-

Additional Chemicals Recommended for Action

No.	Chemical	Working Env. (Man)	General Env. (Man)	General Env. (Non-Human)	Type of Document	Reasons	Remarks
1.	Dioxanes		*		Preliminary study of a single substance	Presence in a wide Range of consumer products and cosmetics	-
2.	Epichlorohydrin		*		Alert/warning	Suspected carcinogen	Information on hazard and problem available but needs to be disseminated
3.	Ethylene and propylene oxides		*		Criteria document	Possible Carcinogens	-
4.	Man made fibres		*		Preliminary study of a single substance	Determine possible adverse effects	-

ANNEX III

International Program on Chemical Safety

IPCS/CEC Joint Task Force on Priority Industrial Chemicals Ispra, Italy, November 17–20, 1980

The following list of chemicals was prepared from the Technical Committee (IPCS) Report (July 1980), the recommendations of the "Consultation on Priority Problems in Toxic Chemicals Control in Europe (WHO-EURO November 1980)", the two consultants' reports, national priority lists and the IRPTC Query Response Service.

Acetonitrile
Acrylamide
Acrylonitrile – ILO
Alkyl epoxides
Aluminium phosphide (see phosphine)
Ammonia – C
Anilines
Anionic detergents – D
Antimony
Arsenic – C
Asbestos

Barium
Beryilium – C
Benzene
Benzidine
Benzo (α) pyrene – C
Bismuth

Cadmium – C
Carbon disulphide – A
Carbon monoxide – A
Chlorinated dibenzo-para-dioxins – C
Chlorinated hydrocarbons – C
Chlorinated naphthalenes
Chlorinated paraffins
Chlorine and hydrogen chloride – C
Chloroacetamide
Chlorobenzenes
Chlorofluorocarbons
Chloromethane (see chlorinated paraffins)
Chlorophenols (see phenols)
Chromium – C
Cobalt – C

DDT – A
Dibromochloropropane (DBCP) – ILO
Dichloromethane
1,2 dichloro-propane
Diethanolamine
Diethyl nitrosoamine
Dimethyl hydrazine (asymmetrical)
Dimethyl sulphate

Ethylamine
Ethylbenzene
Ethylene dichloride
Ethyleneimine

Fluorine and fluorides – C
Formaldehyde

Glycidol and its derivatives

Halogenated alkyl epoxides (see alkyl epoxides)
Hexachloro-1,3 butadene
Hexachlorocyclopentadiene and adducts
Hexachlorophene
Hydrogen chloride (chlorine +) – C
Hydrogen peroxide
Hydrogen sulphide – C

Isophorone

Lead – A

Manganese – B
Mercury – A
Mestyle oxide
4,4'-methylene dianiline
Methyl ethyl ketone
Mirex
Molybdenum

2-naphthyl amine – ILO
"Niax (R) catalyst ESN" – a mixture of 3-(Dimethylamino) propionitrile (95 %) and bis [2-(dimethylamino) ethyl]ether (5 %)
Nickel – C
Nitrates, nitirites and N-nitroso compounds – A
Nitrobenzene
Nitrogen oxides – A
2-Nitropropane (2-NP) – ILO

Organochlorine solvents
Organophosphorus compounds – C
A – Organotins (Tin and)
D-4,4'-Oxydianiline

PBBs
PCBs + PCTs – A
Pentachlorophenol
Perchlorethylene
Petroleum products (selected)
Phenols
Phenylene diamines
Phosphine
Phthalic acid esters
Polynuclear aromatic hydrocarbons – C
Polyvinyl chloride (see vinyl chloride)
Pyridine

Selenium – C
Sulphur oxides – A
Styrene – D

Thallium
Tin (and organotin compounds) – A
Titanium
O-Tolidine
Toluene
2,6-Toluenediamine – D
Triaryl phosphates
1,1,1-Trichloroethane (see chlorinated paraffins)
Trichloroethylene (see organochlorine solvents)
Tricresyl phosphates

Vanadium – C
Vinyl chloride
Vinylidine chloride

Xylenes

ANNEX IV

USA Chemical Manufacturers Association

Biomedical and Environmental Special Programs Budget [a]

Program	Research and Advocacy Commitment	Administrative Expenses	Total
Acrylonitrile	$ 728,484	$ 59,411	$ 787,895
Allyl Chloride	210,600	13,948	224,548
Benzene	1,430,444 [b]	83,526	1,513,970
Butylated Hydroxytoluene	21,944	25,213	47,157
Chlorobenzenes	300,972	22,334	323,306
Epichlorohydrin	214,882	27,332	242,214
Epoxy Resins	– 0 –	9,368	9,368
Ethylene Dibromide	10,000	28,836	38,836
Ethylene Dichloride	288,100	59,376	347,479
Glycol Ethers	– 0 –	– 0 –	– 0 –
Ketones	– 0 –	10,901	10,901
Phosgene	207,912	55,035	262,947
Phthalate Esters	106,471	72,086	178,557
Rubber Additives	27,900	5,867	33,767
Styrene	708,218	54,934	763,152
Titanium Dioxide	30,725	14,615	45,340
Trichloroethylene	490,506	77,152	567,658
Vinyl Chloride	1,326,562	112,958	1,439,520
Vinylidene Chloride	729,482	52,088	781,570
Zinc Dialkyl Dithiophosphates	– 0 –	– 0 –	– 0 –
Subtotal	6,833,202	784,983	7,618,185
Fluorocarbons	7,580,453	509,214	8,089,667
Total	$ 14,413,655	$ 1,294,197	$ 15,707,852

[a] Fluorocarbons program from start thru May 30, 1980. All other programs start to September, 1980.

[b] API is co-sponsoring a portion of this research. Its share ($ 1,587,786) is not shown in this figure. The figure does include $ 303,988 paid to outside legal counsel not shown on the program summary in Appendix A.

ANNEX V

USA Chemical Industry Institute of Toxicology

Priority Chemicals at CIIT

The commodity chemicals selected for toxicological testing are determined by CIIT with the assistance of the Scientific Advisory Panel and suggestions from various representatives of the chemical industry. Criteria for selection include the chemical's volume of production, its physical and chemical properties, its estimated human exposure, toxicological suspicion and opinion, public interest, and the significance of the chemical to society. Chemicals are selected without regard for their importance to any particular member company, and specialty or proprietary compounds are not tested.

CIIT's priority chemical list currently consists of 40 chemicals presently under study or under consideration for study. Of these 40 chronic two-year exposure studies have been completed for the following chemicals:

- Aniline HCI
- Dinitrotoluene
- Ethylene
- Formaldehyde
- Maleic anhydride
- Methyl chloride
- Terephthalic acid
- Toluene

Pilot studies have been conducted for chlorine dimethylamine η-hexane and methyl ethyl ketone. Long-term studies underway or planned for 1981 include:

- Benzene
- Chlorine
- Dimethylamine
- Hexamethylenediamine
- η-Hexane
- Methyl ethyl ketone
- Nitrobenzene

Other chemicals under consideration for future study are:

- Acetone
- Acetylene
- Ammonia
- Benzyl chloride
- Carbon disulfide
- Cresols
- Ethylene diamine
- Ethylene dichloride
- Ethylene glycol
- Ethylene oxide
- Hydrogen cyanide
- Hydrogen sulfide
- Isopropanol
- Methanol
- Methylene chloride
- Phenol
- Phthalic anhydride
- Propylene
- Propylene oxide
- Tetrachloroethylene
- Toluene-2,4-diamine
- Toluene diisocyanate
- Urea
- Vinyl acetate
- Xylenes

potential are performed by contract. The NTP recognizes the need to expand toxicologic assessment of inhaled chemicals to other than NTP laboratories. Methods development and validation is planned.

Chronic inhalation studies on the cardiovascular effects of methyl bromide will continue. Acute or chronic studies on pulmonary response are planned for four epoxides: butylene oxide, ethylene oxide, propylene oxide, and styrene oxide.

Lung fibrogenesis as a consequence of fibers and dusts is a major health concern. A variety of methods are being utilized in an attempt to assess fibrogenic effects including histophathology, fibroblastic activity *in vitro*, macrophage interaction, and bilogical availability using the isolated perfused lung. Chemicals that are being utilized in these studies include:

aluminum salts and organoaluminum
asbestos
copper compounds
fibrous glass
lead oxide
lead sulfide
silica
2 ethoxy ethanol
2 nitropropane

Studies on the dose related pathogenesis and persistence of noncarcinogenic effects of chlordecone in rats are in progress. Toxic parameters being studied include reproduction, fertility, neurobehavior, immunology, hepatotoxicity and blood clotting.

Table 1.—*Chemicals Selected for Teratology Studies*

Chemical	CAS No.
Caffeine	58-08-2
Dimethylaniline	87-62-7
Ethyl Benzene	100414
Ethylene oxide	75218
Ethoxy ethanol*	110-80-5
Formaldehyde	50-00-0
Lead monoxide**	
Pentachlorobenzene	1825-21-4
Toluene	108883
Xylenes:	
O-Xylene	94576
M-Xylene	108383
P-xylene	106423

*Post natal behavioral and nervous system abnormalities will also be evaluated.
**Post natal renal, cardiovascular, metabolic and hematopoietic systems will be evaluated through 10 months of age.

Table 2.—*Chemicals Nominated for Teratology Studies or Screening for Teratogenic Effect*

Chemical	CAS No.
Bisphenol A	80-05-7
Butyl nitrite	
Capsaicin	404-86-4
Cinnamaldehyde	104-55-2
Chlorinated dibenzofurans	
Copper compound(s)	
P-dichlorobenzene	106-46-7

Table 2.—*Chemicals Nominated for Teratology Studies or Screening for Teratogenic Effect*—Continued

Chemical	CAS No.
Gentian violet (hexamethyl-p-rosaniline)	548-62-9
Mercaptobenzothiazole	149-30-4
Oil of nutmeg	
Sulfanilmelamine	57-68-1
Tocopherol	1406-66-2

Table 3.—*Chemicals Tested in Salmonella/Microsome Plate Assays for Comparison With Fischer 344 Rat and $B_6C_3F_1$ Mouse Lifetime Bioassays*

4-Amino-2-nitrophenol—119-34-6
2-Amino-5-nitrothiazole—121-66-4
p-Chloroaniline
3-Chloromethyl pyridine hydrochloride—6959-48-4
N,N'-Dicyclobexylthiourea—1212-29-9
4,4'-bis (Diemthylamino) benzophenone
Dyrene(anilazine)—101-05-3
Ethylene dibromide—106-93-4
Lithocholic acid—434-13-9
4,4'-Methylenebis(n,N'-dimethylaniline)—101-61-1
Nitrilotriacetic acid trisodium salt monohydrate
4-Nitro-o-phenylenediamine—99-56-8
2-Nitro-p-phenylenediamine—5307-14-2
3-Nitropropionic acid—504-88-1
p-Phenylenediamine—106-50-3
Acetylsalicylic acid—50-78-2
Aldicarb—116-06-3
Aniline hydrochloride—142-04-1
o-Anisidine hydrochloride—134-29-0
APD—6003-03-0
1,2,3-Benzotriazole—95-14-7
Caffeine—58-08-2
Cinnamyl anthranilate—87-29-6
tris(2,3-Dibromopropyl)phosphate—126-72-7
1,3-Dichloro-5,5-dimethylhydantoin—118-52-5
Fluometuron—2164-17-2
1,5-Naphthalenediamine—2243-62-1
Proflavin hydrochloride—952-23-8
Reserpine—50-55-5
Styrene—96-09-3
4'-Chloroacetyl(acetanilide)—140-49-8
Coumaphos—56-72-4
m-Cresidine—102-50-1
p-Cresidine—120-71-8
Diazinon—333-41-5
2,4-Dimethoxyaniline—54150-69-5
3,3'-Dimethoxybenzidine-4,4'-diisocyanate ethylenediaminetetra acetic acid, sodium salt—60-00-4
3-Methyl-1-phenyl-2-pyrazotin-5-one
Nitrofen—1836-75-5
5-Nitro-o-toluidine—99-55-8
p-Quinone dioxime—105-11-3
Succinic acid 2,2-dimethylhydrazide—1596-84-5
2,5-Toluenediamine sulfate—6369-59-1
Triphenyltin—76-87-6

Table 4.—*Alphabetical List of Chemicals Selected for Salmonella Mutogenicity Assay*

Acetamide—60-35-5
Acetin—26446-35-5
N-Acetyl-o-toluidine—120-6-1
Acrolein—107-02-8
3-Amino-α·α·α-trifluorotoluene—98-16-8
o-Aminophenol—95-55-6
Amyl nitrite—463-04-7
Aniline—62-53-3
o-Anisidine—90-04-0
p-Anisidine—104-94-9
Anthracene—120-12-7
Arochlor 1254—11097-69-1
l-Aziridineethanol—
Azobenzene—103-33-3
Azodicarbonamide—123-77-3
Benzaldehyde—100-52-7
Benzofuran—271-89-6
p-Benzoquinone dioxime—105-11-3
Benzyl salicylate—118-58-1
Beta-methylumbelliferone—90-33-5
Beta-picoline—108-99-6
Biphenyl—92-52-4
2-Biphenylamine—90-41-5
4-Biphenylamine—92-67-1
2,4'-Biphenylamine—
2,4'-Biphenyldiamine—492-17-1
Bis(chlorendo)furan
Bisphenol—80-05-7
Boric acid—10043-35-3
Bromobenzene—108-86-1
Bromocyclohexanol
Bromoform—75-25-2
2-Butanone peroxide—1338-23-4
n-Butyl para-aminobenzoate—94-25-7
Cacodylic acid—75-60-5
Carbon disulfide—75-15-0
Catechol—120-80-9
Chloral hydrate—302-17-0
Chlorendic acid—115-28-6
2-Chloro-1,3-butsdiene—126-99-8
4-Chloro-α·α·α-trifluorotoluene—98-56-6
4-Chloro-3,5-dinitro-α·α·α-trifluorotoluene—393-75-9
4-Chloro-3-nitro-α·α·α-trifluorotoluene
Chlorobenzene—108-90-7
4-Chloronitrobenzene—100-00-5
2-Chloronitrobenzene—88-73-3
m-Chlorophenol—108-43-0
o-Chlorophenol—95-57-8
p-Chlorophenol—106-48-9
Cinnamaldehyde—104-55-2
Copper acetoarsenite—12002-03-8
m-Cresol—108-39-4
o-Cresol—95-48-7
p-Cresol—106-44-5
Crotonaldehyde—123-73-9
Cyanuric acid—108-80-5
Cyclohexanol—108-93-0
Cyclohexanone—108-94-1
Diacetone acrylamide—2873-97-4
4,4'-Diamino-2,2'-stilbenedisulfonic acid
2,4-Diaminophenol hydrochloride—137-09-7
Debenzofuran—132-64-9
Diborane—19287-45-7
2,3-Dibromo-1-propanol—96-13-9
Di-n-butylamine—111-92-2
1,3-Dichlorobenzene—541-73-1
1,2-Dichlorobenzene—95-50-1
1,4-Dichlorobenzene—106-46-7
cis-Dichlorodiamine platinum—15663-27-1
Dichlorodiphenylethylene—72-55-9
trans-1,2-Diochlorethylene—540-59-0
cis & trans-1,2,3-Dichloroethylene—156-59-2
1,1-Dichloroethylene—75-35-4
3,4-Dichloronitrobenzene—99-54-7
2,3-Dichloronitrobenzene—3209-22-1
2,3-Dichlorophenol—576-24-9
2,5-Dichlorophenol—38048-58-7
2,6-Dichlorophenol—87-65-0

