[3125-01]

COUNCIL ON ENVIRONMENTAL QUALITY

TSCA INTERAGENCY TESTING COMMITTEE

Initial Report to the Administrator, Environmental Protection Agency

As required by section 4(e) of the Toxic Substances Control Act (TSCA), presented herein is the first official report of the Interagency Testing Committee. The Committee has the statutory responsibility to identify and recommend to the Administrator of EPA chemical substances which should be tested to determine their hazard to human health or the environment.

This report reflects the consensus of representatives from all eight member agencies: ten substances and categories of substances are recommended as high priority for testing and designated for consideration by EPA within twelve months.

As required by the statute, the Committee will continue its review process, reporting to the EPA Administrator within six months from the date of this report such additional recommendations as the Committee finds desirable during that period.

Dated: October 5, 1977.

WARREN R. MUIR,
Chairman TSCA Interagency Testing Committee.

EXECUTIVE OFFICE OF THE PRESIDENT,
COUNCIL ON ENVIRONMENTAL QUALITY,
Washington, D.C., October 4, 1977.

Hon. DOUGLAS M. COSTLE,
Administrator,
Environmental Protection Agency,
Washington, D.C.

DEAR MR. COSTLE: The enclosed document is the first official report submitted to you by the Interagency Testing Committee pursuant to Section 4(e) of the Toxic Substances Control Act (TSCA). It reflects the consensus of representatives from all eight member agencies: that the ten listed substances and categories of substances be recommended as high priority for testing under TSCA and designated for consideration by EPA within twelve months.

The report describes the process employed by the Committee in making its recommendations and the rationale for each designation. A supporting dossier for each designation will be forwarded to the Office of Toxic Substances in the next few weeks.

Only a portion of the compounds identified in the July preliminary report has been considered to date. The first revision of our recommendations will be based largely upon further review of those chemicals previously identified. Because this is a continuing process, we will, of course, identify additional chemicals for such review as information becomes available to us.

The Committee has been hampered in its deliberations by the lack of a readily available and consolidated source of data on the many chemicals to which man and the environment are exposed. Other activities under TSCA, e.g., development of coordinated data systems, inventory reporting, and other information collection under Section 8, should be of considerable value in future Committee efforts. Therefore, we expect that a number of additional substances will be listed and integrated in our future reports.

We hope our analysis and recommendations will be helpful to EPA in its implementation of the Toxic Substances Control Act.

Sincerely,

WARREN R. MUIR, Ph. D.,
Chairman, TSCA Interagency Testing Committee.

INITIAL REPORT OF THE TSCA INTERAGENCY TESTING COMMITTEE TO THE ADMINISTRATOR, ENVIRONMENTAL PROTECTION AGENCY

October 1, 1977

CONTENTS

TSCA INTERAGENCY TESTING COMMITTEE

Statutory Member Agencies

Council on Environmental Quality

Warren R. Muir, Member and Committee Chairman

Department of Commerce

Sidney R. Galler, Member

Bernard Greifer, Alternate

Environmental Protection Agency

William M. Upholt, Member

James R. Beall, Alternate

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Carter Schuth, Alternate

National Institute of Environmental Health Sciences

Hans L. Falk, Member

Warren T. Piver, Alternate

National Institute for Occupational Safety and Health

Norbert P. Page, Member

Jean G. French, Alternate

National Cancer Institute

James M. Sontag, Member

Occupational Safety and Health Administration

Grover C. Wrenn, Member

James M. Vail, Alternate

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Department of Interior

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U.S. Consumer Product Safety Commission

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Joseph McLaughlin

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Secretary: Phyllis D. Tucker

ACKNOWLEDGMENTS

The Committee wishes to acknowledge the important contributions of the many individuals and groups who have significantly aided us in our work. These include:

-- Clement Associates, Inc., technical support contractor;

-- the National Science Foundation, for funding and managing the technical support contract and the National Cancer Institute and National Institute of Environmental Health Sciences for assisting in that funding;

-- government experts who assisted in the scoring of biological activity and test needs, including Laurence Fishbein of the National Center for Toxicological Research, Elizabeth Weisburger of the National Cancer Institute, and a number of experts from the Department of Interior;

-- EPA staff members who assisted the Committee in a variety of activities, and particularly:
Donald Barnes, Office of Toxic Substances
Joyce Dain, Interim Secretary to the Committee
John Lyon, Office of General Counsel
Joseph Merenda, staff support to EPA member
Lamar Miller, interim staff support to EPA member
Ralph Northrop, Jr., Office of Toxic Substances

-- the numerous experts who prepared presentations and materials for the Committee; and

-- the many individuals and organizations who submitted comments on the Committee's Preliminary List.

SUMMARY

The Toxic Substances Control Act (TSCA) established the TSCA Interagency Testing Committee, giving it the continuing responsibility to identify and recommend to the Administrator of the Environmental Protection Agency chemical substances and mixtures which should be tested to determine their hazards to human health and the environment. The Committee's initial recommendations are to be published in the Federal Register and transmitted to the EPA Administrator within nine months of the effective date of TSCA. The Committee is to consider additions to its recommendations at least every six months.

In meeting its charge, the Committee has, with the assistance of a technical support contractor, carried out a multi-step screening procedure to identify for its detailed review a limited number of substances and categories of substances likely to have priority for testing to determine their effects on human health and the environment. A number of substances and categories identified by this process have been reviewed by the Committee, which has given careful consideration to each of the eight factors specified in Section 4(e)(1)(A) of TSCA. The Committee has also considered such factors as test programs currently in progress, the current status of regulatory action with respect to a substance, and the need for test data on all members of certain categories rather than on one or more individual members of the category.

In July, 1977, the Committee published a Preliminary List of 330 substances and categories of substances along with a background document describing the methods used by the Committee in making those selections. The Preliminary List included substances and categories selected primarily on the basis of potential for human exposure and environmental release. Public comments received on the Preliminary List were reviewed by the Committee and considered in the development of the Committee's initial recommendations.

Subsequently, the chemicals on the Preliminary List and chemicals added to the Preliminary List based on the public comments were further screened by the Committee based primarily on their potential for adverse human and/or environmental effects, but also continuing to consider their exposure potential. Available data on and potential for carcinogenic, mutagenic, teratogenic and chronic toxic effects, as well as their ability to bioaccumulate or cause deleterious environmental effects were considered. A scoring system which took into account both available information and the lack of it for these factors was used in this process. Using these scoring results and its scientific judgment, the Committee further narrowed the list under consideration to about 80 substances and categories. Aided by information dossiers prepared by its contractor, the Committee reviewed about half of these compounds and has selected for inclusion in its initial recommendations to the EPA Administrator four individual substances and six categories of substances. Each is being

designated by the Committee for consideration by EPA within the next 12 months. They are (arranged alphabetically):

Substance or Category	Testing Recommended
Alkyl Epoxides	Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects, and epidemiological study
Alkyl Phthalates	Environmental effects
Chlorinated Benzenes, Mono- and Di-	Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects, and epidemiological study
Chlorinated Paraffins	Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, and environmental effects
Chloromethane	Carcinogenicity, mutagenicity, teratogenicity, and other chronic effects
Cresols	Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, and environmental effects
Hexachloro-1,3-butadiene	Environmental effects
Nitrobenzene	Carcinogenicity, mutagenicity, and environmental effects
Toluene	Carcinogenicity, teratogenicity, other chronic effects, and epidemiological study
Xylenes	Mutagenicity, teratogenicity, and epidemiological study

The Committee's reasons for each recommendation and a more detailed definition of each of the categories are presented in Section 3.2. The Committee expects that the precise definition of each category will be considered further by EPA in the course of developing testing rules. The Committee also recognizes that certain members of a category may already have been adequately tested for one or more of the effects for which testing of the category has been recommended. In that case, no further testing for that combination of substance and effect would be needed.

A dossier summarizing the information considered by the Committee in selecting each substance or category will be forwarded to EPA in the next few weeks. The Committee will continue its review of the remaining substances and categories already selected for detailed review, and may identify and review others, in anticipation of its next report.

IV

INITIAL REPORT OF THE TSCA INTERAGENCY TESTING COMMITTEE TO THE ADMINISTRATOR, ENVIRONMENTAL PROTECTION AGENCY

October 1, 1977

CHAPTER I. INTRODUCTION

1.1 BACKGROUND

Section 4(e) of the Toxic Substances Control Act (P.L. 94-469, hereafter referred to as TSCA) established the TSCA Interagency Testing Committee. That Committee has the continuing responsibility to identify and recommend to the Administrator of the Environmental Protection Agency chemical substances or mixtures which should be tested to determine their hazard to human health or the environment. The statute provides that the Committee shall make its initial recommendations to EPA by October 1, 1977.

To carry out this responsibility, the Committee has developed and executed a multi-step screening procedure to identify for its detailed review a number of chemical substances and categories of chemical substances expected to have a high priority for testing based on the criteria set forth in Section 4(e)(1)(A) of TSCA. The Committee received extensive technical support in this screening, and in the gathering of data on substances and categories selected for detailed review, from Clement Associates, Inc. under a contract with the National Science Foundation. After reviewing the information available to it on each candidate, including public comments submitted in response to the Committee's July, 1977, publication of a preliminary list of substances under consideration, the Committee has selected the ten substances and categories being recommended to the EPA Administrator in this report. As required by the statute, the Committee will continue its review process, reporting to the EPA Administrator within six months from the date of this report such additional recommendations as the Committee finds desirable during that period.

This report documents the procedures used by the Committee in selecting those substances and categories now being recommended for testing, and, as required by the statute, provides the Committee's reasons for making each such recommendation. In addition to the material contained in this report, the Committee is now finalizing a series of dossiers developed by its technical support contractor which will summarize all of the non-confidential information considered by the Committee in deciding to recommend each substance or category for testing. These dossiers will be transmitted to the EPA in a few weeks.