3,4-Dichlorophenol—95-77-2
3,5-Dichlorophenol—591-35-5
Diethanolamine—111-42-2
7-Diethylamino-4-methylcoumarin—91-44-1
Diethyl carbonate—105-58-8
Diethyldichlorosilane—1719-53-5
Diethyleneglycoldimethylether (diglyme)—111-96-6
Diethyl ethylphosphonate—78-38-6
Di(2-ethylhexyl) phthalate—117-81-7
5,7-Dihydroxy-4-methylcoumarin—2107-76-8
Diisobutylketone—108-83-8
Dimethoxane—828-00-2
1,2-Demthoxybenzene—91-16-7
Dimethylamine—124-40-3
Dimethyl cyanamide—1467-79-4
N,N-Dimethylformamide—68-12-2
2,4-Dimethylphenol—105-67-9
N,N-Dimethylurea—1320-50-9
trans-1,2-Dichloroethylene—156-60-5
cis & trans 1,2-Dichloroethylene—540-59-0
4,6-Dinitro-2-aminophenol—96-91-3
2,4-Dinitrotoluene—121-14-2
Dioctyladipate—123-79-5
1,4-Dioxane—123-91-1
Diphenyl oxide (diphenyl ether)—101-84-8
1,2-Epoxypropane—75-56-9
Ethyl bromide—74-96-4
Ethyl chloride—75-00-3
Ethylene glycol—107-21-1
Ethylenediamine—107-15-3
2-ethylhexyl diphenyl phosphate—1241-94-7
Eugenol—97-53-0
Ferrocene—102-54-5
1-Fluoro-2,4-dinitrobenzene (FDNB)—70-34-8
2-Fluorobenzoyl chloride—393-52-2
Formaldehyde—50-00-0
Furfural—98-01-1
Gallic acid—149-91-7
Cluteraldehyde—111-30-8
Hemotoxylin
Hexabromobenzene—87-82-1
Hexabromobiphenyl—36355-01-8
Hexachlorobenzene—118-74-1
Hexachlorocyclopentadiene dimer—2385-85-5
Hexachloroethane—67-72-1
Hexachlorophene—70-30-4
Hexaclorobutadien—87-68-3
Hexamethly-p-rosaniline-cl—548-62-9
Hydrazine sulfate—10034-93-2
Hydrazinobenzene—100-63-0
Hydroquinone—123-31-9
Hydroquinone dimethyl ether—150-78-7
Hydroquinone monomethyl ether—150-76-5
4-Hydroxyacetanilide—103-90-2
Ligninsulfonic acid sodium salt—8062-15-5
Lithium chloride—7447-41-8
Maleic anhydride—108-31-6
Maleic hydrazide—123-33-1
Melamine—108-78-1
Metchloronitrobenzene—121-73-3
Methacrylic acid methylester—80-62-6
Methylhydrazine—60-34-4
N-Methyl-para-aminophenol—150-75-4
3-Methyl-3-phenylglycidic acid ethyl ester—77-33-8
Methyl salicylate—119-36-8
Ortho-methoxyphenol—90-05-1
8-Methoxyphenol—298-81-7
8-Methoxy psoralin
Morpholine—110-91-8
Neophytadiene—504-96-1
Nickelocene—1271-28-9
1-Nitronaphthalene—86-57-7
p-Nitrophenol—100-02-7
2-Nitropropane—79-46-9
N-Nitrosodiethanolamine—1116-54-7
2-Nitro-a,a,a-trifluorotoluene
3-nitro-a,a,a-trifluorotoluene
Oxalic acid—144-62-7
Paraquat—4685-14-7
Pentachloroaniline—527-20-8
Pentachloroanisole—1825-21-4
Pentachlorobenzene—608-93-5
Pentachloronaphthalene—1321-64-8
Pentachloronitrobenzene—82-68-8
Pentachlorophenol—87-86-5
Pentachlorophenyl methyl ether—1825-21-4
Pentachlorophenyl methyl sulfide—1825-19-0
Phenyl salicylate—118-55-8
Phenytoin—57-41-0
Phorbol ester—17673-25-5
1-(2H)-Phthalazinone—119-39-1
Phthalic anhydride—85-44-9
Picric acid—88-89-1
Piperazine—110-85-0
Peronal—120-57-0
Polybrominated biphenyl—
Propylene Dichloride—78-87-5
1,2-Propylene glycol—57-55-6
Pyridine—110-86-1
Quinoline—91-22-5
p-Quinone—106-51-4
Resorcinol—108-46-3
Rhodanine (Ammonium salt)—1762-95-4
Ricinoleic acid—141-22-0
Semicarbazide hydrochloride—563-41-7
Sodium aluminosilicate—1344-00-9
Sodium dehydroacetate-4418-26-2
Sodium dichloroisocyanurate—13023-28-4, 2893-78-9
Sodium fluoride—7681-49-4
cis-Stilbene—645-49-8
trans-Stilbene—645-49-8
Terephthalic acid—100-21-0
Tert-butyl hydroperoxide—110-05-4
1,2,3,5-Tetrachlorobenzene—634-90-2
1,2,3,4-Tetrachlorobenzene—634-66-2
1,2,4,5-Tetrachlorobenzene—95-94-3
Tetrachloroethylene—127-18-4
Tetrachloronitrobenzene—28804-67-3
Tetrachloronaphthalene
Tetrachlorophthalic anhydride—117-08-8
Tetrakis(hydroxymethyl)phosphonium chloride—124-64-1
Tetraethyllead—78-00-2
Tetramethyllead—75-74-1
Tetranitromethane—509-14-8
Thiazole—288-47-1
Thiocarbonilide
Thioglycolic acid—68-11-1
Toluene—108-88-3
Tributoxyethyl phosphate—Tributyl borate—688-74-4
1,2,3-Trichlorobenezene—87-61-6
1,2,4-Trichlorobenezene—120-82-1
1,3,5-Trichlorobenezene—108-70-3
Trichloronaphthalene—1321-65-9
2,4,6-Trichlorophenol—88-06-2
Triethanolamine—102-71-6
Triphenylphosphine—603-35-0
Trihydroxybutyrophenone—52262-23-4
Tris(4-bromophenyl)phosphate
Tris(2-chloroethyl)phosphite
Tris(2-ethylhexyl)phosphate—78-42-2
Tris(isopropylphenyl)phosphate
Tritolyl phosphate—1330-78-5
Wollastonite os silicates
meta-Xylene—108-38-3
ortho-Xylene—95-47-6
para-Xylene—106-42-3

Table 5.—*Chemicals Selected for a Battery of Mutagenicity Assays*

Chemicals	CAS No.
Allyl chloride	107-05-1
Bisphenol A	80-05-7
Butylene oxide	26249-20-7
Cyclohexanone	108-94-1
N,N-dimethyl acetimide	
Dimethylformamide	68-12-2
Ethoxyethanol	110-80-5
Ethyl benzene	100-41-4
Ethylene oxide	75-21-8
Hexachlorobutadiene	87-68-3
Mercaptobenzenethiazole	149-30-4
Methyl bromide	74-83-9
2 Methoxyethanol	109-86-4
Bis 2 methoxyethoxyethyl ether	143-24-8
N methyl dicyclohexylamine	
Styrene oxide	100-42-5
1,1,2,2-tetrachlorethane	127-18-4
Vinyl toluene	

TABLE 6.—*International Collaborative Study of Mutagenicity Assay Systems; Compounds To Be Tested*

Carcinogen/Noncarcinogen Pairs	
4-Nitroquinoline-N-oxide—56-57-5	Chloroform—67-66-3
3-Methyl-4-nitroquinoline-N-oxide—14073-00-8	1,1,1-Trichloroethene—71-55-6
Benzidine—92-87-5	2-Acetylaminofluorene
3,3',5,5'-Tetramethylbenzidine—54827-17-7	4-Acetylaminofluorene
4-Dimethylaminoazobenzene (Butter Yellow)—60-11-7	N-Nitrosomorpholine—59-89-2
4-Dimethylaminoazobenzene-4-sulphonic acid	Diphenylnitrosamine—86-30-6
Sodium salt (Methyl Orange)	Dinitrosopentamethylene tetramine
Urethane—51-79-6	1-Naphthylamine—134-32-7
O-Isopropyl-N-3-chlorophenylcarbamate—101-21-3	2-Naphthylamine—91-59-8
Benzo(a)pyrene—	Dimethyl carbamoyl chloride—79-44-7
Pyrene—129-00-0	Dimethylformamide—68-12-2
Propiolactone—57-57-8	Methylazoxymethanol acetate—592-62-1
Butyrolactone—96-48-0	Azoxybenzene—495-48-7
9,10-Dimethylanthracene—781-43-1	d,l Ethionine—
Anthracene—120-12-7	Methionine—63-68-3

Miscellaneous Compounds

Hydrazine sulphate—10034-93-2
Hexamethylphosphoramide (HMPA—680-31-9
Ethylenethiourea—96-45-7
Diethylstilbestrol—56-53-1
Safrole—94-59-7
Cyclophosphamide—50-18-0
Epichlorhydrin—
3-aminotriazole
4,4'-Methylenebis (2-chloroaniline)—101-14-4
Sugar (sucrose)—57-50-1
O-toluidine—95-53-4
Ascorbic acid—50-81-7
Auramine

Table 7.—*International Collaborative Study of Mutagencity Assay Systems Utilized*

Prokaryotic Systems

Repair deficiency assays:
- Bacillus subtilis—rec
- Escherichia coli—rec
- Escherichia coli—pol A

Point mutation assays:
- Salmonella typhimurium/microsome (Ames test)
- Salmonella typhimurium 8-azaquanine resistance
- Escherichia coli WP-2
- Escherichia coli 343-113

Eukaryotic Systems

Fungus:
- Saccharomyces cerevisiae—mitotic recombination
- Saccharomyces cerevisiae—reversions
- Schizosaccharomyces pombe—forward mutations
- Saccharomyces cerevisiae—mitochondrial mutations
- Neurospora crassa—ad-3 reversions

Plant:
- Tradescantia—stamen hair system

Insect:
- Drosophila melanogaster—sex-linked recessive lethals

Mammal (in vitro):
- Unscheduled DNA Synthesis (human cells)
- Sister chromatid exchange (CHO cells)
- Chromosome aberrations (hamster and rat cells)
- Specific Locus mutations—
  - L5178Y cells—TK and HGPRT
  - P388F cells—TK and HGPRT
  - CHO cells—HGPRT
  - Human fibroblasts—HGPRT

Mammal (in vivo):
- Micronucleus (mouse)
- Chromosome aberrations
- Sister-chromatid exchange (mouse, rabbit)
- Sperm morphology (mouse)

Nongenetic Systems

- Hydroxylation of Biphenyl
- Local Graying of Hair
- *In vitro* Nuclear Enlargement
- Rabins Test
- Transformation (BHK Cells)

Table 8.—*Chemicals for Which Lifetime Bioassays Are In Progress*

Chemical	CAS No.	Route	Spec.
Acid black 52		Feed, intratr	RH
Acid orange #3	6373-74-6	Feed	RM
Agar agar	9002-18-0	Feed	RM
Agaritine	2757-90-6	Water	RM
Aldicarb	116-06-3	Feed	RM
Allyl isothiocyanate	57-06-7	Gav	RM
Allyl isovalerate	2835-39-4	Gav	RM
Aminoundecanoic acid	27325-47-3	Feed	RM
Aniline, p-chloro	106-47-8	Feed	RM
Antimony oxide	1309-64-4	Feed	RM
Asbestos, amosite		Feed	RH
Asbestos, chrysotile SR		Feed	RH
Asbestos, chrysotile IR		Feed	RH
Asbestos, chrysotile SR		Inhal	R
Asbestos, chrysotile IR		Inhal	R
Asbestos, crocidolite		Feed	R
Ascorbic acid	50-81-7	Feed	RM
Benzene	71-43-2	Gav	RM
Benzoin	119-53-9	Feed	RM
Benzyl acetate	140-11-4	Gav	RM
Benzyl chloride	100-44-7	IP/IJ	M
2-biphenylamine HCl	90-41-5	Feed	RM
Bisphenol A	80-05-7	Feed	RM
HC blue 1	2784-94-3	Feed	RM
Blue 15B	574-93-6	Feed	RM
Bromoform	75-25-2	Gav	RM
Bromodichloromethane	75-27-4	Gav	RM
Butylated hydroxytoluene (BHT)	128-37-0	Feed	RM
Butyl benzyl phthalate	85-68-7	Feed	RM
n-Butyl chloride	109-69-3	Gav	RM
t-Butyl alcohol	75-65-0	Water	RM
Caprolactam	105-60-2	Feed	RM
Castor oil	8001-79-4	Feed	RM
Chlorobenzene	108-90-7	Gav	RM
Chlorodibromomethane	124-48-1	Gav	RM
3-Chloro-2-methylpropene	563-47-3	Gav	RM
C.I. disperse yellow 3	2832-40-8	Feed	RM
Cinnamyl anthranilate	87-29-6	Feed	RM
Coconut oil acid diethanolamine (con 2/1)	8040-31-1	SP	RM
Cyclohexanone	108-94-1	Water	RM
Cytembena	2126-70-7	IP/IJ	RM
D & C red No. 9	5160-02-1	Feed	RM
DBCP	96-12-8	Inhal	RM
Decabromodiphenyl oxide	1163-19-5	Feed	RM
Diallylphthalate	131-17-9	Gav	RM
Dibenzo-p-dioxin, 1,2,3,6,7,8-hexachloro	34465-46-8	SP	M
Dibenzo-p-dioxin, 1,2,3,6,7,8-hexachloro	34465-46-8	Gav	RM
Dibenzo-p-dioxin, 2,3,7,8-tetrachloro	1746-01-6	SP	M
Dibenzo-p-dioxin, 2,3,7,8-tetrachloro	1746-01-6	Gav	RM
Diesel fuel marine		Gav	R
Diesel fuel marine		SP	M
1,4-diamino-2,6-dichlorobenzene		Feed	RM
o-Dichlorobenzene	95-50-1	Gav	RM
p-Dichlorobenzene	106-46-7	Gav	RM
1,1-dichloroethylene	75-35-4	Gav	RM
Cis/trans-1,2-dichloroethylene	156-59-2 540-59-0	Gav	RM
1,2-dichloropropane	78-87-5	Gav	RM
Diethanolamine	111-42-2	Water	RM
Di(2-ethylhexyl)adipate	103-23-1	Feed	RM
Di(2-ethylhexyl)phthalate	117-81-7	Feed	RM
Diglycidylresorcinol ether	101-90-6	Feed	RM
n,n-Dimethyldodecylamine oxide	1643-20-5	Water	RM
Dimethylhydrogenphosphite	868-85-9	Gav	RM
Dimethyl methylphosphonate	756-79-6	Gav	RM
Dimethyl morpholinophosphoramidate	597-25-1	Gav	RM
Dimethylvinylchloride	513-37-1	Gav	RM
Diphenylamine, n-nitroso	86-30-6	Feed	RM
4,4'-diphenylmethane diisocyanate	101-68-8	Gav	RM
Disperse blue #1	2475-45-8	Feed	RM
Disperse yellow #3		Feed, intratr	RH
Dodecyl alcohol, ethoxylated	29718-44-3	Feed	RM
Ethane, 1,2-dibromo	106-93-4	Inhal	RM
Ethane, 1,1,1-trichloro	71-55-6	Gav	RM
Ether, bis(2-chloro-l-methylethyl)	108-60-1	Gav	M
Ether, bis(2-chloro-l-methylethyl)	108-60-1	Gav	R
Ethyl acrylate	140-88-5	Gav	RM

Table 8.—*Chemicals for Which Lifetime Bioassays Are In Progress—Continued*

Chemical	CAS No.	Route	Spec
Ethyl tellurac	30145-38-1	Feed	RM
Ethylene chlorohydrin	107-07-3	SP	RM
Ethylene glycol monoethyl ether	110-80-5	Water	RM
Eugenol	97-53-0	Feed	RM
Fibrous glass		Inhal	R
Fluometuron	2164-17-2	Feed	RM
Fluorescein, disodium salt	518-47-8	Water	RM
Geranyl acetate	105-87-3	Gav	RM
Gitsonide	(2002-43-6	SP	RM
Guar gum	9000-30-0	Feed	RM
Gum arabic	9000-01-5	Feed	RM
Gum tara		Feed	R
HC blue #2		Feed	RM
HC red #3		Feed	RM
8-hydroxyquinoline	148-24-3	Feed	RM
Lauric acid diethanolamine (Con I/I)	120-40-1	SP	RM
Lead dimethyl dithiocarbamate	19010-66-3	Feed	RM
Locust bean gum	9000-40-2	Feed	RM
Malaoxon	1634-78-2	Feed	RM
Malathion	121-75-5	Feed	R
Maleic hydrazide diethanolamine salt	5716-15-4	Water	RM
Malonaldehyde	542-78-9	Gav	RM
Mannitol	69-65-8	Feed	RM
Melamine	108-78-1	Feed	RM
Methapyrilene	91-80-5	Feed	RM
Methylenedianiline	101-77-9	Feed	RM
Methylene chloride	75-09-2	Gav	RM
Methylene chloride	75-09-2	Inhal	RM
Mirex	2385-85-5	Feed	R
Molybdate orange	12656-85-8	Feed	RM
Monuron	150-68-5	Feed	RM
Naphthalene	91-20-3	Gav	RM
Nitrofurantoin	67-20-9	Feed	RM
Oleic acid diethanolamine (Con I/I)	13961-66-9	SP	RM
Orange #10	1936-15-8	Feed	RM
4,4 -oxydianiline	101-80-4	Feed	RM
Pentachloroethan	76-01-7	Gav	RM
Phenol	108-95-2	Water	RM
Phenylbutazone	50-33-9	Water	RM
Phenytoin		Feed (prenatal/ postnatal)	RM
Phthalocyanine green	1328-53-6	Feed	RM
Polychlorinated biphenyl		Feed (prenatal/ postnatal)	RM
Propyl gallate	121-79-9	Feed	RM
Pyridine	110-86-1	Gav	RM
Red #14	3567-69-9	Feed	RM
Reserpine	50-55-5	Feed	RM
p-Rosaniline HCl	569-61-9	Feed	RM
Selenium sulfide	7488-56-4	Gav	RM
Selenium sulfide	7488-56-4	SP	M
Selsun	UNK	SP	M
Sodium dodecyl sulfate	151-21-3	Feed	RM
Sodium(2-ethylhexyl)alcohol sulfate	126-92-1	Feed	RM
Stannous chloride	7772-99-8	Feed	RM
Styrene oxide	96-09-3	Gav	RM
Sudan 1	842-07-9	Feed	RM
Sun yellow FCF	2783-94-0	Feed	RM
Telone	542-75-6	Gav	RM
1,1,1,2-tetrachloroethane	630-20-6	Gav	RM
Tetrachloroethylene	127-18-4	Inhal	RMH
Tetraethylthiuram disulfide	14239-68-0	Feed	RM
THPC	124-64-1	Feed	RM
THPS	UNK	Feed	RM
Toluene disocyanate	584-84-9	Gav	RM
Tremolite		Feed	R
Trichlorfon	52-86-6	Feed	RM
Trichloroethylene	79-01-6	Gav	RM
Tris(2-ethylhexyl)phosphate	78-42-2	Gav	RM
Violet 3	1325-82-2	Feed	RM
Witch hazel	84400-12-7	SP	RM
Zearalenone	7645-23-0	Feed	RM
Ziram	137-30-4	Feed	RM

Table 9.—*Chemicals selected for Extensive Evaluation of Toxic Effects Including Carcinogenesis*