1.2 COMMITTEE ESTABLISHMENT AND RESPONSIBILITIES

The Committee, as established by Section 4(e) of TSCA, has eight members, appointed by the eight Federal agencies identified for membership in Section 4(e)(2)(A) of the Act. In addition, a number of alternates have been designated as permitted by Section 4(e)(2)(B)(i). The Committee has adopted the name "TSCA Interagency Testing Committee", which is frequently shortened in this report to "Committee". As provided by Section 4(e)(2)(B)(iii), it has selected a chairman from among its members. The Committee has also invited several other Federal agencies with programs related to the control of toxic substances, but which were not included in the statutory membership of the Committee, to designate liaison representatives to attend Committee meetings. Current Committee members, alternates, and liaison representatives are identified in the frontispiece.

The Committee's testing priority recommendations are required by Section 4(e) to be published in the Federal Register and transmitted to the EPA Administrator within nine months of the January 1, 1977, effective date of TSCA. At least every six months thereafter, the Committee is required to review its recommendations and make such revisions as are necessary.

The Committee's recommendations are to be in the form of a list of chemical substances or mixtures set forth, either individually or in groups, in the order in which the Committee determines the EPA Administrator should consider taking action under Section 4(a) in developing and promulgating testing regulations. The Committee is authorized to designate up to 50 of these substances or groups for which the EPA Administrator must within 12 months either initiate rulemaking requiring their testing or publish reasons for not taking such action.

In developing its recommendations, the Committee is directed by Section 4(e)(1)(A) of TSCA to consider, along with all other relevant factors: the production volume, environmental release, occupational exposure, and non-occupational human exposure to the substance or mixture; the similarity of the substance or mixture in question to others known to present unreasonable risk of injury to health or the environment; the extent of data on the effects of the substance or mixture in question on health or the environment and the extent to which additional testing of the substance or mixture may produce data from which effects can reasonably be determined or predicted; and the reasonably foreseeable availability of facilities and personnel for performing the testing being recommended. The Committee is also directed by Section 4(e) to give priority attention in establishing its list of recommendations to substances or mixtures which are known or suspected to cause or contribute to cancer, gene mutations, or birth defects.

The Committee's specific reasons for including each substance or mixture in its recommendations are required to be published in the Federal Register and transmitted to the EPA Administrator along with the priority list.

While Section 4(e) refers to the Committee's recommendations as a list of "chemical substances and mixtures", Section 26(c)(1) authorizes the EPA Administrator to take actions (including the promulgation of Section 4(a) testing regulations) with respect to categories of chemical substances or mixtures as well. A category is defined in TSCA as a group whose members are similar in molecular structure; in physical, chemical, or biological properties; in use; in mode of entrance into the human body or into the environment; or in any other way, so long as the grouping is not based solely on its members being "new chemical substances" as defined in the Act. Since the EPA Administrator is authorized to promulgate testing regulations for categories of chemical substances or mixtures, the Committee has concluded that its recommendations to the EPA Administrator may also include categories (or groups) of chemical substances or mixtures, as well as individual substances and mixtures. This conclusion is consistent with Section 4(e) which states that the Committee's recommendations for testing "shall be in the form of a list of chemical substances and mixtures which shall be set forth, either by individual substance or mixture or by groups of substances or mixtures... ."

In order to maintain consistency in this report and in keeping with its meaning in TSCA, the term "category" will be used to reflect groupings of substances. "Substance" will be used to refer to both individual chemicals as well as mixtures.

CHAPTER 2. DEVELOPMENT OF THE COMMITTEE'S INITIAL RECOMMENDATIONS

2.1 SELECTION OF THE COMMITTEE'S BASIC APPROACH

Estimates of the number of chemical substances and mixtures subject to TSCA range from tens of thousands to over 100,000; the number and identities of these substances and mixtures will not be established until after the completion of the chemical inventory under Section 8(b) of TSCA. Nevertheless, all of these substances and mixtures, together with others which may be manufactured in the future, are subject to the promulgation of testing rules under Section 4(a) and are thus within the purview of the Interagency Testing Committee.

At the same time, Section 4(e) of TSCA specifies a number of factors which the Committee is to consider in determining whether to recommend a substance for testing. Careful consideration of these factors requires the collection and review of a substantial amount of data concerning the production, use, chemical and biological activity, and previous testing of each substance or category of substances under consideration.

As a result, because of the lack of a comprehensive and readily accessible data base on current chemicals, the large number of potential candidates for the Committee's consideration, and the statutory deadline for the Committee's initial recommendations to EPA, the Committee has had to select for its detailed consideration only a small subset of the possible candidates.

In considering alternative approaches to selecting a limited number of substances for detailed review, the Committee met with a number of experts on chemical data systems and chemical characterization. Several possible approaches were identified. One was a nomination approach in which Committee members or other experts would nominate specific chemicals for consideration. Another was to use structure-activity relationships to identify for review substances chemically similar to others of known hazard. Yet another approach was to focus the Committee's attention on those substances known to have high levels of production volume, environmental release, or human exposure.

After considering these alternatives, the Committee decided to adopt a combined strategy employing features of each. This resulted in a multi-step screening process wherein a relatively large number of substances were considered initially and at each subsequent step a smaller subset was selected for collection of more data and more intensive review.

The basic steps in the process adopted by the Committee, which are illustrated in Figure 1 and are described in more detail in subsequent sections, were as follows:

a. Establishment of an INITIAL LISTING of about 3,650 substances and categories of substances previously identified as potential hazards to human health or the environment,

b. Compilation of a smaller MASTER FILE (about 1,700 substances and categories) through elimination from the INITIAL LISTING of substances not in commercial production or used predominantly as pesticides, food additives, or drugs,

c. Selection of a PRELIMINARY LIST of about 330 substances and categories for further consideration based on evaluation of the production volume, environmental release, occupational exposure, and general human exposure levels of the substances in the MASTER FILE,

d. Selection of about 80 substances and categories for detailed review based on evaluation of the potential biological activity and need for health and ecological effects testing of substances appearing on the PRELIMINARY LIST,

e. Selection of substances and categories recommended for testing after review of preliminary dossiers prepared by the Committee's contractor, public comments on the PRELIMINARY LIST, and other pertinent information available to the Committee from various agencies,

f. Documentation of the Committee's reasons for including each substance or category in its list of recommendations and completion of a final dossier summarizing the information considered by the Committee in reaching its decision.

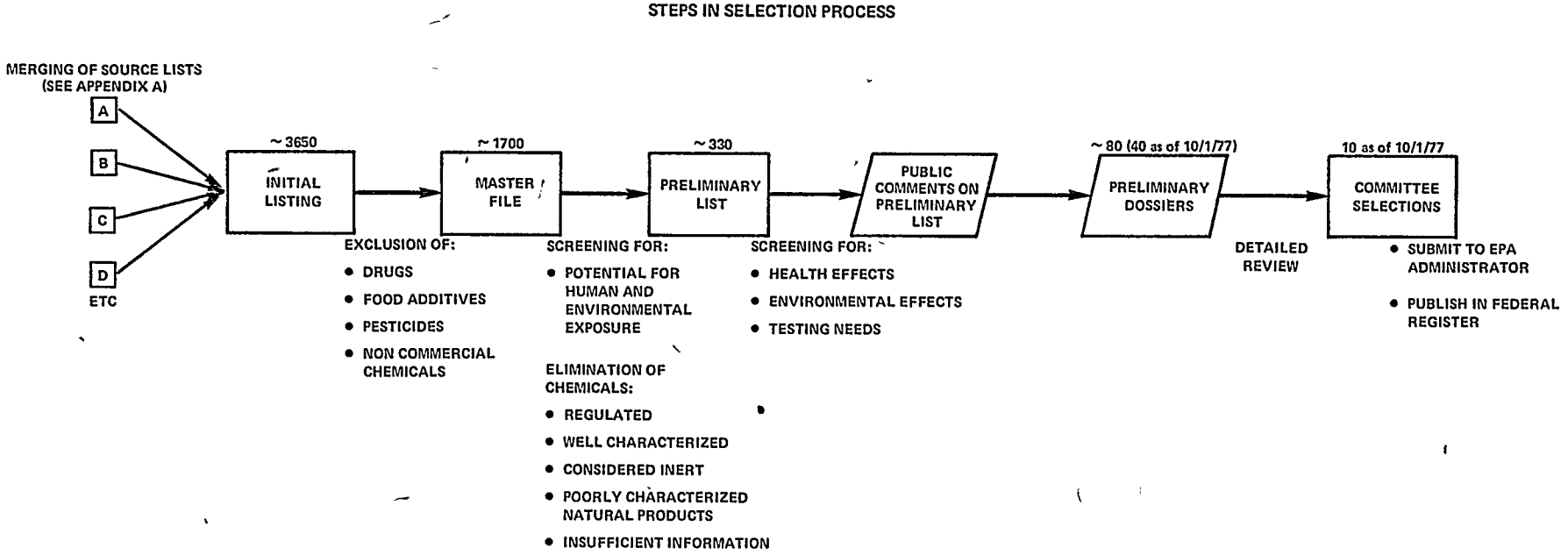

FIGURE 1 SELECTION SCHEME USED BY THE TSCA INTERAGENCY COMMITTEE IN SELECTING ITS INITIAL RECOMMENDATIONS TO THE EPA ADMINISTRATOR (OCTOBER 1977)

Carrying out this multi-step process required the collection, review, coding, and analysis of data on a large number of chemical substances, as well as the application of scientific judgment in many areas where adequate data were unavailable. The Committee was supported extensively in these efforts by Clement Associates, Inc. under a contract with the National Science Foundation (Contract No. NSF ENV77-15417 with partial funding by the NIEHS and NCI. The contractor employed expert consultants from a variety of disciplines in carrying out its tasks under the contract. In addition, many U.S. Government agencies made data and expertise of their employees available to the Committee for these efforts.

Several of the steps of the Committee's procedure employed quantitative scoring of the substances under consideration. Members of the Committee used their professional expertise and judgment in applying these scores to the decisions at each step.