Compound	NCI No.	CAS No.
2-Amino-4-nitrophenol	C55995	99-57-0
2-Amino-5-nitrophenol	C55870	121-88-0
Ampicillin	C56086	69-53-4
Amyl nitrite (butyl nitrite)	C50179	110-46-3
Arsenicals, organic		
Benzathine penicillin G	C56100	1538-0-6
Benzofuran	C56166	271-89-6
Benzyl alcohol	C06111	100-51-6
2,2-Bis(bromomethyl)-1,3-propanediol	C55516	3296-90-0
Boric acid		11113-50-1
Bromobenzene	C55492	108-86-1
1,3-Butadiene	C50602	106-99-0
2-Butanone peroxide	C55447	1338-23-4
Caffeine	C02730	58-08-2
Capsaicin		404-86-4
Carbon disulfide	C04591	75-15-0
Chloramine	C56382	55-86-7
Chlorendic acid	C55072	115-28-6

Table 9.—*Chemicals selected for Extensive Evaluation of Toxic Effects Including Carcinogenesis*—Continued

Compound	NCI No.	CAS No.
Chlorinated trisodium phosphate	C56754	56602-89-4
Chloroacetophenone	C55107	532-27-4
Chlorobenzalmalononitrile	C55118	
Chlorowax 40	C53546	51990-12-6
Chlorowax 500	C53667	56509-64-9
Chlorpheniramine maleate		113-92-8
Cineol (eucalyptol)		470-67-7
Cinnamaldehyde	C56111	104-55-2
2,3-Dibromo-1-propanol	C55436	96-13-9
1,4-Dichlorobenzene	C54955	106-46-7
2,4-Dichlorophenol	C55345	120-83-2
Dichlorvos	C00113	62-73-7
Dimethylaniline	C56186	87-62-7
Diphenhydramine HCL	C56075	147-24-0
DMBA (positive control)	C03918	57-97-6
Ephedrine sulphate	C55852	299-42-3
Epinephrine HCL	C55663	55-31-2
1 2-Epoxybutane	C55527	106-88-7
1 2-Epoxyhexadecane	C55536	7320-37-8
Erythromycin stearate	C55674	114-07-8
Ethyl alcohol	C00134	64-17-5
Ethylbenzene		100-41-4
Ethyl bromide	C55481	74-96-4
Ethyl chloride	C06224	75-00-3
Ethylene oxide	C50086	75-21-8
Formaldehyde	C02799	50-00-0
Furosemide	C55936	54-31-9
Gibberellic acid	C55823	77-06-5
Glutaraldehyde	C55425	111-30-8
Glycidol	C55549	556-52-5
Hematoxylin	C55889	517-28-2
Hexabromobiphenyl (FF-1)	C53634	85355-01-8
Hexafluoroacetone	C08413	00057-27-9
Hexamethyl-p-rosaniline (gentian violet)	C55969	548-62-9
Hexylresorcinol	C55787	136-77-6
Hydrochlorothiazide	C55925	58-93-5
Hydroquinone	C55834	123-31-9
L-Hydroxytryptophan		56-69-9
Iodinated glycerol	C55469	5634-39-9
Isophorone	C55618	78-59-1
Isopropyl glycidyl ether		
d-Limonene	C55572	5989-27-5
Mercaptobenzothiazole		149-30-4
4-Methoxyprorsalen	C55903	298-81-7
Methylbenzyl alcohol	C55685	98-85-1
Methyl carbamate	C55594	598-55-0
Methyldopa	C55721	555-30-6
Methyl methacrylate	C50680	80-62-6
Mycotoxins (ochratoxin, penicillic acid).		
Nalidixic acid	C56199	389-08-2
Naphthalene		91-20-3
1-Naphthylamine, N petinyl	C02915	1 10-88-6
5-Nitro-2-furaldehyde		698-63-5
Nitrofurazone	C56064	59-87-0
Oil of nutmeg		
Oxalic acid	C55209	144-62-7
Pentachloroanisole		1825-21-4
Pentachloronitrobenzene	C00419	82-68-8
Pentachlorophenol	C54933	87-86-5
Phenol	C50124	108-95-2
Phenolphthalein	C55798	77-09-8
Phenylephrine hydrochloride	C55641	5768-67-6
1-Phenylphenol	C50351	61-76-7
Polyurethane		90-43-7
Propylene	C50077	9009-54-5
Propylene oxide	C50099	115-07-1
Pyrrolizidine alkaloids		75-56-9
Retene	C55390	643-20-9
Rhodamine 6G	C56122	483-65-8
Rotenone	C55210	989-38-8
Sodium aluminosilicate	C55505	83-79-4
Sodium dichloroisocyanurate	C55732	1344-00-9
Sodium fluoride	C55221	2893-78-9
Succinic anhydride	C55696	7681-49-4
Sucrose		108-30-5
		25702-74-3
		9012-95-1
		27816-49-5
Sulfamethazine		57-68-1
2,3,7,8-Tetrachlorodibenzofuran		51207-31-9
Tetrachloroethylene (perchloroethylene)	C04600	127-18-4
Tetracycline hydrochloride	C55661	64-75-6
Tetracycline, clay	C55606	79-57-2
Tetranitromethane	C55647	509-14-8
Tocopherol		1406-66-2
Toluene	C07272	108-88-3
Trimellitic anhydride		552-30-7
Vinylcyclohexene	C54998	106-64-1
Vinyl toluene		622-97-9
Wollastonite Ca-silicates	C55470	13983-17-0
Xylenes, mixed	C55232	1330-20-7

TABLE 10.—*Chemicals nominated for Toxicologic or Carcinogenic Evaluation*

Compound	NCI No.	CAS No.
1-amino-2, 4-dibromoanthraquinone		81-49-2
amphetamine	C55710	60-13-9
azodicarbonamide	C55981	123-77-3
benzaldehyde	C56133	100-52-7
benzilic acid, 4,4'-dichloroethyl ester	C00408	510-15-6
N-butyl chloride	C06155	109-69-3
gama-butyrolactone	C55878	96-48-0
beta-cadinene (oil of cade)	C56008	523-47-7
carvone (caraway, dill seed)	C55867	99-49-0
catechol	C55856	120-80-9
chloramphenicol	C55709	56-75-7
chlordecone (Kepone)	C00191	143-50-0
chlorinated dibenzofurans		
chlorinated naphthalenes		
p-chloroaniline	C02039	106-47-8
chlorpromazine	C05210	69-09-0
chromium inorganic	C04273	7440-47-3
copper and inorganic compounds	C08515	7440-50-8
corn oil	C00577	8001-30-7
curcumin		458-37-7
2,4-diaminophenol hydrochloride		
4,4-diamino-2,2 stilbenedisulfonic acid		
cis-dichlorodiamine platinum (II)	C55776	15663-27-1
1,1-dichloroethylene	C54262	75-35-4
cis- & trans 1,2 dichloroethylene	C51581	156-59-2
dichloropropane		26638-19-7
diethyl pinthiaste		84-66-2
3,4-dihydrocoumarin	C55890	119-84-6
dimethioxane ("dioxin")	C56213	828-00-2
3,3 dimethoxybenzidine	C02175	91-93-0
dimethyl sulfoxide	C00873	67-68-5
ethoxyethanol	C54853	110-80-5
ethylene glycol	C00920	107-21-1
furan	C56202	110-00-9
furfural	C56177	98-01-1
furfuryl alcohol	C56224	98-00-0
glycidol	C00617	9005-65-6
HC yellow No. 4	C58019	52551-67-4
hexachlorobutadiene		87-68-3
hexachlorocyclopentadiene	C55607	77-47-4
hexachloroethane	C04904	67-72-1
hormones		
hydroxyacetanilide		
4-hydroxyacetanilide	C55801	103-90-2
indomethacine	C56144	53-86-1
iron compounds		
isobutererenol HCL	C55630	7683-59-2
lead oxide		1335-25-1
lithium and compounds		7439-93-2
manganese compounds	C02517	7439-96-5
mercury (metal)	C04375	7439-97-6
mercuric chloride		7487-94-7
		43412-44-9
phenyl mercuric acetate		
methapyrilene	C09018	91-80-5
methyl coumarin	C55812	92-48-8
p-methylhydroxylamine		67-62-9
methyl ethyl ketone peroxide		1338-23-4
monochloroacetic acid	C08264	79-11-8
monochloroethane		75-003
monosodium methane arsenate		
navy fuels JP-5	C54784	
nitrobenzene		98-95-3
nitrophenols		
p-nitrophenol	C55992	100-02-7
N-nitrosodiethanolamine	C55583	1116-54-7
nitrotoluene		1321-12-6
octachlorodibenzodioxin	C09676	3268-87-9
oleic acid, methyl ester, cis		
organophosphates		
palladium (2+) chloride		
pentachloroethane	C55804	76-01-7
pentaerithrityl tetranitrate	C55743	78-11-5
petroleum distillates		
phenol, 2,2'-thiobis(4,6-dichloro)	C02946	97-18-7
D-phenylalanine		673-06-3
N-phenylhydroxylamine		100-65-2
pichloram	C00937	1918-08-1
platinum and compounds		7440-06-4
polyvinylpyrrolidone polymers		
potassium azide		20762-60-1
probenecid	C56097	57-66-9
quercetin		522-12-3
p-quinone	C55845	106-51-4
resorcinol	C05970	108-46-3
rhodamine	C56122	989-38-8
sodium azide	C06462	26628-22-8
sodium dichloroisocyanurate	C55732	2893-78-9
styrene	C02200	100-42-5
talc	C06006	14807-96-6
L-taurine		107-35-7
tellurium		13494-80-9
tetrahydrofuran		109-99-9
tetraks (hydroxymethyl) phosphonium chloride.	C55061	124-64-1
titanium & compounds—titanium	C04251	7440-32-6
titanium oxide	C04240	13463-67-7
titanium ferrocene	C04502	1271-19-8
trichloroethylene	C04546	79-01-6
trichloropropane		25735-29-9
2,4,6-trinitrotoluene	C56155	118-96-7
tris (4-bromophenyl) phosphate		115-96-8
tris (2-chloroethyl) phosphate		
vinyl cyclohexene dioxide		
vinylidene fluoride		
vitamin D		1406-18-2
vitamin D_3		67-97-0
witch hazel	C50544	84400-12-7
xylenesulfonic acid, sodium salt	C55403	1300-72-7
2,6-xylidine	C56186	87-62-7

Table 11.—*Chemicals Studied for Behavioral or Neurologic Effect*

Chemicals	CAS No.
Carbon disulfide *	75-80-5
Chlordecone	143-50-0
Caffeine *	58-08-2
Ethanol *	64-17-5
Ethylene oxide	75-21-8
Lithium carbonate	554-13-2
Mercaptobenzothiazole	149-30-4
Methyl bromide	74-83-9
Methyl chloride *	74-87-3
Methylethyl ketone	78-93-3
Polybrominated biphenyl	
Propylene oxide	75-56-9
Selenium	7488-56-4
Toluene *	108-88-3
Valium *	439-14-5
Xylene	1330-20-7

* Human subject study

† Includes human subject study and interaction of methyl chloride caffeine ethanol and valium

‡ Includes human subject study and interaction of toluene, methyl ethyl ketone and xylene

[FR Doc. 79-22733 Filed 7-23-79; 8:45 am]

BILLING CODE 4110-85

Michael J. van den Heuvel

A View of the Resource Needs for the Appraisal of Toxicological Information on Existing Chemicals

A pre-requisite for any decisions taken, either nationally or internationally, on the need or otherwise for the further testing of an existing chemical in order to fill gaps in knowledge of its toxicological or ecotoxicological properties, is the collection and critical scientific appraisal of all the already available, relevant, information on the substance.

Appraisal of Information on Human Health Effects

In the United Kingdom, the Data Appraisal Unit of the Health and Safety Executive has been engaged for some time in the toxicological appraisal of existing substances and so has practical experience of the resource costs, both financial and in scientific manpower terms, of such work. During the past two years, the unit has ,for example, collected and critically appraised the available toxicity data on a number of substances including benzene, styrene, carbon disulphide and formaldeyhde.

In discussing resource costs, however, it is desirable to indicate the exact nature of the work which is involved at each stage of a critical appraisal.

Stage 1 – Data Collection

The first stage of the appraisal involves the identification and retrieval of available toxicological information. Whilst chemical firms often hold unpublished information on substances which they market and should not be overlooked as an important source of information, the principal source of data on existing chemicals is undoubtedly the published scientific literature. This information is identified by means of computer searches of commercial scientific data bases. There are a large number of such data bases in existence including Toxline, Exerpta Medica, Toxicological Abstracts, Medline, Chemical Abstracts, Pestdoc and International Pharmacology Abstracts. In our experience a search of Toxline and Exerpta Medica produces a generous coverage of the important published toxicity information for most substances, although supplementary searches of two or three of the more specialist data bases are often also necessary. Having identified the individual published papers, a copy of each paper has then to be obtained and, where necessary, translated into English.

Stage 2 – Validation of Data

After retrieval, each scientific paper must be 'validated' by an experienced toxicologist – that is, the experimental procedures which were used in the study must be scrutinized to determine how closely they follow current thinking on methodology. For example, such aspects as the species/strain, number, age and sex of animals and the method, frequency and level of dosing used in a laboratory study need to be considered; in epidemiological studies the requirement for adequate matching controls is paramount. Reported results need to be checked against the experimental data and statistical procedures verified as being both appropriate and accurate. Such testing of the validity of a reported study is absolutely essential to establish the level of confidence which can be placed in the reported results of a study.

Stage 3 – Interpretation

Following validation, studies conducted in the laboratory involving the use of biological systems other than man, must be interpreted. Each individual study must be assessed for its applicability to man. To do this, the toxicologist the reported results of the study in the light of the known physical, chemical and toxicological properties of the substance.

Stage 4 – Report

Finally, a report must be prepared drawing together information on acute, chronic and other laboratory studies, epidemiological evidence, etc. The reasons for accepting or rejecting each piece of evidence need to be given in detail, together with an indication of the level of confidence which can be placed in the results of the various studies. In most cases an overall assessment is made in which the toxicological properties of the substance are identified and attention drawn to gaps in the data and/or to areas where the data is conflicting and where there is thus a need for further investigation.

Resource Costs

Obviously, the costs of toxicity appraisals in terms of money and staff time will vary considerably from chemical to chemical dependent upon the volume and nature of the published information. The experience in the United Kingdom is that substances selected for toxicity appraisal tend to be those which have given rise to some serious concern or which are in very wide use and alleged to be responsible for some degree of ill health in those handling the substance in industry. For this reason they inevitably seem to have been the subject of considerable research. The costs given below are per substance, based on experience of toxicity appraisal work in the United Kingdom:

Stage 1	Cost of computer searches (including staff time)	£ 50–£ 200
	Cost of Reprints	£ 200–£ 400
	Cost of Translation Services	£ 1000 +
Stage 2 & 3	Cost of Staff Time (Two or three scientists/ toxicologists for 2 to 3 months)	£ 10,000–£ 15,000
Stage 4	Cost of Final Report (preparation and assessment)	£ 1000–£ 2000

Thus the total cost for completing toxicity appraisals of existing substances in the UK has varied in practice between £ 12,250 and £ 18,600.

Appraisal of Information on Environmental Effects

An appraisal of the ecotoxicological information is identical procedurally to that required for toxicity information appraisal. In the United Kingdom, critical appraisals of information on environmental effects of existing chemicals have been conducted, for example, on pesticides (principally the organochlorine insecticides), chlorinated phenols, PCB's heavy metal compounds and sulphur dioxide.

It has, unfortunately, proved difficult for administrative reasons to identify the cost of these appraisals in the same way as was done for toxicity appraisals. It is reasonable, however, to expect that for most – but not all – industrial chemicals costs of ecotoxicological appraisal will be lower if only because the potential environmental effects of such chemicals are seldom the subject of intense investigation.

Nevertheless, it will always be necessary to institute the computer searches to retrieve any available information and for information retrieved to be critically appraised and reported upon by experienced ecotoxicologists. Where a substantial amount of published information on environmental effects is identified, the costs of conducting the required critical appraisal may be similar to those attributed earlier for toxicity appraisal.

The average overall cost in the United Kingdom for the conduct of a critical appraisal of information on the human health and environmental effects of an existing substance is thus of the order of £ 20,000–£ 30,000.

P. Menke-Glückert

Concluding Remarks by the General Chairman

This workshop was an exchange among experts and it was part of an exercise of OECD which will have many other follow-up exercises. In this sense it is just one little step forward. I believe that the theme of this meeting as well as the achievements here in Berlin showed clearly that there is a great interest among OECD Member Countries and, moreover, a sincere sense of cooperation among these nations when it comes to dealing with problems in controlling toxic chemicals, here in particular existing chemicals. The international scientific community has responded to the challenge to diminish risks of toxic chemicals.

In the past it has been customary to deal with industrial existing chemicals, as need arose, case by case. This workshop showed beyond any doubt that this approach will no longer suffice. Ways must be found to deal with the multitude of problems surrounding the existing chemicals in a systematic and internationally harmonized manner. This means we need a global strategy; we need a list of priorities.

I think it also very positive that we are realistic and not trying to portray a situation as if the solutions have already been found. For most of the problems there are *not* enough resources available on national levels when considering all the problems we need to solve:

It was estimated that the laboratory investigation of each of the existing chemicals may cost as much as 1 to 2 million dollars, most likely less.

In view of the magnitude of this problem it is now commonly felt that only close international cooperation between governments, scientists and industry, too, and sharing of resources will yield acceptable progress.

Very careful preparations are necessary to establish an international program of cooperation to deal with class II chemicals. The government of the Federal Republic of Germany has therefore proposed a major international study to delineate solution alternatives. This study is presently prepared by a pre-study, whose results should become available early in 1982.

The government of the Federal Republic of Germany offered to hold a follow-up workshop, perhaps already within one year, whereby it was agreed that the subject to be discussed would be more specific than was the case in the workshop during June of 1981, where the most important task was to take stock in the present overall problems arising from existing chemicals. I think we should give clear indications how to solve the problem, and I think that we should use as far as possible all the available existing resources, such as the data collections from IRPTC, or the inventories which exist in some OECD Member Countries.

Specifically this workshop suggested, among many other recommendations, the following actions to be taken:

- The OECD secretariat should prepare in 1981 a meeting with other international organizations to discuss improved cooperation, so as to minimize costly duplication of efforts.
- Agreement must be sought with respect to a list of such dangerous chemicals, or classes of chemicals, of which one may assume that sufficient information is already in hand, so that "chemical reviews" could be composed (*class I* existing chemicals, perhaps several hundred). Possibly the IPCS list could form an acceptable basis.

- There is a need for agreement on the data components which must be covered in such chemicals reports. It was also recommended that these chemicals reports should only contain the necessary, quality-screened individual data components, without attempting to reach regulatory recommendations. It was felt that the latter would have to remain a primarily national concern.
- Once agreement has been reached on the necessary data components (MED = Minimum Required Existing Data Components) and also on ways to ascertain quality assurance, ways must be found to produce quickly and efficiently the "chemical reviews" for the class I chemicals. Thus we can avoid duplication over and over by international institutions and national agencies (e.g. for cadmium, asbestos, PCB, etc.).
- The vast majority of existing chemicals will be those for which very little information is presently available (maybe as many as 50,000) (*class II* existing chemicals). For these, the establishment of appropriate selection criteria for screening out particularly suspicious chemicals was recommended.
- In agreement with industry, it was felt that there may be as many as 5,000 such suspicious chemicals.
- The problem of confidentiality must be settled.

At the end let me re-emphasize that we should not create data cemeteries within national administrations: We have to do first things first, which means to start on the basis of MED with chemical reviews of class I chemicals.

Concluding remarks

This is the moment, on behalf of the OECD, to thank the German Authorities for organizing this Workshop. I did indicate last night our gratitude to the Authorities of the Federal Government and the Senate of Berlin for their hospitality. While I am on the topic of last night's reception could I just diverge to say that there is no truth in the ugly rumour that the marvellous interpreter at the reception had difficulty in translating my remarks into English.

I also want to thank the speakers for the interesting surveys of issues, which taken together must virtually have covered every important facet of existing chemicals – and, of course, all those who have contributed to the discussion.

I have been asked by various participants how I judge the progress made. I would say it has been very successful.

Firstly, because all the interested parties have settled down to discuss management of existing chemicals – a topic which has been considered in back-rooms in the red-light district until the recent past.

Secondly, because we have arrived at some useful conclusions and have identified some areas of common concern.

Thirdly, because the presentations and the voluntary contributions have shown the complexity of managing existing chemicals, the interfaces between the many issues and the need to build step-wise. After all, the ventilation of divergent views and the opportunity of all the interested parties to contribute is an essential ingredient if effective international harmonization is an objective in any area.

Fourthly, I was personally gratified to hear the industry delegates at this meeting talking about the breadth and availability of data, their suggestions on the orientation of further work and their offers to contribute to this work on existing chemicals. This has been important to us in OECD in making progress to date. It has been equally important that we build on existing work.

Fifthly, I was pleased to see representatives of the broader community. They have, I believe, made the point that there should be more open and well-understood decision-making processes which include appropriate mechanisms for public participation, including access to information held by industy. This is not just a matter of industry image, but an important facet of democracy at work.

Lastly, as I said in my remarks in the first session, OECD is not the only master-builder. Here in this meeting we have established the need for collaboration between international institutions and as well much existing work in these institutions has been commended as building blocks.

Now I should like to turn to OECD specifically.

The products of this Workshop will be placed before the Chemicals Group and the Management Committee of the OECD. We have talked a lot about selection criteria over recent days. The first step within OECD in starting our work will be to apply selection criteria to the papers, discussion and conclusions at this meeting. The results of this analysis will govern what is appropriate, manageable and affordable in OECD and how we phase in this work. Further impetus may well be given by the up-coming High Level Meeting. We in the OECD Secretariat would welcome further discussion and we will be reflecting on all this through the summer months.

Thank you Chairman for a most interesting meeting on a most challenging topic. We have enjoyed your vigour in the chair and the ideas you have injected into the meeting – could I comment personally that it is a captivating experience to watch you in full flight. Of course, I should also recognise the continuing leadership of Dr. Hartkopf in this field and the way in which he set the stage for the meeting. Then I would like to thank Prof. Schmidt-Bleek and all his co-workers and to thank them for all their efforts and hospitality.

APPENDICES

AGENDA

Workshop on the Control of Existing Chemicals under the Patronage of the Organization for Economic Co-operation and Development
June 10–12, 1981
Berlin (West)
Reichstagsgebäude

Wednesday, June 10, 1981

General Chairman: P. Menke-Glückert
General Co-Chairman: P. Crawford
Chief-Rapporteur: N. King

Opening of the workshop

Introduction by Günter Hartkopf, Staatssekretär, Federal Ministry of the Interior

TOPIC I

International Co-operation in Controlling Specific Existing Chemicals

Section-Chairman: M. Bracken
Rapporteurs: I. Fuller
C. Morawa

M. Mercier
(International Programme on Chemical Safety):
Present and planned activities of IPCS on existing chemicals

J. I. Waddington
(World Health Organization/Euro):
The programme on European co-operation on environmental health aspects of the control of chemicals.

J. Smeets
(Commission of the European Communities):
The control of existing chemicals in the European Community

P. Crawford
(Organization for Economic Co-operation and Development):
International harmonization of chemicals control in OECD countries

Thursday, June 11, 1981

TOPIC II

Analysis of the Legal and Administrative Powers to Control Existing Chemicals in OECD Member Countries

Section-Chairman: W. Irwin
Rapporteurs: P. Rudolph
B. Wagner

S. Johnson
Survey of legal and administrative powers to control existing chemicals – based, in part, upon the results of the questionnaire circulated by the host country

Short prepared statements by national experts on Topic II:

E. W. Langley (United Kingdom); *V. Silano* (Italy); *P. Deschamps* (France); *J. Exsteyl* (Belgium); *H. Schulze* (Federal Republic of Germany).

TOPIC III

Identification and Quantification of Criteria for Selecting Existing Chemicals for Gathering Information, Testing and Assessment on a Case by Case Basis

Section-Chairman: R. Lønngren
Rapporteurs: A.-W. Klein
E. Smith

J. Brydon
Selecting priority existing chemicals for review and testing – based, in part, upon the results of the questionnaire circulated by the host country

K. Kobayashi
Safety examination of existing chemicals in Japan – Selection, testing, evaluation and regulation

M. C. Bracken
U. S. experience in the selection of chemicals for testing under the Toxic Substances Control Act

J. Huismans
The international register of potentially toxic chemicals: Its usefulness for the selection of priority existing chemicals for assessment and hazard control

T. Mill
Minimum data needed to estimate environmental fate and effects for hazard classification of synthetic chemicals

U. Woelcke
Selecting existing chemicals under the aspect of occupational hazards

A. Somogyi
Health Risk Assessment

B. Broecker
Contribution of the European Council of Chemical Manufacturer's Federations on the problem of selecting priority chemicals

Short prepared statements by national experts on Topic III:
W. H. Könemann (Netherlands); VCI (Verband der Chemischen Industrie – Association of the German Chemical Industry) – *Helmut Kainer* (Federal Republic of Germany); Berufsgenossenschaft of the Chemical Industry – *J. Oberhansberg* (Federal Republic of Germany); Deutscher Gewerkschaftsbund – IG Chemie, Papier, Keramik – Trade Union for Chemicals Paper and Earthenware – *Gerd Albracht* (Federal Republic of Germany); *E. W. Langley* (United Kingdom); *M. J. Flux* (United Kingdom); *R. L. Bohon* (USA); *J. Exsteyl* (Belgium); *H. G. Nösler* (Federal Republic of Germany); *W. Niemitz* (Federal Republic of Germany); *D. F. Gascoine* (Australia); *F. S. Rowland* (USA); *E. H. Blair:* A framework of consideration for setting priorities for the testing of chemical substances.

Friday, June 12, 1981

TOPIC IV

Identification of Resource Needs for Testing and Evaluating Existing Chemicals

Section-Chairman: F. Schmidt-Bleek
Rapporteurs: W. Haberland
A. Walker

A. S. Welinder
A survey of resource for testing and evaluating existing chemicals

D. McCollister
Resource needs for selection, evaluating and testing existing chemicals as illustrated by present national and international institution programs

M. J. van den Heuvel
A view of the resource needs for the appraisal of toxicological information on existing chemicals.

List of Authors of Papers and of *Statements*

Dipl.-Chem. Gerd Albracht
IG Chemie-Papier-Keramik
Hauptvorstand
Postfach 30 47
Königsworther Platz 6
D-3000 Hannover 1

Dr. Etcyl H. Blair
Vice President
The Dow Chemical Company
2020 Dow Center
USA-Midland, Michigan 48 640

Dr. Robert L. Bohon
3 M Co., ee and pc
21-2w-05
P. O. Box 33 331
USA-St. Paul, Minnesota 55 133

Dr. Marilyn C. Bracken
Associate Assistant Administrator
for Toxics Integration
US Environmental Protection Agency
401 M Street
USA-Washington D.C., 20 460

Dr. Bernhard Broecker
Hoechst Aktiengesellschaft
Postfach 80 03 20
D-6230 Frankfurt am Main 80

Dr. Jim Brydon
Director, Contaminants Control Branch
Environmental Protection Service
Environment Canada
CDN-Ottawa, Ontario K1A 108

Dr. Peter J. Crawford
Head of the Chemicals Division
Environment Directorate
Organization for Economic
Co-operation and Development
2, rue André Pascal
F-75 775 Paris Cédex 16

M. Pascal Deschamps
Chargé de Mission
Ministère de l'Environnement
et du Cadre de Vie
14, boulevard du Général Leclerc
F-92 522 Neuilly-sur-Seine/Cédex

Mr. Jacques Exsteyl
Inspecteur Chimiste en Chef Directeur
Ministère de l'Emploi et du Travail
rue Belliard 53
B-1040 Bruxelles

Mr. Michael J. Flux
Company Environment Adviser
Imperial Chemical Industries Limited
Imperial Chemical House
Millbank
GB-London SW1P 3Jf

Mr. D. F. Gascoine
Assistant Secretary
Environment Assessment Branch
Department of Home Affairs
and Environment
P. O. Box 1252
AUS-Canberra City, ACT, 260

Staatssekretär Dr. Günter Hartkopf
Bundesministerium des Innern
Graurheindorfer Str. 198
D-5300 Bonn 1

Mr. Michael van den Heuvel
Health and Safety Executive
Room 601
Baynards House
1 Chepstow Place
Westbourne Grove
GB-London W2 4TF

Dr. Jan W. Huismans
Director
International Register of Potentially
Toxic Chemicals (IRPTC)
United Nations Environment Programme
Palais des Nations
CH-1211 Geneva 10

Mr. Stanley Johnson
30 Maida Avenue
GB-London W2 1ST

Dr. Helmuth Kainer
BASF Aktiengesellschaft
D-6700 Ludwigshafen

Dr. Norman J. King
Department of the Environment
Room S 10/02
2 Marsham Street
GB-London SW 1P 3EB

Mr. K. Kobayashi
Ministry of International Trade and Industry
1–3 Kasumigaseki
Chiyoda-ku
JAP-Tokyo 100

Dr. W. H. Könemann
Division of Ecology and Environmental Toxicology
Ministry of Health and Environmental Protection
Dokter Reijersstraat 12
NL-BA Leidschendam

Mr. E. W. Langley
Deputy Chief Inspector of Factories
Health and Safety Executive
25, Chapel Street
GB-London NW 2

Mr. Paul Lemerle
Deputy Secretary-General
Organization for Economic Co-operation and Development
2, rue André Pascal
F-75 775 Paris Cédex 16

Mr. Harald Lindemann
Bundesministerium für Wirtschaft
Villemombler Straße 76
D-5300 Bonn 1

Dr. Rune Lønngren
Swedish National Products Control Board
P.O. Box 1302
S-17 125 Solna 1

Donald D. McCollister
Director,
International Regulatory Affairs
Health and Environmental Sciences
1803 Building
USA-Midlang, Michigan 48 640

Professor M. Mercier
Manager, International Programme on Chemical Safety
Division of Environmental Health
World Health Organization
CH-1211 Geneva 27

Dr. Theodore Mill
Department Director
Physical Organic Chemistry Department
Stanford Research International
333 Ravenswood Ave.
USA-Menlo Park, California 94 025

Prof. Dr. W. Niemitz
Institut für Wasser-, Boden- und Lufthygiene des Bundesgesundheitsamtes
Corrensplatz 1
D-1000 Berlin 33

Dr. Heinz Günter Nösler
Henkel KGaA
Postfach 11 00
D-4000 Düsseldorf

Dr. Joachim Oberhansberg
Berufsgenossenschaft der Chemischen Industrie
Postfach 10 14 80
D-6900 Heidelberg

J. P. Parenteau
Direction de la Prévention des Pollutions et Nuisances
Ministère de l'Environnement et du Cadre de Vie
14, boulevard du Général Leclerc
F-92521 Neuilly-sur-Seine

Prof. Dr. F. S. Rowland
Institut für Physikalische
und Theoretische Chemie
der Technischen Universität München
D-8046 Garching

permanent address:
Department of Chemistry
University of California
USA-Irvine, California 92 717

Prof. Dr. Dr. Hanno Schulze
Bayerisches Staatsministerium für
Landesentwicklung und Umweltfragen
Rosenkavalierplatz 2
D-8000 München 81

Prof. Vittorio Silano
Istituto Superiore di Sanità
Department of Toxicology
Viale Regina Elena 299
I-Roma 00161

Prof. A. Somogyi
Bundesgesundheitsamt
Thielallee 88–92
D-1000 Berlin 33

Dr. J. Ian Waddington
Director, Promotion of Environmental Health
World Health Organization
Regional Office for Europe
8, Scherfigsvej
DK-2100 Copenhagen

Dr. Albert S. Welinder
Head of Division
Ministry of the Environment
National Agency of Environmental Protection
Strandgade 29
DK-1401 Copenhagen

List of Participants

Ministerialrat
Dr. Friedrich Ahrens
Ministerium für Arbeit,
Gesundheit und Soziales
des Landes Nordrhein-Westfalen
Horion-Platz 1
D-4000 Düsseldorf

Dipl.-Chem. Gerd Albracht
IG Chemie-Papier-Keramik
Hauptvorstand
Postfach 30 47
Königsworther Platz 6
D-3000 Hannover 1

Dr. Bernd Bayer
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Hans Becker
Biologische Bundesanstalt für
Land- und Fortwirtschaft
Messeweg 11–12
D-3300 Braunschweig

Mr. Trevor John Beckmann
Director
Government Chemical Laboratory
William Street
AUS-Brisbane Q. 4000

M. Jean Birden
Ingénieur
Directeur Adjoint
Inspection du Travail
46, avenue de la gare
Luxemburg

Dr. Etcyl H. Blair
Vice President
The Dow Chemical Company
2020 Dow Center
USA-Midland, Michigan 48 640

Dr. Oluf Chr. Bockman
Norsk Hydro a.s.
Research Center
N-3901 Porsgrunn

Dr. Ulrich Boehringer
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Robert L. Bohon
3 M Co., ee and pc
21-2w-05
P.O. Box 33 331
USA-St. Paul, Minnesota 55 133

Dr. Marilyn C. Bracken
Associate Assistant Administrator
for Toxics Integration
US Environmental Protection Agency
401 M Street
USA-Washington D.C., 20 460

Dr. Bernhard Broecker
Hoechst Aktiengesellschaft
Postfach 80 03 20
D-6230 Frankfurt am Main 80

Dr. Jim Brydon
Director, Contaminants Control Branch
Environmental Protection Service
Environment Canada
CDN-Ottawa, Ontario K1A 1C8

Mr. Rob Coppock
Wissenschaftszentrum Berlin
Institut für Umwelt und Gesellschaft
Potsdamer Str. 58
D-1000 Berlin 30

Dr. P. J. Corcoran
Department of the Environment
2 Marsham Street
GB-London S.W. 1

Mrs. Betty Cordier
Expert Ministry of Economic Affairs
Chemical Division
c/o ECOCHEM – FIC
Square Marie-Louise, 49
B-1040 Brussels

Dr. Peter J. Crawford
Head of the Chemicals Division
Environment Directorate
Organization for Economic
Co-operation and Development
2, rue André Pascal
F-75 775 Paris Cédex 16

Dr. Lennart Danielson
Chemicals Division
Environment Directorate
Organization for Economic
Co-operation and Development
2, rue André Pascal
F-75 775 Paris Cédex 16

M. Pascal Deschamps
Chargé de Mission
Ministère de l'Environnement
et du Cadre de Vie
14, boulevard du Général Leclerc
F-92 522 Neuilly-sur-Seine/Cédex

Mr. Wim H. Dobbe
Ministerie van Economische Zaken
Postbus 20 101
NL-2500 EC's-Gravenhage

Mr. Jacques Exsteyl
Inspecteur Chimiste en Chef Directeur
Ministère de l'Emploi et du Travail
rue Belliard 53
B-1040 Bruxelles

Dr. A. Peter Fletcher
Senior Medical Officer
Department of Health and Social Security
Market Tower, Room 1016
1 Nine Elms Lane
GB-London SW8 5NQ

Mr. Michael J. Flux
Company Environment Adviser
Imperial Chemical Industries Limited
Imperial Chemical House
Millbank
GB-London SW1P 3Jf