2.2 ESTABLISHMENT OF THE INITIAL LISTING

In order to focus its initial attention on substances likely to require health and/or ecological effects testing, and for which sufficient preliminary data were likely to be available to permit more detailed reviews at later steps, the Committee chose to limit its initial consideration to substances or categories of substances which had already been identified in previous reviews as being of concern because of potential adverse effects on human health or the environment or as having large production volumes and a potential for substantial human exposure or environmental release. Nineteen separate source lists of this type were identified by the Committee and pooled to produce the INITIAL LISTING of about 3,650 substances, mixtures, and categories. The individual source lists are identified and described briefly in Appendix A.

2.3 REDUCTION TO THE MASTER FILE

The INITIAL LISTING included a number of substances having pesticide, food additive, or drug uses, all of which are regulated under other Federal statutes and are exempted from regulation by TSCA. To identify them, the INITIAL LISTING was compared with lists of pesticides prepared by the EPA and lists of food additives and drugs prepared by the Food and Drug Administration, using Chemical Abstracts Service (CAS) Registry Numbers. This initial purge of substances subject to other statutes was incomplete, since some entries on source lists did not include CAS numbers. To compensate for this, a further manual purging was required. Consideration was also given to the fact that a substance used as a pesticide, food additive or drug may also have other uses that are subject to the authority of TSCA. Since pesticides, food additives, and drugs are generally produced in limited volumes, substances identified as such but having annual production over 10 million pounds were considered likely to have other uses as well and were retained on the truncated list for further review of their uses. Substances identified as pesticides, food additives, or drugs but known to the Committee or its contractor to have other uses within the jurisdiction of TSCA were also retained.

The resulting file was reduced further by the elimination of chemicals which were judged not likely to be in commercial production. This was accomplished by comparing the file against EPA's Candidate List of Chemical Substances, prepared by the Office of Toxic Substances (dated April 1977). Again, the basis of comparison for this purge was an assigned CAS number. Consequently, this purge did not affect those chemicals on source lists for which no CAS number was given. In an attempt to eliminate substances which are not in commercial production, the following rule was adopted: any substance not identified by a CAS number which appeared on the NIOSH Registry (Source List 13 of Appendix A) and on none of the other source lists was judged not likely to be in commercial production. This decision was based on the fact that the NIOSH Registry lists any substance for which toxic effects have been reported, including research chemicals. A scan of the substances eliminated by the application of this rule demonstrated its usefulness: few of the purged substances were recognized to be in commercial production.

As a result of the purges described above, a MASTER FILE of approximately 1700 substances emerged.

2.4 SELECTION OF THE PRELIMINARY LIST

Having developed a MASTER FILE of substances to be considered for possible recommendation to EPA for testing, the Committee began to apply the eight factors explicitly identified for its consideration in Section 4(e)(1)(A). While recognizing that there would be advantages to applying all of the first seven factors* simultaneously in evaluating the relative priorities for detailed review of the substances under consideration, the Committee concluded that assembling and evaluating the necessary data for all substances on the MASTER FILE would not be feasible within the time schedule established by statute, considering the limitations of current chemical information systems and the number of professional judgments which would have to be made. Evaluation of the fifth, sixth, and seventh factors (relating to chemical similarity to substances of known hazard, existing health and environmental effects data, and need for testing) was anticipated to require more independent review and judgment and to be the more time-consuming portion of the task. Hence, the Committee decided to further reduce the number of substances under consideration before explicitly evaluating those factors which had, to some extent, already been reflected in the choice of source lists.

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* The eighth factor, the reasonably forseeable availability of facilities and personnel for performing the needed testing, was considered principally by the Committee in terms of the aggregate facilities and personnel needs for carrying out all of the Committee's recommendations. See Section 2.8 for further discussion of this factor.

This reduction, which resulted in the selection of the PRELIMINARY LIST, was based principally on evaluation of the first four factors identified for the Committee's consideration in Section 4(e)(1)(A) of TSCA. These are:

(i) quantity of the substance produced annually

(ii) amount of the substance released into the environment

(iii) number of individuals occupationally exposed and duration of their exposure

(iv) extent to which the general population will be exposed.

Using a combination of published data and judgment, the Committee's contractor made an attempt to score each substance in the MASTER FILE for these four factors. Appendix B describes in more detail how scores were assigned to substances. Information on the use or uses of a substance was critical to the assignment of scores for environmental release and general population exposure, and scores for those factors could not be assigned if use information could not be found by the contractor. For about 1,000 of the 1,700 substances in the MASTER FILE this was the case; as a result, for only about 700 of the substances was it possible to assign scores. By combining the scores for the four factors, as described in Appendix C, a rank-ordered list of the scored substances was prepared for the Committee's consideration.

In selecting the approximately 330 substances and categories included on the PRELIMINARY LIST, the Committee considered all of the scored substances and eliminated from current consideration a number of them which in the Committee's professional judgment were found to be:

a. Currently under stringent regulation or of lower priority for the Committee's purposes because their hazard is reasonably well characterized (e.g., vinyl chloride and mercury);

b. Essentially inert materials (e.g. certain polymers) or substances reasonably well characterized as having low toxicity (e.g., methane);

c. Covered by testing requirements under food, drug and cosmetic or pesticide legislation (e.g., citric acid); or

d. Certain natural products (e.g., asphalt) whose consideration should be deferred pending better characterization for testing purposes.