Mr. Dietrich Fuchs
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Mr. Ryozo Fujiwara
Director, Environment and Safety
Department
Mitsui Toatsu Chemicals Inc.
Kasumigaseki 3 – 2 – 5
Chiyoda-ku
JAP-Tokyo

Dr. Irving Fuller
Office of Pesticides and Toxic Substances
US Environmental Protection Agency
401 M Street S.W.
USA-Washington D.C., 20460

Dr. Tiziano Garlanda
Montedison
Foro Bonaparte 31
I-Milano

Mr. D. F. Gascoine
Assistant Secretary
Environment Assessment Branch
Department of Home Affairs
and Environment
P. O. Box 1252
AUS-Canberra City, ACT, 260

Dr. Friedrich Geiss
Joint Research Centre
Commission of the European
Communities
I-21020 Ispra

Mr. Michael Gilbertson
Toxic Chemicals Management Centre
Environment Canada
CDN-Ottawa, Ontario K1A 1C8

Dipl.-Phys. Walter Gill
Gesellschaft für Systemtechnik GmbH
Am Westbahnhof 2
D-4300 Essen 1

Professor Dr. Miki Goto
Institute of Ecotoxicology
Gakushuin University
1-5-1 Mejiro
Toshima-ku
JAP-Tokyo 171

Mr. R. Grainger
Chemical Industries Association
Alembic House
93 Albert Embankment
GB-London SE 1

Dr. Klaus-Otto Günther
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Sam Gusman
The Conservation Foundation
1717 Massachusetts Ave., N.W.
USA-Washington D.C., 20036

Dr. Hans Gysin
Consultant
Environmental Secretariat of the OECD
Im Klosteracker 29
CH-4102 Binningen

Dr. Wolfram Haberland
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Jürgen Hahn
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Staatssekretär Dr. Günter Hartkopf
Bundesministerium des Innern
Graurheindorfer Str. 198
D-5300 Bonn 1

Mr. Michael van den Heuvel
Health and Safety Executive
Room 601
Baynards House
1 Chepstow Place
Westbourne Grove
GB-London W2 4TF

Dr. Joseph H. Highland
Chairman, Toxics Chemical Program
Environmental Defense Fund
1525 18th Street N.W.
USA-Washington D.C., 20036

Mr. Immanuel Huhtanen
Chemical Industry Federation
P.O. Box 330
SF-00101 Helsinki 10

Dr. Jan W. Huismans
Director
International Register of Potentially
Toxic Chemicals (IRPTC)
United Nations Environment Programme
Palais des Nations
CH-1211 Geneva 10

Mrs. Judith Hushon
Programme Manager
Enviro Control Inc.
11300 Rockville Pike
USA-Rockville, Maryland 20852

Dr. Will A. Irwin
US Department of the Interior
Office of Hearing and Appeals
Interior Board of Surface Mining
and Reclamation Appeals
4015 Wilson Boulevard
USA-Arlington Va., 22203

Mr. Stanley Johnson
30 Maida Avenue
GB-London W2 1ST

Mr. Stephen Johnson
Senior Advisor for Chemical
Testing and Science Policy
Office of Toxic Substances
US Environmental Protection Agency
USA-Washington D.C., 20460

Dr. Helmuth Kainer
BASF Aktiengesellschaft
D-6700 Ludwigshafen

Dr. Detlev Kayser
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Imre Kerner
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Norman J. King
Department of the Environment
Room S 10/02
2 Marsham Street
GB-London SW 1P 3EB

Mr. M. Kitano
Chemicals Inspection & Testing
Institute, Japan
4-1-1 Higashimukojima
Sumidaku
JAP-Tokyo 131

Dr. Albrecht Wilhelm Klein
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Werner Klein
Gesellschaft für Strahlen- und
Umweltforschung
Institut für Ökologische Chemie
Ingolstädter Landstraße 1
D-8042 Neuherberg
Post Oberschleißheim

Dr. Jürgen Knebel
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Mr. K. Kobayashi
Ministry of International Trade and
Industry
1–3 Kasumigaseki
Chiyoda-ku
JAP-Tokyo 100

Dr. Willem Hans Könemann
Division of Ecology and
Environmental Toxicology
Ministry of Health and
Environmental Protection
Dokter Reijersstraat 12
NL-BA Leidschendam

Ms. Judy Kosovich
Project Officer, Policy Section
Office of International Activities
Environmental Protection Agency, A-106
401 M Street S.W.
USA-Washington D.C., 20460

Dr. Harm A. Kuiper
Ministry of Agriculture and Fisheries
Direction VKA
Bezuidenhoutseweg 73
NL-Den Haag

Mr. Yusuke Kuroda
General Assistant Manager
Technical Division
Japan Chemical Industry Association
Ministry of International Trade and
Industry
Kasumigaseki 1–3
Chiyoda-ku
JAP-Tokyo

Dr. Arno W. Lange
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Mr. E. W. Langley
Deputy Chief Inspector of Factories
Health and Safety Executive
25, Chapel Street
GB-London NW 2

Mr. Paul Lemerle
Deputy Secretary-General
Organization for Economic
Co-operation and Development
2, rue André Pascal
F-75 775 Paris Cédex 16

Dr. Heinrich von Lersner
Präsident des Umweltbundesamtes
Bismarckplatz 1
D-1000 Berlin 33

Mr. Harald Lindemann
Bundesministerium für Wirtschaft
Villemombler Straße 76
D-5300 Bonn 1

Dr. Rune Lønngren
Swedish National Products
Control Board
P.O. Box 1302
S-17125 Solna 1

Donald D. McCollister
Director,
International Regulatory Affairs
Health and Environmental Sciences
1803 Building
USA-Midland, Michigan 48 640

Dr. Hans-Wilhelm Marquart
Bayer AG
LE Umweltschutz / Produkte
D-5090 Leverkusen

Min. Dir. Peter Menke-Glückert
Abteilungsleiter Umwelt
Bundesministerium des Innern
Graurheindorfer Str. 198
D-5300 Bonn 1

Dr. Horst Mierheim
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Theodore Mill
Department Director
Physical Organic Chemistry
Department
Stanford Research International
333 Ravenswood Ave.
USA-Menlo Park, California 94 025

Mr. Konrad von Moltke
Director
Institute for European
Environmental Policy
Adenauerallee 214
D-5300 Bonn 1

Mrs. Christa Morawa
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Mr. Georges Mosselmans
Commission of the European
Communities
DG XI: General Directorate for
Environment, Consumer Protection and
Nuclear Safety
200 Rue de la Loi
B-1049 Brussels

Dr. Norbert Moulin
Expert, Ministry of Economic Affairs
Chemical Division
c/o ECOCHEM – FIC
Square Marie-Louise, 49
B-1040 Brussels

Mr. A. Neff
Director, Technical Affairs
The Canadian Chemical
Producers' Association
CDN-Ottawa K1H 6E3, Ontario

Prof. Dr. W. Niemitz
Institut für Wasser-, Boden- und
Lufthygiene des Bundesgesundheitsamtes
Corrensplatz 1
D-1000 Berlin 33

Dr. Heinz Günter Nösler
Henkel KGaA
Postfach 11 00
D-4000 Düsseldorf

Dr. Joachim Oberhansberg
Berufsgenossenschaft der
Chemischen Industrie
Postfach 10 14 80
D-6900 Heidelberg

Mrs. Anne Mari Opheim
State Pollution Control Authority
P.O. Box 8100
N-Dep-Oslo 1

Mr. B. M. O'Reilly
Hazardous Substances Division
Health and Safety Executive
25 Chapel Street
GB-London NW1 5DT

Dr. Jiri Parizek
International Programme on
Chemical Safety
World Health Organization
CH-1211 Geneva 27

Ms. Sue H. Patterson
Office of Environment and Health
Department of State
USA-Washington D.C., 20520

Mr. Heinz-Jochen Poremski
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Drs. Lammert C. Rinzema
Dow Chemical Europe S.A.
Bachtobelstr. 3
CH-8810 Horgen

Dr. Hilliard Roderick
International Institute on
Environmental Health Risks
c/o 20 Lloyd Road
GB-Hove BN3 6NL

Dr. Claudia Rosicky
Abteilung III. 2
Bundesministerium für
Gesundheit und Umweltschutz
Stubenring 1
A-1010 Wien

Dr. Ralph T. Ross
US Department of Agriculture
USA-Washington D.C., 20250

Dr. Elke Roßkamp
Bundesgesundheitsamt
Thielallee 88–92
D-1000 Berlin 33

Dr. Jerome Rothenberg
Center for International Studies
Massachusetts Institute of Technology
USA-Cambridge, Massachusetts 02139

Prof. Dr. F. S. Rowland
Institut für Physikalische und
Theoretische Chemie
der Technischen Universität
München
D-8046 Garching

permanent address:
Department of Chemistry
University of California
USA-Irvine, California 92717

Mr. Peter Rudolph
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Mr. Jacques Salamitou
Rhône Poulenc
22, avenue Montaigne
F-75008 Paris

Dr. Hans Peter Saxer
Lonza AG
Postfach
CH-4002 Basel

Dr. Helmut K. Schäfer
Hoechst Aktiengesellschaft
Gebäudenummer C 769
Postfach 80 03 20
D-6230 Frankfurt am Main 80

Professor Dr. Friedrich Schmidt-Bleek
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Prof. Dr. Dr. Hanno Schulze
Bayerisches Staatsministerium für
Landesentwicklung und Umweltfragen
Rosenkavalierplatz 2
D-8000 München 81

Mr. Noriaki Shigeno
Senior Staff
Office of Health Studies
Environment Agency
3-1-1 Kasumigaseki
JAP-Tokyo 100

Prof. Dr. Günther Siebert
Lehrstuhl für experimentelle
Zahnheilkunde
Pleicherwall 2
D-8700 Würzburg

Prof. Vittorio Silano
Istituto Superiore di Sanità
Department of Toxicology
Viale Regina Elena 299
I-Roma 00161

Dr. Edward M.B. Smith
Chief Medical Officer
Albright & Wilson Ltd.
1 Knightsbridge Green
GB-London SW 1X 7QD

Prof. A. Somogyi
Bundesgesundheitsamt
Thielallee 88–92
D-1000 Berlin 33

Ir. W. J. M. Sprong
Division of Ecology and Environmental
Toxicology
Ministry of Health and Environmental
Protection
Dokter Reijersstraat 12
NL-BA Leidschendam

Mrs. Margareta Stackerud
National Environment Protection Board
P.O. Box 1302
S-17125 Solna

Mrs. Merethe Steen
State Pollution Control Authority
P.O. Box 8100
N-Dep-Oslo 1

Dr. Jens Steensberg
Chief Medical Officer
National Agency of Environmental
Protection
Strandgade 29
DK-1401 Copenhagen K

Dr. Alwig Stingele
Joint Research Centre
Commission of the European
Communities
I-21020 Ispra, Varese

Mr. Andre de Swaef
Attaché du Ministre
Ministère de l'Emploi et du Travail
rue Belliard 51–53
B-1040 Brussels

Dr. W. Töpner
Bundesministerium für Jugend,
Familie und Gesundheit
Deutschherrenstraße 87
D-5300 Bonn 2

Dr. Peter Toft, Chief
Monitoring and Criteria Division
Bureau of Chemical Hazards
Environmental Health Directorate
Health and Protection Branch
Health and Welfare Canada
Tunney's Pasture
CDN-Ottawa, Ontario K1A OL2

Mr. Y. Tsuji
Ministry of International Trade and
Industry
1–3 Kasumigaseki
Chiyoda-ku
JAP-Tokyo 100

Dr. Lisia Turri
NO / COM – ANIC SpA
San Donato
I-Milano

Mr. Reinhard Ueberhorst
Senator für Gesundheit und Umweltschutz
An der Urania 12
D-1000 Berlin 30

Mr. Garrett Upstill
Chemicals Division
Environment Directorate
Organization for Economic Co-operation and Development
2, rue André Pascal
F-75 775 Paris Cédex 16

Mrs. Suzanne Veltzé
Head of Division
Agency of Environmental Protection
29 Strandgade
DK-1401 Copenhagen K

Dr. J. Ian Waddington
Director, Promotion of Environmental Health
World Health Organization
Regional Office for Europe
8, Scherfigsvej
DK-2100 Copenhagen O

Dr. Burkhard Wagner
Chemicals Division
Environment Directorate
Organization for Economic Co-operation and Development
2, rue André Pascal
F-75 775 Paris Cédex 16

Dr. Arthur P. Walker
Procter & Gamble Ltd.
Whitley Road, Longbenton
P.O. Box Forest Hall No. 2
GB-Newcastle upon Tyne NE 12 9TS

Dr. Albert S. Welinder
Head of Division
Ministry of the Environment
National Agency of Environmental Protection
Strandgade 29
DK-1401 Copenhagen

Mr. Eberhard Westheide
Ref. U II 9
Bundesministerium des Innern
Graurheindorfer Str. 198
D-5300 Bonn 1

Ms. Cynthia Whitehead
Lawyer
Königstraße 12 B
D-5300 Bonn 1

Mr. Julian Wilbourn
International Agency for Research on Cancer
World Health Organization
150, cours Albert-Thomas
F-69 372 Lyon Cédex 2

Mr. Theo Witteman
Co-ordinator Chemicals
Vereniging van de Nederlands Chemische Industrie
Postbus 80504
NL-2508 GM 's-Gravenhage

Dr. Uwe Wölcke
Bundesanstalt für Arbeitsschutz und Unfallforschung
Vogelpothsweg 50–52
D-4600 Dortmund-Dorstfeld

Dr. Wolfgang Wohlleben
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Mrs. Monika Zimmermann
Bundesverband Bürgerinitiativen und Umweltschutz (BBU) e.V.
Ermanstraße 16
D-1000 Berlin 41

Guests:

Prof. Dr. Wolfgang Hertel
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Hans-Dieter Schenke
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Mr. Werner Schenkel
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Jan Dieter Schmitt-Tegge
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Gabriele Studinger
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

Dr. Martin Uppenbrink
Umweltbundesamt
Bismarckplatz
D-1000 Berlin 33

Mrs. Sigrid Warmburg
Umweltbundesamt
Bismarckplatz 1
D-1000 Berlin 33

IPCS/CEC Joint Task Force on Priority Industrial Chemicals Ispra, Italy, November 17–20, 1980

The following list of chemicals was prepared from the Technical Committee (IPCS) Report (July 1980), the recommendations of the "Consultation on Priority Problems in Toxic Chemicals Control in Europe (WHO-EURO November 1980)", the two consultants' reports, national priority lists and the IRPTC Query Response Service.

Acetonitrile
Acrylamide
Acrylonitrile – ILO
Alkyl epoxides
Aluminium phosphide (see phosphine)
Ammonia – C
Anilines
Anionic detergents – D
Antimony
Arsenic – C
Asbestos

Barium
Beryilium – C
Benzene
Benzidine
Benzo (α) pyrene – C
Bismuth

Cadmium – C
Carbon disulphide – A
Carbon monoxide – A
Chlorinated dibenzo-para-dioxins – C
Chlorinated hydrocarbons – C
Chlorinated naphthalenes
Chlorinated paraffins
Chlorine and hydrogen chloride – C
Chloroacetamide
Chlorobenzenes
Chlorofluorocarbons
Chloromethane (see chlorinated paraffins)
Chlorophenols (see phenols)
Chromium – C
Cobalt – C

DDT – A
Dibromochloropropane (DBCP) – ILO
Dichloromethane
1,2 dichloro-propane
Diethanolamine
Diethyl nitrosoamine
Dimethyl hydrazine (asymmetrical)
Dimethyl sulphate

Ethylamine
Ethylbenzene
Ethylene dichloride
Ethyleneimine

Fluorine and fluorides – C
Formaldehyde

Glycidol and its derivatives

Halogenated alkyl epoxides (see alkyl epoxides)
Hexachloro-1,3 butadene
Hexachlorocyclopentadiene and adducts
Hexachlorophene
Hydrogen chloride (chlorine +) – C
Hydrogen peroxide
Hydrogen sulphide – C

Isophorone

Lead – A

Manganese – B
Mercury – A
Mestyle oxide
4,4′-methylene dianiline
Methyl ethyl ketone
Mirex
Molybdenum

2-naphthyl amine – ILO
"Niax (R) catalyst ESN" – a mixture of 3-(Dimethylamino) propionitrile (95 %) and bis [2-(dimethylamino) ethyl]ether (5 %)
Nickel – C
Nitrates, nitirites and N-nitroso compounds – A
Nitrobenzene
Nitrogen oxides – A
2-Nitropropane (2-NP) – ILO

Organochlorine solvents
Organophosphorus compounds – C
A – Organotins (Tin and)
D-4,4′-Oxydianiline

PBBs
PCBs + PCTs – A
Pentachlorophenol
Perchlorethylene
Petroleum products (selected)
Phenols
Phenylene diamines
Phosphine
Phthalic acid esters
Polynuclear aromatic hydrocarbons – C
Polyvinyl chloride (see vinyl chloride)
Pyridine

Selenium – C
Sulphur oxides – A
Styrene – D

Thallium
Tin (and organotin compounds) – A
Titanium
O-Tolidine
Toluene
2,6-Toluenediamine – D
Triaryl phosphates
1,1,1-Trichloroethane (see chlorinated paraffins)
Trichloroethylene (see organochlorine solvents)
Tricresyl phosphates

Vanadium – C
Vinyl chloride
Vinylidine chloride

Xylenes

Dipl. Phys. Walter Gill, Gesellschaft für Systemtechnik, Essen

Summary of the Response to the Questionnaire under Contract with the Umweltbundesamt
Contract No.: 10604009

1. Introduction

The following summary of the questionnaire shall give an outline of the international situation concerning "existing chemicals". The "questionnaire on existing chemicals" was developed by GST Gesellschaft für Systemtechnik mbH under contract of the Umweltbundesamt Berlin in preparation of the workshop on the control of existing chemicals in Berlin, June 10–12, 1981.

This questionnaire was sent to all OECD-member countries.

The summary is based on the topics 2, 3 and 4 of the OECD-workshop program and can be used as an informational guide to the workshop.

The table on the next page shows which countries and which authorities have so far answered to the questionnaire. These answers are included in this summary.

survey concerning the response to the questionnaire

land/organisation	responding authority	questionnaire answered	percentage of sales in chemicals in the world
Australia	department of home affaires & environment	yes	
Austria	Bundesministerium für Gesundheit und Umweltschutz	yes	0.4
Belgium	ministry of the environment	yes	1.7 *)
Canada	department of environment and department	yes	
Denmark	miljostyrelsen	yes	0.3
Finland			
France	ministere de l'environnement	yes	4.5
Germany	department of interior	yes	7.7
Greece			
Iceland			
Ireland			
Italy	ministero della sanita, istituto igiene di sanita	yes	3.1
Japan	1. environment agency; 2. ministry of international trade and industry	yes	9.4
Luxemburg	inspection du travail et des mines	no	1.7 *)
Netherlands	min. van volksgezondheid en milieuhygiene	yes	1.7 *)
New Zealand	department of health, division of public health	yes	
Norway	state pollution control authority	yes	0.5
Portugal			
Spain			
Sweden	the national swedish environment protection board	no	0.6
Switzerland	1. Bundesamt für Gesundheitswesen; 2. federal office for the protection of the environment	yes	1.1
Turkey			
United Kingdom	department of the environment	yes	5.4
United States of America	environmental protection agency (on behalf of itself: the departments of labor and health and human services, and the consumer product safety commission)	yes	22.0
Yugoslavia			
CEC	commission of the european communities	no	
FAO			
CEE			
ILO	international labour office	no	

*) percentage is the total of the three countries Belgium, Netherlands and Luxemburg ≈ 61 %

Topic 2. Analysis of the Legal and Administrative Powers to Control "Existing Chemicals" in OECD Member Countries

2.1. Remarks:

This chapter contains the answers of the questions which have been numbered in the questionnaire as follows: 2.1, 4.1, 5.1, 5.2, 5.3, 5.4, 5.6, 5.7, 5.8, 5.9, 5.10, 5.11, 5.12, 4.5, 4.6

2.2. Summary of the Response to the Questionnaire

Question: how is the term "existing chemicals" defined in your country?

Country	by law	by lists	other	no definition
Australia *)		x		
Austria				x
Belgium			x	
Canada *)			x	
Denmark	x			
France *)	x			
Germany	x			
Japan	x			
Netherlands	x			
New Zealand				x
Norway				x
Switzerland	x			
United Kingdom *)			x	
United States of America	x			
Italy				x

* *The following remarks were given to this question:*

Country:	
Australia:	there is no formal definition for "existing chemicals" but an inventory of chemicals already in use is planned which will provide definition – by – membership.
Canada:	there is no formal definition for "existing chemicals" though the term is used in Canada to denote chemicals that are not new to Canadian commerce.
France:	put on the French market before the 1/VII/1979.
United Kingdom:	the UK has no statutory definition for the term "existing chemicals". However, directive 67/548/EEC (the 6th amendment) defines the term in the context of that directive.
United States of America:	the toxic substances control act defines "existing chemicals" in terms of an inventory (required to be established and published as a list). Other laws do not define "existing chemicals" as such. The requirements for registration of pesticides contained in the federal insecticide, fungicide, and rodenticide act results in a listing of active ingredients and products registered for use, but the lists are not published. Food additives, color additives, and drugs must be approved under the authority of the federal food, drug, and cosmetic act; lists of these three categories are maintained, but not published.
Italy:	In the next future, existing chemicals will be defined by law as those included in the EEC inventory now in preparation (EEC-directive 79/831)

Question: Are there legally-binding regulations which stipulate the selection of a certain number of "existing chemicals" for examination within a certain time?

Countries:		
Australia	no	
Austria	no	
Belgium	no	
Canada	no	
Denmark	no	
France	no	
Germany	no	
Japan	yes	
Netherlands		planned
New Zealand	no	
Norway	no	
Switzerland	no	
United Kingdom	no	
United States of America	no *)	
Italy		planned

*) although toxic substances control act authorizes selection of up to fifty chemicals for recommendation for testing rules

Question: Please state the legally-binding regulations in your country which can be used to regulate the chemicals which have been recognized as dangerous to health or the environment.

In which areas are these regulations valid?
Is the legal procedure already in use?

Country	Regulations	Validity	in use
Australia	commonwealth law including the therapeutic goods act and the customs (prohibited imports) regulation states laws to schedule and control poisons, register and regulate use of pesticides and veterinary drugs, therapeutic substances, food additives etc. air quality and water quality laws or administer discharge standards.	federal state	yes
Austria	BGBl. 99/1947 and 399/1977 124/1948 and 503/1974	whole country	yes yes
Belgium		whole country	yes
Canada	environmental contaminants act; pest control products act; fisheries act; clean air act; hazardous products act; atomic energy control act; food and drug act; plus various provincial acts	certain regions and whole country	yes
Denmark	act on chemical substances and products; statutory order on classification, packaging, labelling etc. of chemical substances and products	whole country	yes
France	chemicals control act of 12/VII/1979 (art 7)	whole country	yes

Country	Regulations	Validity	in use
Germany	§ 17 German chemicals act and § 19 ordinance on workplaces § 35 German federal immission control act and several statutory ordinances; foodstuffs and commodities act; feed act; drugs act; petrol/lead act; diseases of animals act; federal epidemics control act; DDT-act; plan protection act; fertilizers act; waste disposal act; water management act; detergents act; regulations by employers; liability insurance; statutory ordinance on chemicals at the workplace	whole country	yes
Italy	see page 335		
Japan	legally, chemical substances that have persistency potential and those which could be danger to human health when ingested continuously are regulated under article 27 of chemical substances law. Case by case, laws concerning the control of chemical substances other than the chemical substances control might be exercised.	whole country	yes
Netherlands	the minister of health and environmental protection may impose a broad spectrum of regulatory measures necessary to protect the environment, covering the whole life cycle of a chemical, varying from an obligation to apply certain safety procedures to a complete ban of the chemical. Classification and labelling will be according to the EC directive. (According to the draft WMS)	whole country	no
New Zealand	Poisons act 1960; poisons regulations 1964; noxious substances regulations 1954	whole country	yes
Norway	product control act 1976; specific acts which regulate air and water pollution, pesticides, food additives cosmetics, transportation of hazardous goods, water protection act	whole country	yes
Switzerland	toxicity law of march 21, 1969; law for water protection of Oct. 8, 1971; agriculture law of Oct. 3, 1951; in particular order of Feb. 4, 1955, on trade in agricultural auxiliary substances (law for the protection of the environment planned)	whole country	yes
United Kingdom	health and safety at work etc. act 1974; control of pollution ch. 40 1974; consumer protection ch. 15 1971; carcinogenic substances regulations 1967; pesticides are regulated according to the European community directive (council directive 79/117)	whole country	yes
United States of America	federal insecticide, fungicide and rodenticide act; federal food, drug and cosmetic act; toxic substances control act; federal water pollution control act; clean air act; resource conservation and recovery act;	whole country	yes

Country	Regulations	Validity	in use
	marine protection, research, and sanctuaries act; safe drinking water act; atomic energy act; occupational safety and health act; federal mine safety and health act; hazardous materials transportation act; ports and waterways safety act; consumer product safety act; flammable fabrics act; federal hazardous substances act; railroad safety act; comprehensive environmental releases, compensation, and liability act.		
Italy	toxic gas act (1926) and subsequent modifications; basic health law (1934) and subsequent modifications; fisheries act (1931) and subsequent modifications; waste management and disposal act (1941) and subsequent modifications; health and safety at work act (1956) and subsequent modifications; atomic energy control act (1964) and subsequent modifications; foodstuffs and food additives act (1962) and subsequent modification; clean air act (1966) and subsequent modifications; pest control products act (1968) and subsequent modifications; clear water act (1976); national health service act (1978);	whole country	yes

Question: With which countries and via which international authorities are the above mentioned laws and the provisions for their execution harmonized?

The laws and the provisions for their execution are harmonized as follows:

Belgium Denmark France Germany Italy Netherlands United Kingdom	within EC
Canada Switzerland United Kingdom United States of America	within OECD
Australia	not at all so far as is known

Question: Are there voluntary agreements between government and industry which provide for regulations concerning the production, industrial use and use patterns of certain chemicals?

Has industry ever voluntarily withdrawn chemicals from the market because of a recognized danger to the environment?

Country identification sign	Agreement	Examples	withdrawn	Examples
A	yes	FC		
B	no		yes	PCB, dibromochloropropane alkylbenzene, propansulfon, benzidine, based colorants
CAN	yes	PCB, CFC, insulating material	yes	triorthocresylphosphate, methylenechloride
DK	no		no	
D	yes	CFC		
NL	yes	PCB, PCT, phosphates	yes	PCB, PCT, phosphates
NZ	no		yes	CFC
N	yes	phosphates	yes	asbestos, benzene
CH	yes	FCC, PCB, pigments		
UK	yes	pesticides, CFC, chemicals for north sea oil operation and water treatment	yes	alkylmercury
USA	yes	pesticides pharmaceuticals	yes	PCB, NTA *)
AUS	yes	PCB's non-biodegradable detergents	yes	Tris
F	yes	CFC		
I	yes	CFC's in aerosols	yes	some dyestuffs for textiles

Case I:

The submitting company reported that as a result of mutagenicity and other safety information submitted to EPA under section 8 (e), the company has dropped acid green 3 from any further consideration in experimental products. In addition, the company reported that acid green 3 was not being used in any other company product applications at the time of the filling of the 8 (e) notice.

Case II:

Based on positive results from ames tests on electrophotographic toners, the submitting company informed the suppliers of the tested materials that no further toners would be accepted until such time as the toners were demonstrated to be negative for mutagenicity. The submitting company reported that it was resuming acceptance of the subject materials.

Case III:

The submitting company reported that based on the results of a 13-week intraperinoneal injection study which showed neurotoxicological effects in rats, the company was dropping its activities with both methylene bis acrylamide and 2-hydroxy ethylacrylate for the use (unspecified) it had planned.

Case IV:

Based on the positive results obtained from a skin sensitization test in guinea pigs, the submitting company reported that it would probably not continue with its development of a product containing VARISOFT 222 (90%).

Question: Once an existing chemical has been designated for further laboratory examination, specific tests will be applied to verify or dispel its dangerous nature. While it is recognized that average (or a range of) costs are somewhat difficult to specify, it is of considerable importance to obtain estimates of both costs and time for these laboratory investigations

Country	estimated range of costs *) (10^3 DM)	estimated average costs *) (10^3 DM)	estimated range of time (years)	estimated average time (years)
Canada	18 to 540	900	0.04 to 3	2 . . . 3
Germany	1000 to 2000		1 to 4	
Netherlands	9 to 910	182	0.1 to 2.5	1
Norway	43 to 1070	535	0.5 to 3	1
Switzerland			2	0.5
United States of America	toxicological test 2 to 321 *)	107 . . . 214	0.1 to 3	2 . . . 3
	laboratory audits 2 . . . 7	5		45–50 h per audit, field time only
Australia		not	available	
Japan		10 . . . 48		2 . . . 4 month
Italy	4 to 400		0.5 to 3	1

* not including primate or inhalation studies
*) currency conversion table see next page

Currency Conversion Table (April, 1st, 1981)

Country	Currency	DM
Australia	1 A $	2.54
Austria	100 ÖS	14.26
Belgium	100 bfrs	5.98
Canada	1 can $	1.82
Denmark	100 dkr	32.60
Finland	100 fmk	52.65
France	100 ff	43.25
Greece	500 Dr	4.55
Irland	1 Ir	3.76
Italy	5000 Lit	2.09
Japan	100 yen	0.96
Luxemburg	100 lfrs	5.98
Netherlands	100 hfl	91.30
Norway	100 nkr	40.00
Portugal	100 Esc	4.15
Spain	500 Ptas	2.58
Sweden	100 skr	46.75
Switzerland	100 sfrs	110.75
Turkey	100 Ltq	2.50
United Kingdom	1 £	4.81
United States of America	1 US $	2.14

Question: Please state, how many among the presently marketed chemicals are potentially dangerous
- **to man during the chemicals designated application**
- **to the environment (including man as part of the environment)**

Country	to man	to the environment
Denmark	6 to 10 000	3 to 5000
Germany	appr. 20 %	5 % to 10 %
Netherlands	500	1000
Switzerland	9500 *)	
United States of America	industrial chemicals appr. 20 %	appr. 20 %
	pesticides: potentially all.	potentially all
	pharmaceuticals: potentially all.	potentially all
Italy	some thousands	some thousands

*) official estimate

Question: Which existing chemicals or groups of chemicals have been restricted in production and/or in being placed on the market and/or in use in your country either by arrangement with industry or by legislation when and how?

Detailed lists of chemicals named in response to this question are given in annex I.

Question: Are there legally – binding regulations by which, for reasons of health or environmental protection the manufacturer or importer can be compelled to make confidential data available to authorities?
Please state the regulations.

Country	Regulations existing	Regulations
Australia	yes	commonwealth state agreement for regulation of pesticides and agricultural chemicals, pharmaceuticals, veterinary drugs and poisons and food additives
Austria	yes	Spezialitätenordnung BGBl. Nr. 99/1947 BGBl. Nr. 399/1977 Pflanzenschutzmittel BGBl. Nr. 124/1948 BGBl. Nr. 503/1974
Belgium	yes	
Canada	yes	environmental contaminants act, section 3 (1), 4 (1) and 4 (6) clean air act § 14 hazardous products act
Denmark	yes	act on chemical substances and products
France	yes	chemicals control act
Germany	planned	see § 4 para 6 of the German chemicals act
Japan	no	
Netherlands	planned	draft wet milieugevaarlijke stoffen
New Zealand	planned	poison act 1960
	yes	toxic substances act 1979
Norway	yes	law concerning product control of 1976

Country	Regulations existing	Regulations
Switzerland	yes	– art. 6 toxicity law of march 1969 – art. 17 implementing order – law of water protection of Oct. 1971 – agriculture law of Oct. 1951 – law for the protection of the environment (draft, Oct. 1979)
United Kingdom	yes	health and safety at work etc. act. 1974; consumer protection act. 1971; there are general provisions in other acts which can be used depending on circumstances
United States of America	yes	section 8–10 federal insecticide, fungicide and rodenticide act; federal food, drug and cosmetic act; toxic substances control act; most of the laws listed on p. 333
Italy	planned	EEC-directive 79/831; new pest control products act (in preparation)

Topic 3 Identification and Quantification of Criteria for Selecting Existing Chemicals for Gathering Information, Testing and Assessment on a Case by Case Basis

3.1. Remarks:

This chapter contains the answers of the questionnaire which have been numbered in the questionnaire as follows: 3.2, 3.3, 3.6, 3.4, 3.5, 3.7, 3.8, 2.2, 2.3, 2.5, 2.6

3.2. Summary of the Response to the Questionnaire

Question: From which lists of chemicals do you select "existing chemicals" which pose a danger to man and/or the environment?
Which of the Chemicals lists known to you should form the basis for the selection of chemicals which are to be tested for their potential danger to man or the environment if such criteria exist?
For which reasons were the lists selected?

Country	Name of the lists	Status	Reasons
Belgium	IARC, EEC, WHO	are used	int. agreements
	IARC, WHO	should be used	nat. regulations int. competence
Canada	DOE/NH & W priority list of chemicals	are used	nat. regulations
	great lakes list	should be used	int. agreements
Denmark	lists from enforcement, guidance sessions etc. or from consumers, industry, science or authorities in other countries	are used	
Germany	from all available lists	are used	supranational laws
	impending EEC-inventory of substances on the community market by 18 September 1981 (EPA-TSCA chemical subst. inventory) (MITI-inventory)	should be used	nat. regulations (§ 4 para. 5 German chemical act)
Netherlands	BIOKON-report, EC list no. ENV/118/77, toxic pollutants in point source water effluent discharge, ENV/RE/PL/80.68 of the OECD OSHA-list, IARC, MAC-list TSCA section 4 (e)	used or should be used	those which are relevant within the scope of the 6th amendment
Australia	US-EPA-list Canadian list	used	
Japan	list of existing chemical substances (chemical substances control law); existing chemical substances list (occupational safety and health law); registry of toxic effects of chemical substances (NIOSH, USA, 1977)	used	nat. regulations

Country	Name of the lists	Status	Reasons
Norway	official norwegian list; IARC-monographs; EEC classification; hazardous substances list – US EPA; NIOSH-Registry	used	
	ITC-lists IPCS/CEC (Italy 1980) EPA-IARC-lists of potential carcinogens	should be used	
Switzerland	official list (Giftliste); list of toxic substances acc. to federal law on trade (march 21st, 1969)	used	nat. regulations int. agreements
	convention for the protection of the Rhine against chemical pollution (Dec. 3rd, 1976)	should be used	
United Kingdom	the UK does not select "existing chemicals" on the basis of lists		
United States of America	reports of the national cancer institute of the national toxicology program; lists under FFDCA-authority (drugs, color-additives, food additives); TSCA inventory; registry of toxic effects of chemical substances, publ. by the national institute for occupational safety	used	nat. regulations
	registered active ingredients lists, together with test data submitted in support of registration or reregistration. TSCA-interagency testing committee recommendations; other national toxicology program tests	should be used (planned)	
Italy	IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans; EPA-TSCA Lists; IRPTC working list of selected chemical substances; TSCA section 4, Priority list; list of substances for the application of article 5 EEC proposal for a Council Directive on the Major Accident Hazards of certain chemicals; OSHA's candidate List; List of Aromatic Amines; ministerial circular No. 46; list of chemicals tested at the National Cancer Institute; IPCS/CEC joint task force on priority industrial chemicals; EEC classification of hazardous substances list; occupational exposure limits for airborne toxic substances; RTECS publ. by NIOSH;	should be used	nat. regulations; intern. agreements; to study and set up health preventive measures

Question: Please give a complete list of the chemicals which you have so far selected as "suspicious existing chemicals" needing closer attention i.e. testing and control?