Others of the scored substances were specifically selected by the Committee for inclusion on the PRELIMINARY LIST based on judgment of members that further review was needed. The remainder of the scored substances were considered for inclusion on the PRELIMINARY LIST based on their relative ranking in the scoring process.

In addition to the scored substances, the Committee also considered in selecting the PRELIMINARY LIST the unscored substances from the MASTER FILE and a limited number of additional substances recommended by Committee members or the Committee's contractor. A number of substances from these sources were included on the PRELIMINARY LIST based on the Committee's knowledge of the substance and its uses or the Committee's professional judgment that the substance should be further evaluated.

In reviewing substances for possible inclusion on the PRELIMINARY LIST, the Committee also considered the desirability of grouping substances into categories. In several cases the Committee grouped chemically-related substances from the MASTER FILE while in other cases the Committee retained groups which had already appeared in one of the source lists. About 15% of the entries on the PRELIMINARY LIST were categories.

2.5 PUBLIC COMMENT ON THE PRELIMINARY LIST

The PRELIMINARY LIST, together with a background document describing its development, was published by the Committee in July, 1977. Notice was published by the Committee in the Federal Register (42 FR 30531 and 42 FR 40756) announcing the availability of the list and background document and requesting public comment. Comments were specifically requested on:

a. The methodology used by the Committee in developing the PRELIMINARY LIST;

b. Substances not appearing on the PRELIMINARY LIST which commentors might recommend for consideration by the Committee and the commentor's reasons for the recommendation;

c. Substances appearing on the PRELIMINARY LIST which commentors might recommend that the Committee not consider further and the reasons for that recommendation; and

d. Comments on the needs for and relative priority of testing of the substances being considered by the Committee.

As an additional aid to commentors and others interested in the Committee's activities, copies of the list of substances comprising the MASTER FILE and a tabulation of the scores for production volume, environmental release, and occupational and general population exposure considered by the Committee in selecting the PRELIMINARY LIST were made available for public inspection at the headquarters and regional offices of the Environmental Protection Agency.

Comments on the PRELIMINARY LIST were received from about 65 industrial firms, trade associations, environmental organizations, government agencies, and individuals. About two-thirds of the

commentors recommended deletion from the Committee's further consideration of one or more substances or categories appearing on the PRELIMINARY LIST, while four commentors recommended additional substances for the Committee's consideration. About one-fifth of the commentors included comments on the methodology employed by the Committee in developing the PRELIMINARY LIST and about one-third included comments on other issues related to the Committee's activities. Such issues were the use of categories in the Committee's recommendations to EPA, documentation of the Committee's reasons for its decisions with respect to specific substances, and provision of opportunity for public comment on the Committee's actions.

Public comments on the PRELIMINARY LIST have been reviewed by the Committee and considered in the development of the Committee's initial recommendations. Four of the seven additional substances recommended by commentors were added to the PRELIMINARY LIST for consideration in selecting substances and categories for detailed review. Because of the large number of comments recommending deletions of substances from the Committee's consideration and the limited time available under the statutory deadline, pertinent comments were considered on a substance-by-substance or category-by-category basis during the Committee's review of preliminary dossiers and consideration of reasons for and against recommending testing. Comments on the Committee's methodology have been reviewed and will be considered in subsequent activities of the Committee. In the Committee's judgment, the recommended changes in methodology would not, if implemented, alter its initial recommendations. Comments dealing with use of categories, documentation of the Committee's reasons for actions, and other more general issues were also reviewed and considered in the development of the Committee's recommendations.

2.6 SELECTION OF SUBSTANCES FOR DETAILED REVIEW

This step of the Committee's procedure extended the scoring of the substances under consideration to factors (v) through (vii) of Section 4(e)(1)(A). These factors are:

> (v) the extent to which the substance or mixture is closely related to a chemical substance or mixture which is known to present an unreasonable risk of injury to health or the environment;
>
> (vi) the existence of data concerning the effects of the substance or mixture on health or the environment; and
>
> (vii) the extent to which testing of the substance or mixture may result in the development of data upon which the effects of the substance or mixture on health or the environment can reasonably be determined or predicted.

To accomplish this, each substance on the PRELIMINARY LIST was scored for each of seven biological activity factors by a number of experts available through the Committee's contract. The factors were: carcinogenicity, mutagenicity, teratogenicity, acute toxicity, other toxic effects such as reproductive effects or organ-specific toxicity, bioaccumulation, and ecological effects. After reviewing a summary of information on the biological activity of the substance developed by the contractor based on the open literature, each of the contractor's scorers assigned a score to the substance for the effect(s) for which that scorer was responsible.

A total of nine scorers was used by the contractor, with two or three scorers separately evaluating each effect in most cases. Each scorer considered both the summary information provided by the contractor and his personal knowledge of the substance and chemically-related substances in assigning scores. Any substantial discrepancies among individual scorers were identified, discussed among the scorers, and a consensus reached; in the case of minor discrepancies in the scores for any factor, the scores of the several scorers were averaged.