Detailed lists of chemicals in response to this question are given in annex II.

Question: Should you have an official list of "existing chemicals" please specify the information which your authorities have acquired for the chemicals in this list from the notifiers.

Please state which of these information is confidential.

Country	Acquired information
Belgium	name, structural formula, composition of the substance, purity effects, other information
Canada	remark: not applicable
Germany	name, cas no, composition of the substance
Netherlands	remark: not applicable
Norway	name, cas no, composition *), purity, quantities marketed *), other information
Switzerland	name, structural formula *), composition *), purity *), effects *), other information *) (toxicological)
United Kingdom	remark: not applicable
United States of America	name, cas no, structural formula, composition, quantities, other information (any or all data elements may be claimed confidential) (toxic substances control act inventory)
Japan	name
Italy	production method, quantities marketed, data to identify the substance

*) confidential information

Question: Which of the following criteria are used in your country at present or are to be used in the future to select "existing chemicals" which pose a danger to health?

direct criteria	Country identification sign AUS	B	CDN	DK	D	I	NL	NZ	N	CH	UK	USA	JPN
acute toxicity	○	○+	○+	○+	○+	○+	+	○	○+		○+	○+	○
mutagenicity	○	○+	○+	+	○+	○+	+	○	○+		○+	○+	○
carcinogenicity in humans	○	○+	○+	○+	○+	○+	+	○	○+		○+	○+	○
proven carcinogenicity in animal experiments	○	○+	○+	○+	○+	○+	+	○	○+		○+	○+	○
teratogenicity	○	○+	○+	○+	○+	○+	+	○	○+		○+	○+	○
persistence	○	○+	○+	○+	○+	○+	+	○	○+		○+	○+	○
chronic toxicity	○	○+	○+	○+	○+	○+	+	○	○+		○+	○+	○
indirect criteria													
amount produced	○		○+		+	○+	+	○	○+		○+	○+	○
method of production	○		○+		+	○+	+	○	○+		○+	○+	
use patterns	○	○+	○+	○+	+	○+	+	○	○+		○+	○+	○
structure/activity relationship	○	○+	○+	○+	○+	○+	+	○	○+		○+	○+	○
other criteria													
taste/odour										+			
metabolism studies		+			+				+	+	○+		
reproduction studies		+	+								+		
reproductive effects		+				+						+	
bioaccumulation			+		+								
biodegradation			+										
physical degradation			+										
environmental levels			+									+	○
occupational levels			+										
phys./chem. properties/data			+		+							+	
pharmacodynamics			+										
structure/activity relationship			+									+	
amount imported			+										
amount in storage			+										

other criteria	Country identification sign AUS	B	CDN	DK	D	I	NL	NZ	N	CH	UK	USA	JPN
corrosivity				+						+			
skin irritation/sensitization				+	+				+				
exposure					+	+							
neurotoxicity					+	+	+					+	
behavioural effects							+			+		+	
social											○+		
case and epidemiological reports in occupational medicine					+								
exposure at the workplace					+								
number of workers exposed					+							+	
methods of processing, handling, transport, storage disposal					+								
number of workers employed					+								
toxic waste production													

○ at present,
+ in the future

Question: Which of the criteria listed on page 32 would suffice as the sole criterion for the selection of "existing chemicals" which pose danger to health or which combination of criteria would suffice?

Criteria	country identification sign									
	B	CDN	D	I	NL	NZ	N	UK	USA	JPN
chronic toxicity	x	x				x	x	x	x	x
carcinogenicity	x	x	x			x	x	x	x	x
acute toxicity		x				x	x	x	x	x
proven carcinog. in animal exp.		x				x	x	x	x	x
persistence		x				x		x		x
use patterns		x				x		x	x	x
long term toxicity			x							
mutagenicity							x	x	x	x
teratogenicity							x	x	x	x
allergic sensitisation							x			
reproductive toxicology								x		
toxic metabolites								x		
epidemiology								x		
amount produced								x		x
social judgement								x		
lack of antidote									x	
structure activity relationship										
combination of criteria										x
toxic effect and exposure		x		x						
any individual effect with any individual persistence criterion		x								
any individual quantity and use criterion		x								
any combination of health effect and exposure criteria			x							x
any combination of health effect and exposure criteria only combinations			x							x
sufficient					x					
combination of direct and indirect criteria					x					
persistence and amount produced and use-pattern							x			
reaction products/ metabolic products and use pattern								x		
structure/activity relationship		x				x	x	x	x	
any combination of 2 or more with exception of carcinogenicity lack of antidote and mutagenicity									x	
persistence and specific effect on health									x	
amount produced/toxicity				x						
production and use patterns/toxicity				x						

Combinations of criteria	country identification sign B	CDN	D	I	NL	NZ	N	UK	USA	JPN
chronic toxicity including carcinogenicity				x						
reproductive toxicology and teratogenicity				x						

Question: Which of the following criteria are at present used in your country or which are to be used in the future to select "existing chemicals" which pose a danger to the environment?

criteria	country identification sign													
	A	B	CDN	DK	D	I	NL	NZ	N	CH	UK	USA	AUS	JPN
amount produced			○+		+	○+	+	+	○+	+	○+	○+	○	○
amount marketed			○+		+	○+	+	+	○+	+	○+	○+	○	○
use patterns		○+	○+	○+	+	○+	+	+	○+	+	○+	○+	○	○
persistence	+	○+	○+	○+	+	○+	+	+	○+	+	○+	○+	○	○
compartimentalisation into air/water/soil	+	○+	○+	○+	+	○+		+	○+		○+	○+	○	○
bioaccumulation	+	○+	○+	○+	+	○+	+	+	○+	+	○+	○+	○	○
abiotic accumulation potential	+	○+	○+	+	+	○+	+	+	○+	+	○+	+	○	+
biodegradability	+	○+	○+	+	+	○+	+	+	○+	+	○+	○+	○	○
abiotic degradability	+	○+	○+		+	○+	+	+	○+	+	○+	+	○	○+
toxicity	+	○+	○+	+	+	○+	+	+	○+	+	○+	○+	○	+
ecotoxicity	+	○+	○+	○+	+	○+	+	+	○+	+	○+	○+	○	○
structure/activity relationships		○+	○+	○+	+	○+	+	+	○+		○+	○+	○	○
other criteria														
irreversible effects			○+											
population dynamics			○+											
reproduction effects			○+											
physical/chemical properties			○+	+										
other criteria														
estimated environmental mobility					+									
mutagenicity (screening)					+									
actual contamination										+				
monitoring data											○+	○	+	+
episode reports											+			
amount of release											+	○		
production of toxic waste							+							

○ at present,
+ in the future

Question: Which of the criteria listed on page 36 would suffice as the sole criterion in the selection of "existing chemicals" which pose an environmental danger or which combination of criteria would suffice?

criteria	country identification sign													
	A	B	CND	DK	D	I	NL	NZ	N	CH	UK	USA	AUS	JPN
compartimentalisation into water/air/soil					+				+		+	+		+
bioaccumulation potential	+	+			+			+	+		+	+		+
degradability	+				+			+	+		+	+		+
toxicity	+				+			+	+		+	+		+
ecotoxicity	+	+				+		+	+		+	+		+
persistence		+						+	+		+	+		+
abiotic accumulation					+						+			+
abiotic degradation					+						+			
water solubility					+						+			
physical state					+						+			
molecular structure					+						+			
structure/activity relationship					+			+	+		+	+		+
all existing toxicological data								+			+			
production of toxic wastes						+								
any of the environmental criteria possible											+	+	+	
use and production data											+	+		
amount produced											+	+		
use patterns											+	+		
combinations of criteria														
two of the following: – compound is in commerce – organisms are exposed – organisms are experiencing toxic effects			+											
persistence and bioaccumulation				+										+
persistence and ecotoxicity				+										
compartimentalisation and structure relationship				+										

criteria	country identification sign A	B	CND	DK	D	I	NL	NZ	N	CH	UK	USA	AUS	JPN
amount produced/marketed, use patterns and structure activity relationship with one of the other criteria							+							
amount produced/marketed and use patterns and compartimentalisation into air/water/soil								+						
amount marketed with accumulation parameters and use patterns										+				
use patterns										+	+			
actual contamination with toxicity/ ecotoxicity										+				
amount released into the environment/persistence						+								

Topic 4 Identification of Resource Needs for Testing and Evaluating Existing Chemicals

4.1. Remarks:

This chapter contains the answers of the questionnaire which have been numbered in the questionnaire as follows: 4.1, 5.11, 5.10, 4.7, 4.8, 4.3, 4.9, 4.14, 4.10, 4.11, 4.12, 4.13, 4.5, 4.6

4.2. Summary of the Response to the Questionnaire

Question: Are there legally-binding regulations which stipulate the selection of a certain number of "existing chemicals" for examination within a certain time?

Countries:		
Austria	no	
Belgium	no	
Canada	no	
Denmark	no	
Germany	no	
Netherlands		planned
New Zealand	no	
Norway	no	
Switzerland	no	
United Kingdom	no	
United States of America	no *)	
Australia	no	
Japan	yes	
France	no	
Italy		planned

*) although toxic substances control act authorizes selection of up to fifty chemicals for recommendation for testing rules

Question: Please state, how many among the presently marketed chemicals are potentially dangerous

- **to man during the chemicals designated application**
- **to the environment (including man as part of the environment)**

Country	to man	to the environment
Denmark	6 to 10.000	3 to 5.000
Germany	appr. 20 %	5 % to 10 %
Netherlands	500	1.000
Switzerland	9.500 *)	
United States of America	industrial chemicals appr. 20 % pesticides: potentially all; pharmaceuticals: potentially all	appr. 20 % potentially all potentially all
Italy	some thousands	some thousands

*) official estimate

Question: Once an existing chemical has been designated for further laboratory examination, specific tests will be applied to verify or dispel its dangerous nature. While it is recognized that average (or a range of) costs are somewhat difficult to specify, it is of considerable importance to obtain estimates of both costs and time for these laboratory investigations

Country	estimated range of costs *) (10^3 DM)	estimated average costs (10^3 DM)	estimated range of time (years)	estimated average time (years)
Canada	18 to 540	900	0.04 to 3	2 . . . 3
Germany	1000 to 2000		1 to 4	
Netherlands	9 to 910	182	0.1 to 2.5	1
Norway	43 to 1070	535	0.5 to 3	1
Switzerland			2	0.5
United States of America	toxicological tests 2 to 321 * laboratory audits 2 . . . 7	107 . . . 214 5	0.1 to 3	2 . . . 3 45–50 h per audit, field time only
Japan		10 . . . 48		2 . . . 4 month
Italy	4 to 400		0.5 to 3	

* not including primate or inhalation studies
*) currency conversion table see page 337

Question: Who bears the cost of selecting chemicals to be examined and in what proportions?

Who bears the cost of the laboratory examinations which are to be carried out and in what proportions?

Country	costs of selecting	costs of examinations
Belgium	100 % government	100 % industry
Canada	80 % . . . 100 % government 20 % . . . 0 % industry	
Denmark	100 % government	0 % . . . 100 % government 100 % . . . 0 % industry
Germany	100 % government	normally 100 % industry
Netherlands	100 % government	?
New Zealand	remark: not applicable	90 % government 10 % industry
Norway	100 % government	100 % industry
Switzerland	mainly government	mainly industry
United Kingdom	remark: applicable	agriculture: 100 % industry pesticides: 100 % industry ford science. 50 % industry 50 % government
United States of America	100 % government	pre-approval for drugs and color additives; data for pesticides registration; required TSCA testing; 100 % industry other contexts government 100 %
Australia	100 % government	100 % industry
Japan	100 % government	100 % government
France	no costs of selection	100 % industry
Italy	100 % government	20 % government 80 % government

Question: From which sources is information about "existing chemicals" derived before the decision is made to proceed with laboratory investigations?

information source	country identification sign											
	B	DK	D	F	NL	NZ	N	CH	UK	USA	JPN	I
literature	x	x	x	x	x	x	x	x	x	x	x	x
official authorities	x	x	x	x	x	x	x	x	x	x	x	x
industry	x	x	x	x	x	x	x	x	x	x	x	x
abroad	x	x	x	x	x	x	x	x	x	x	x	x
private research institutes	x	x	x	x	x	x	x	x	x	x		x
universities	x	x	x	x	x	x	x	x	x	x		x
other			x	x	x	x	x	x		x		
other												
governmental institutes			x							x		
data banks				x				x		x		
environmental survey											x	

Question: Who carries out the laboratory examinations at present or who is to carry them out in the future?

institution	country identification sign												
	A	B	DK	D	NL	NZ	N	CH	UK	USA	AUS	JPN	I
official institutions	○	○	○+	+		○+	○+	○		○+		○	○+
industry	○	○	+	+		○+	○+	○+		○+	○+		○+
universities	○	○	○+	+		○+	○+			○+		○	○+
private institutions		○	○+	+		○+	○+			○+			○+
no regulations					○+			○	○+				

○ at present, + in the future

Question: Please name the institution which evaluates the results of the examinations

Country	Institutions
Belgium	IHE, IRC, laboratory for industrial toxicology
Germany	responsible federal authorities
New Zealand	testing laboratory registration council
Norway	national institute of public health
Switzerland	– federal office for the protection of the environment – swiss laboratory for testing materials (EMPA) – others, not yet determined
United States of America	EPA, OPP, FDA, national toxicology program, outside consultants, chemical industry institute of toxicology
Japan	Chemical Products Council, Central Pharmaceutical Affairs Council after referring to the "Test and Assessment Committees" Environment Agency taking note of experts' comments
France	Ecotoxicity evaluation commission
Italy	Consiglio Superiore di Sanità Istituto Superiore di Sanità National Committee for the study of mutagenic, carcinogenic and teratogenic effects of chemicals

Question: Are there prescribed test guidelines for the examinations? Are there prescribed regulations on "good laboratory practice" Which institution ensures that they are adhered to?

Country	test guidelines and institution	good laboratory praxis and institution
Austria	OECD-test guidelines *)	GLP-principles of the OECD *)
Australia	OECD-guideline *)	GLP-principles of the OECD *)
Belgium	– institute of hygiene and epidemiology – institute of chemical research – laboratory for industrial toxicology	within framework of 6th modification of EEC-directive – IHE – IRC – laboratory for industrial toxicology
Denmark	OECD-test guidelines *)	statens tekniske proven vn
France	OECD-test guidelines *)	GLP-principles of the OECD *)
Germany	OECD-test guidelines *) EEC-directive 79/83	GLP-principles of the OECD *)
Japan	MITI-test, adapted in the OECD-guideline	GLP-principles of the OECD
Netherlands		GLP-proposal in the decrees for the wet milieugevaarlijke Stoffen
New Zealand		testing laboratory registration council
Norway	OECD-test guidelines *)	*)
Switzerland	swiss laboratory for testing materials (EMPA) for detergents, for others are planned	*)
United Kingdom		GLP, 6th amendment
United States of America	GLP adopted by FDA and NIH at present and rules planned by EPA OECD guidelines *)	FDA and NIH GLP's EPA GLP.'s OECD GLP principles *)
Italy	OECD test guidelines * – ministry of health and its technical and scientific body (Istituto Superiore di Sanità)	OECD GLP principles *

*) planned

Question: Are there legally – binding regulations by which, for reasons of health or environmental protection the manufacturer or importer can be compelled to make confidential data available to authorities?
Please state the regulations.

Country	regulations existing	regulations
Australia	yes	commonwealth state agreement for regulation of pesticides and agricultural chemicals, pharmaceuticals, veterinary drugs and poisons and food additives
Austria	yes	Spezialitätenordnung BGBl. Nr. 99/1947 BGBl. Nr. 399/1977 Pflanzenschutzmittel BGBl. Nr. 124/1948 BGBl. Nr. 503/1974
Belgium	yes	
Canada	yes	environmental contaminants act, section 3 (1), 4 (1) and 4 (6) clean air act § 14 hazardous products act
Denmark	yes	act on chemical substances and products

Country	regulations existing	regulations
France	yes	chemicals control act
Germany	planned	see § 4 para 6 of the German chemicals act
Italy	planned	EEC-directive 79/831 new pest control act
Japan	no	
Netherlands	planned	draft wet milieugevaarlijke stoffen
New Zealand	planned	poison act 1960
	yes	toxic substances act 1979
Norway	yes	law concerning product control of 1976
Switzerland	yes	– art. 6 toxicity law of march 1969 – art. 17 implementing order – law of water protection of Oct. 1971 – agriculture law of Oct. 1951 – law for the protection of the environment (draft, Oct. 1979)
United Kingdom	yes	health and safety at work etc. act. 1974; consumer protection act 1971 there are general provisions in other acts which can be used depending on circumstances
United States of America	yes	sections 8–10 federal insecticide, fungicide and rodenticide act; federal food, drug and cosmetic act; toxic substances control act; most of the laws listed on p. 334

Annex I Detailed lists of chemicals named in response to the following question: Which existing chemicals or groups of chemicals have been restricted in production and/or in being placed on the market and/or in use in your country either by arrangement with industry or by legislation? When and how?