In addition, three of the effects (carcinogenicity, mutagenicity, and ecological effects) were separately scored by government experts from the National Cancer Institute, National Center for Toxicological Research, and Department of Interior, respectively. These scores were averaged with those of the contractor's scorers.

Scores assigned for the various effects took the form of either a numerical score (generally 0, 1, 2, or 3) or a letter score (generally x, xx, or xxx). Assignment of a numerical score indicated a judgment that further testing of the substance is not needed for the effect under consideration, while the magnitude of the score indicated the degree to which the effect had been confirmed or the dose level at which it had been found. Assignment of a letter score, on the other hand, indicated a judgment that further testing should be carried out, with the number of "x's" assigned reflecting a judgment as to the level of numerical score that might be anticipated after testing. For example, in scoring a substance for carcinogenicity a score of 3 meant that the substance is well established as a carcinogen in humans or experimental animals, while a score of xxx meant that the substance is strongly suspected of carcinogenic activity but has not been adequately tested. In averaging the scores assigned to a substance by the several scorers for a given factor, no mixing of numerical and letter scores was permitted. Any discrepancies between scorers in chosing the numerical or letter scale were discussed among the scorers and resolved. The criteria applied by the scorers in assigning scores for the various factors are described in more detail in Appendix D.

Categories of substances appearing on the PRELIMINARY LIST were not generally scored as entities, but rather, scores were assigned separately for each of the example substances listed under the category heading in the list.

Using these scores, the contractor provided the Committee a series of lists of the substances appearing on the PRELIMINARY LIST ranked according to various criteria. These included separate lists for each factor ranked by the average score a substance received for that factor (identifying those substances judged most in need for testing for a single effect) and a list ranked by the sum of the letter scores received by a substance for all factors (identifying substances requiring testing for a number of effects). Also tabulated on each list was an exposure index for each substance which was derived from the earlier scoring of production volume, environmental release, and occupational and general population exposure. For the human health effects factors and total letter score lists the exposure index used was the sum of the production volume, occupational exposure, and general population exposure scores, while for the bioaccumulation and ecological effects factors, the exposure index was the sum of the production volume and environmental release scores. The Committee also received from its contractor a list of those substances evaluated by the scorers which were known or might be anticipated to have additional adverse health or environmental effects as a result of contaminants appearing in the commercial product or degradation products of the substance under consideration.

The Committee's selection of substances and categories from the PRELIMINARY LIST to be carried forward for detailed review used the various lists provided by its contractor as guides, but reflected the independent judgments of the members of the Committee. First, the scores themselves were reviewed, with any major discrepancies between the contractor's scores and those of the government scorers or the judgments of individual Committee members being considered. Then, the Committee turned to the various ranked lists, reviewing in turn the substances ranked most in need of testing on the sum-of-letter-scores list or the lists for the individual factors. Each substance appearing in the top 75 to 100 positions on one or more of these lists was considered by the Committee and a decision made whether to select it for detailed review.

Particular attention was paid by the Committee to substances known or suspected to be carcinogens, mutagens, or teratogens, in keeping with the statutory guidance provided the Committee in Section 4(e)(1)(A) of TSCA. This emphasis was reflected not only in the Committee's consideration of individual substances and categories, but also in its structuring of the review process, since these effects were scored individually and, in effect, received greater attention than did other effects scored in groups (e.g., other toxic effects or ecological effects).

Categories of substances appearing on the PRELIMINARY LIST were also reviewed in terms of the scoring of their example members and the Committee's judgment as to retaining them. A number of decisions to modify previous categories or define new categories were made by the Committee during this review process.

In reviewing these lists, more than two-thirds of the individual substances scored by the contractor were explicitly considered by the Committee. Approximately eighty substances and categories were selected by the Committee for the drafting of preliminary dossiers and further detailed review. Of these, about half were individual substances and half categories.

2.7 CONSIDERATION FOR LISTING AND DESIGNATION

For each of the approximately eighty substances and categories selected for detailed review, preliminary dossiers have been (or are being) prepared by the Committee's contractor. Within the time period allowed by the statute for development of the Committee's initial recommendations, preliminary dossiers were drafted for about one-half of the substances and categories for detailed review. Consideration of these and other information resulted in the initial recommendations transmitted by this report. Consideration of the remaining substances and categories already selected for detailed review, and others which may subsequently be selected, will continue and will be reflected in subsequent recommendations to EPA by the Committee.

The preliminary dossiers summarized information obtained from the open literature relating to the identification, relevant chemical and physical properties, production volume, uses, environmental release, and exposure to the substance 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 chemically similar substances was also included where available. Preliminary dossiers for categories of substances included these types of information for specific members of the category, generally the example members identified in the PRELIMINARY LIST.