Country: Australia

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
poisons				
pesticides				
agricultural chemicals				
veterinary drugs				
food additives				
feed additives				
pharmaceuticals				
explosives				

Country: Canada

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
PCB	ban or manufacture, importation or selected uses	1977–80	environmental contaminants act	
PCT	total ban	1979	environmental contaminants act	
PBB	total ban	1979	environmental contaminants act	
Mirex	total ban	1978	environmental contaminants act	
CFC	ban on selected uses	1980	environmental contaminants act	
Pb in gas (petrol)	restriction on concentration	1973	clean air act	
Hg in paint	restriction on concentration		pest control products act	

Country: Denmark

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
detergents	ban on use of detergents with less than 90 % biodegradability	1975	statutory order	
lead, cadmium	use restrictions for Pb- and Cd-containing glazes	1977	statutory order	
methanol	is not allowed in antifreeze mixtures	1977	statutory order	
benzene	compounds containing in excess of 0.2 % of benzene are for the purpose of sale and use to be considered toxic	1977	statutory order	
arsenic, antimony	certain restrictions on use in paints	1977	statutory order	
pentachloro-phenols	ban on the use of chlorophenols as wood preservatives, with the exemption of pentachlorophenol of a certain purity	1977	statutory order	
mercury and mercury compounds	ban on use (except for mercurychloride) in paints	1980	statutory order	
formaldehyde	limits for the amount given off from particle boards etc. in buildings and furniture	1980	statutory	

Country: France

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
PCB and PCT	use only in closed systems	1975	order	
Cd		1972	administrative act	
Hg		1974		
Detergents	must be biodegradable	1977	order	
CFC	production and use limitations	1979	voluntary agreement	
VCM	ban on use in aerosol sprays	1975	order	
Asbestos	use limitations	1977	order	
Agrochemicals	must be licensed			
Drugs	must be licensed			
Food additives	must be licensed			

Country: Germany

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
DDT	production ban import and export ban; marketing ban; use ban	7.8.72	DDT act	
lead tetraethyl	control of content of lead compounds in otto fuels	5.8.71	lead in petrol act	
PCB, PCT vinylchlorid	marketing ban	26.7.78	statutory ordinance to the federal immission control act	
arsenic asbestos	reduction of use	1.10.80	statutory ordinance on chemicals in the workplace	
benzene	reduction of use			
pentachlorethane	reduction of use			
tetrachloro-methane	reduction of use			
tetrachlorethane	reduction of use			
silikogene	reduction of use			
strahlmittel	reduction of use			
acrylonitril	reduction of use			
aldrin	reduction of use			
aramite	reduction of use			
arsenic compounds	reduction of use			
ethylene oxid	reduction of use			
lead compounds	reduction of use			
cadmium compounds	reduction of use			
camphechlor (toxaphene)	reduction of use			
chlordan	reduction of use			
chloroform	reduction of use			
chloropicrin	reduction of use			
dieldrin	reduction of use			
fluorene	reduction of use			
acetic acids and its compounds and derivates				
heptachlor	reduction of use			
HCH, technical	reduction of use			
benzene, hexachloro	reduction of use			
isobenzan	reduction of use			
isodrin	reduction of use			
morfamquat	reduction of use			
mercury compounds	reduction of use			
selenic compounds	reduction of use			
strobane	reduction of use			
carbon tetra chloride	reduction of use			

Country: Italy

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
lead tetraethyl	control of content of lead compounds in fuels	1954 and following years	Ministerial Decree (M.D.)	
white lead in paint	ban	1961	M.D.	
food additives and dyes	restrictive measures	1963 and following years	M.D.	
constituents and impurities of food	restrictive measures	1963 and following years	M.D.	
benzene	restrictive measures	1963	law	
cyclodiene-chlorine pesticides	restrictive measures	1968	M.D.	
DDT-insecticides	restrictive reasures	1970	M.D.	
2, 4, 5-T and 2, 4, 5-TP	ban	1970	M.D.	
detergents	ban on use of anionic detergents with less than 80 % biodegradability	1971	law	
some chemotherapeutics for agriculture	ban	1971	M.D.	
some active substances for agriculture	restrictive measures	1972	M.D.	
Hg-antiparasitic agents	ban	1972	M.D.	
creosote-phyto-pharmaceuticals	ban	1972	M.D.	
DDT-antiparasitic agents	restrictive measures	1973	M.D.	
p- and m-creosol-phytopharmaceu-ticals	ban	1973	M.D.	
cyclodiene-chlorine pesticides	ban	1973	M.D.	
quintozene-phytopharma-ceutical agents	ban	1973	M.D.	
MNFA-Phyto-pharmaceutical agents	ban	1974	M.D.	
ATA-phytopharma-ceutical agents	ban	1974	M.D.	
BHC-phytopharma-ceutical agents	ban	1974	M.D.	
lindane phyto-pharmaceutical agents	restrictive measures	1975	M.D.	
chlorofluoro-carbons	reduction of use as propellant in aerosols	1976		voluntary agreement with industry

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
diallate, triallate and sulfallate	ban	1977	M.D.	
DDT-phytopharmaceutical agents	ban	1978	M.D.	
textile dyestuffs	withdrawal	1981		voluntary agreement with industry

Country: Japan

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
PCBs	production, importation are banned	1973	law concerning the examination and regulation of manufacture, etc. of chemical substances	
HCB	production, importation are banned	1979	law concerning the examination and regulation of manufacture etc. of chemical substances	
PCN	production, importation are banned	1979	law concerning the examination and regulation of manufacture, etc. of chemical substances	

Country: Netherlands

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
PCB's/PCT's	prohibition of marketing PCB/PCT and PCB/PCT containing products (with few exceptions)	1979	PCB decree based on chemical waste act	a voluntary agreement preceded the decree
vinylchloride	prohibition of use as propellant in aerosols	1979	PCB decree	
CFC's	obligation of labelling spray cans with a warning regarding the reduction of ozon in the stratosphere	1978	CFC's in spray cans decree, based on air pollution act	
asbestos	prohibition of certain uses; reduction of concentration at the workplace	1977	asbestos decree based on silicosis act	

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
phosphates	reduction of phosphates in laundry detergents	1980		voluntary agreement with industry
propanesulton	prohibition of certain uses at the workplace	1976	decree, based on the health and safety at work act	
lead, benzene, sulfur	limitation of their content in fuels	1977 1977 1974	decrees, base on air pollution act	

Country: Norway

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
CFC's	production and import ban concerning use of all fully halogenated CFC's as propellant in aerosol cans	1.7.81	product control act	regulation
PCB's	it is prohibited to produce, import, distribute or use PCB or PCB-containing products	1.1.80	product control act	regulation
detergents	in the mjosaarea it is prohibited to advertise phosphate containing detergents in the local papers and to exhibit such products in the store	20.2.78	product control act	regulation
oil dispersants	regulations applying to composition and use of dispersants to combat oil spiells	2.2.80	product control act	regulation

Country: United Kingdom

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
PCB's & PCT's	restriction on use	1972 1980	control of pollution act – s.i. 1980/638. control of pollution (supply and use of injurious substances) regulations	voluntary agreement with industry

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
VCM	ban on use in aerosol sprays	1980	consumer protection act – s.i. 1980/136. The dangerous substances and preparations (safety) regulations	
cadmium and lead in cook-ware	restriction on leachable cadmium and lead	1975	consumer protection act – s.i. 1975/1241. Clayed ceramic ware (safety) regulations	
cadmium and lead in cook-ware (continued)	restriction on leachable cadmium and lead	1976	s.i. 1976/454 vitreous enamel ware (safety) regulations	
crocidolite ("blue" asbestos)	control limit in air in the work-place (threshold limit-value TLV) in effect made its processing uneconomic in the work place and hence avirtual ban on its use	1969	factories act asbestos regulations	
"hard" detergents	requirement for regradability hence	1964		voluntary agreement
	restricting the range of substances which might be used	1978	s.i. 1978 (564 and s.i. 1978/1546). Detergents composition regulations	with industry
pesticides				voluntary agreement with industry
CFC's				voluntary agreement with industry
chemicals used in north sea oil operations				voluntary agreement with industry
chemicals used in water treatment and distribution				voluntary agreement with industry

Country: United States of America

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
pesticides	registration (1500 active ingredients; 34,000 products)	1948–present	FIFRA	
60 pesticide active ingredients	classified for restricted use	1975–present	FIFRA	
BAAM	conditional registration	1979	FIFRA	

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
thallium sulfate	suspension/cancellations	1972	FIFRA	
vinyl chloride	suspension/cancellations	1975	FIFRA	
DBCP, silvex 2, 4, 5-T	suspension/cancellations	1979	FIFRA	
26 pesticides	cancellation	1971–present	FIFRA	
100 pesticides	tolerances in raw agricultural commodities	1971–present	FFDCA	
color additives (unknown)	approval for use in foods, drugs and cosmetics required	1976–present	FFDCA	
human drugs	premarket approval requiring safety and effectiveness	1946–present	FFDCA	
veterinary drugs	premarket approval requiring safety and effectiveness	1946–present	FFDCA	
food additives shown to cause cancer (e.g., red dye cyclamate) in humans or animals	removal from market mandatory	1958–present	FFDCA	
PCB's	marking and disposal requirements	1978	TSCA 6 (e)	
	ban on most uses (rule partially overturned in litigation)	1979	TSCA 6 (e)	
CFC's	ban on most aerosol uses	1979	TSCA 6	
PBB's Tris	advance notice of intent to initiate or resume manufacture required	1980	TSCA 8	
590 industrial chemicals	threshold limit values for exposure	1970–present	OSH Act	
22 chemical carcinogens	engineering and practice controls to minimize exposure to limit feasible	1970–present	OSH Act	
8 toxic metals	requirement to test wastes for content if found to exceed toxic concentrations; wastes are subject to handling and manifest rules	1980	RCRA	
85 waste streams	subjected to handling and manifest rules	1980	RCRA	
122 chemicals	wastes in excess of 1 kg are subject to handling and manifest rules	1980	RCRA	
239 chemicals	wastes in excess of 1000 kg are subject to handling and manifest rules	1980	RCRA	
360 chemicals	wastes known to contain any of these are subject to handling and manifest rules	1980	RCRA	
129 chemicals	waste quality criteria published	1980, 1981	FWPCA	

Name of chemical or group of chemicals	restrictive measure applied e.g. production ban	date of measure	which legal instrument was applied?	what kind of agreement was reached?
9 chemicals	toxic pollutant effluent standards	1977	FWPCA	
390 chemicals	rules governing spills	1978	FWPCA	
6 chemicals or categories	criteria pollutants ambient air quality standards	1971–78	CAA	
asbestos beryllium mercury vinyl chloride	hazardous air pollutant emission standards final	1973–76	CAA	
benzene	hazardous air pollutant emission standards proposed (others to be published 1981, 1982)	1980	CAA	
arsenic	listed for development of hazardous air pollutant emission standard (inorganic compounds)	1980	CAA	
asbestos lead, CFC's	restrictions on use in consumer products	1977	CPSA	

Annex II **Detailed lists of chemicals named in response to the following question:**
Please give a complete list of the chemicals which you have so far selected as "suspicious existing chemicals" needing closer attention i.e. testing and control.

Country: **Australia**

PCBs
asbestos
cadmium
mercury
alkyl phthalates
arsenic trioxides and other arsenic compounds
chlorine
copper-chrome-arsenate
cyanides
ethylene dichloride
fluorides, including hydrogen fluoride
heavy metals (chromium and nickel in particular)
methylene choride
trichloroethylene
organic peroxides
organo-tin compounds
pentachlorophenol
phenols
polycyclic aromatic hydro carbons
toluene diisocyanate

Country: **Belgium**

confidential

Country: **Canada**

PCB; CFC; cadmium; chlorophenols; chlorobenzenes HCBD; hexachlorocyclopentadine and adducts; mercury; organotins; phthalic acid esters, triaryl phosphates; aromatic amines; chlorinated naphtalenes, paraffins and styrenes; halogenated diphenyl esters, ethanes and ethylenes and methanes, toluenes; bromobenzenes and fluorobenzenes

Country: **Denmark**

mercury, cadmium, CFC, hydrazine, chromates, formaldehyde, pentachlorophenols

Country: **France**

chemicals in antifouling paints

Country: **Germany**

acetamide
allyl chloride
4-amino-2-nitrophenol
antimony trioxide
benzal chloride
benzotrichloride
N-Phenyl-2-naphtylamine
synthetic mineral fibers
o-tolidine
o-toluidine
toluylendiamine
1,1,2-trichlorethane

benzyl chloride
bitumen, not blended
cadmium and its compounds
chlordane
chlorinated diphenyl (technical products)
chloroform
chromate, alkaline
chromium carbonyl
chromium trioxide
2,4-diaminoanisole
4,4′-diaminodiphenylmethane
o-dianisidine
2,2′ dichlorodiethyl ether
1,2-dichlorethane
1,3-dichlorpropene (cis and trans)
diethylcarbamoyl chloride
diglycidylether
dioxane
epoxypropene
ethylenoxide
formaldehyde
heptachlor
isopropyl oil (product of isopropyl alcohol production)
kepone
lead chromate
phenylglycidylether
phenylhydrazine
trichlorethylene
vinylidene chloride
2,4-xylidene

Country: **Italy**

aromatic amines
some pesticides
some monomers for plastics in food packaging (e.g. vinyl chloride, ethyl-enoxid)
some solvents (e.g. chloroform, trichloro-ethylene)
some hair and paper dyes (2-nitro-*p*-fenilendiammina, 4-nitro-o-fenil-endiammina, 2,4-diammino-anisolo, auramina)
some human and animal drugs (e.g. arprinocid, ronidazole)
nitrosamines
heavy metals
asbestos
dichlorvos
p-dichlorobenzene
trinitrofluorene
formaldehyde
synthetic sweeteners
PCB and PCT
halogenated dibenozodioxins and dibenzo-furans
IARC list of carcinogenic chemicals

Country: **Japan**
Upon consideration of "amount produced" and "use patterns", chemicals are selected successively and submitted to testing.

Country: **Netherlands**
asbestos, formaldehyde, Hg, Pb, PCB, PCT, CFC

Country: **New Zealand**
it is not possible to give such a "complete list"

Country: **Norway**
as named in their
- list of carcinogenic substances
- list of allergenic substances
- list of toxic, harmful, irritant and corrosive substances

Country: **Switzerland**
e.g.
chloroform, epichlorhydrine, vinylchloride, benzene, Hg, As, Pb, hexachlorobenzene, toxaphene, heavy metals, organohalogen compounds, additives to plastics, pesticides, detergents, road salts

Country: **United Kingdom**
It is not possible to give a complete list. All substances are potentially dangerous and their proposed mode and pattern of use are important considerations. The aim is to eliminate danger or reduce it as far as is reasonably practical.

Country: **United States of America**
pharmaceuticals
food additives and color additives
pesticides
PCB's, PBB's, dioxins
volatile chlorinated solvents
volatile early eluting chlorinated organics
low volatility chlorinated organics
aromatic amines
toxic metals
radionuclides
naturally occurring toxins
national toxicology program (NTP) chemicals in test or scheduled for testing
chemicals recommended for testing by the interagency testing committee under TSCA.
chemicals showing positive results in one or more on the national cancer institute (NCI-NTP) bioassays.
EPA-designated priority pollutants
wastes and waste streams designated under sec. 3001 of the resource conservation and recovery act.
special pesticides review status (april 81)

LIST OF ABBREVIATIONS

BIAC	BUSINESS AND INDUSTRY ADVISORY COMMITTEE TO THE OECD
CEC	COMMISSION OF THE EUROPEAN COMMUNITIES
CEFIC	EUROPEAN COUNCIL OF CHEMICAL MANUFACTURERS FEDERATIONS
CIIT	CHEMICAL INDUSTRY INSTITUTE OF TOXICOLOGY
CMA	CHEMICAL MANUFACTURERS ASSOCIATION
EC	EUROPEAN COMMUNITIES
ECDIN	ENVIRONMENTAL CHEMICALS DATA AND INFORMATION NETWORK OF THE EC
ECE	ECONOMIC COMMISSION FOR EUROPE (UN)
ECETOC	EUROPEAN CHEMICAL ECOLOGY AND TOXICOLOGY CENTRE
EEC	EUROPEAN ECONOMIC COMMUNITY
EPA	ENVIRONMENTAL PROTECTION AGENCY (USA)
FAO	FOOD AND AGRICULTURE ORGANIZATION (UN)
FDA	FOOD AND DRUG ADMINISTRATION (USA)
GLP	GOOD LABORATORY PRACTICES
IARC	INTERNATIONAL AGENCY FOR RESEARCH ON CANCER
ILO	INTERNATIONAL LABOR ORGANIZATION
IPCS	INTERNATIONAL PROGRAMME ON CHEMICALS SAFETY
IRPTC	INTERNATIONAL REGISTER OF POTENTIALLY TOXIC CHEMICALS
MITI	MINISTRY OF INTERNATIONAL TRADE AND INDUSTRY (JAPAN)
NCI	NATIONAL CANCER INSTITUTE (USA)
NIH	NATIONAL INSTITUTE OF HEALTH (USA)
NIOSH	NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (USA)
NSF	NATIONAL SCIENCE FOUNDATION
NTP	NATIONAL TOXICOLOGY PROGRAM
OECD	ORGANIZATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT
OSHA	OCCUPATIONAL AND HEALTH ADMINISTRATION (USA)
TSCA	TOXIC SUBSTANCES CONTROL ACT
WHO	WORLD HEALTH ORGANIZATION