Using the information summarized in the preliminary dossier, together with information submitted in public comments on the PRELIMINARY LIST, information available to the Committee from various Federal agencies, and the members' individual knowledge, the Committee reviewed each substance or category. Each of the factors specified in Section 4(e)(1)(A), as well as any other relevant factors identified by the Committee on a case-by-case basis, was considered. In particular, in considering factor (vi) of Section 4(e)(1)(A), the existence of data concerning the effects of the substance on helath or the environment, the Committee considered test programs currently in progress, as well as data already generated. Another factor considered in certain instances was the status of current regulatory action relative to the substance. In each case where a category of substances was under consideration the appropriate definition of the category and the need for data on all members of the category were considered. Where relevant to the particular type of testing under consideration for a substance or category, factor (viii) of Section 4(e)(1)(A), the availability of test facilities and personnel, was discussed on a case-by-case basis. In general, however, this factor was considered in the aggregate after the Committee's tentative recommendations for all substances and categories had been identified. The Committee's consideration of this factor is discussed further in section 2.8 of this report.

After reviewing and thoroughly discussing the information available to the Committee on the substance or category under consideration, a decision was made regarding whether to recommend the development of test rules by EPA and, if so, for which effects. Subsequently, one or more Committee members participated in the drafting of the supporting reasons for each recommendation and these reasons were again reviewed by the Committee. A final decision to recommend the substance or category for testing represents a consensus by the Committee members that such testing is needed to evaluate the effects of the substance (or of each individual substance falling within the definition of a category) on human health and the environment, and that priority attention should be given by EPA to requiring the conduct of such testing. The Committee recognized, of course, that some members of recommended categories may have already been adequately tested for the effects of concern and would not require further testing.

Several substances and categories reviewed by the Committee were deferred for further consideration because of insufficient information to adequately define the categories or to determine the needs for testing.

Assignment of priority order to the substances and categories recommended for testing was also considered. The Committee concluded that all of the substances and categories being recommended at this time should be given equal priority in EPA's development of test rules. Factors contributing to this decision were the limited number of recommendations being made, the Committee's decision to designate all recommended substances and categories for consideration by EPA within 12 months, and the Committee's understanding of EPA's plans to develop its test rules for various effects, e.g., carcinogenicity, rather than for individual substances or categories. The Committee recommends that these substances and categories be included in the first applicable "effects rule".

2.8 CONSIDERATION OF AVAILABILITY OF TESTING FACILITIES AND PERSONNEL

One of the criteria listed in Section 4(e)(1)(A), that the Committee was required to consider, is the reasonably foreseeable availability of facilities and personnel for performing the testing it recommends. The Committee reviewed the results of recent surveys of toxicology testing capabilities conducted by the Society of Toxicology (SOT) and the DHEW Committee to Coordinate Toxicology and Related Programs (CCTRP). While the SOT surveyed general toxicology testing capabilities, the CCTRP specifically assessed inhalation test capabilities. The Committee also reviewed the capabilities and plans of the National Center for Toxicological Research (NCTR), the possible impact of the FDA's Good Laboratory Practices, and the logistics and practical considerations for carcinogenicity, mutagenicity, and reproductive effects testing. It also was briefed on ecological test capabilities and needs in that area.

Based upon these reviews, the Committee has concluded that there are sufficient toxicology testing capabilities in the U.S. to carry out the health effects testing recommended by the Committee in this report.

A more difficult area to assess was that of environmental or ecological testing. Capabilities for acute studies are probably adequate, but the National capability for conducting long-term tests of chemical pollution on the environment will be less certain until the test standards and protocols are defined through the rulemaking process. The Committee feels, however, that the testing burden likely to result from recommendations in this report is reasonable.

CHAPTER 3. RECOMMENDATIONS OF THE COMMITTEE

3.1 SUBSTANCES AND CATEGORIES OF SUBSTANCES RECOMMENDED FOR TESTING

As described in Chapter 2 of this report, the Committee has, with the assistance of a technical support contractor, carried out a multi-step screening procedure to identify for its detailed review a limited number of substances and categories of substances likely to have priority for testing to determine their effects on human health and the environment. A number of substances and categories identified by this process have been reviewed by the Committee, which has given careful consideration to each of the eight factors specified in Section 4(e)(1)(A) of TSCA. The Committee has also considered such other factors as it judged relevant on a case-by-case basis. Such additional factors have included test programs currently in progress, the current status of regulatory action with respect to a substance, and the need for test data on all members of certain categories rather than on one or more individual members of the category.

The eighth factor specified in Section 4(e)(1)(A) for the Committee's consideration, the reasonably foreseeable availability of facilities and personnel for performing the recommended testing, has (as described in Section 2.8 of this report) been considered by the Committee with respect to the aggregate requirements of all of the testing recommendations made here, as well as for each individual testing recommendation. In the Committee's judgment there are, or can be made available within the next few years, adequate facilities and personnel for conducting the testing now being recommended by the Committee. Furthermore, any specific limitations of facilities or personnel which cannot now be identified by the Committee would be expected to be short-term in nature and can be taken into account by EPA in establishing the time periods for submission of the test data under Section 4(b)(1).

In selecting substances and categories for inclusion in its initial recommendations, the Committee has also given priority attention to substances known or suspected to cause cancer, gene mutations, or birth defects.

Based on its consideration of the factors identified in Section 4(e)(1)(A) and all other relevant factors identified by the Committee, and using all of the information available to it, including the knowledge and professional judgment of its members, it is the consensus of the TSCA Interagency Testing Committee that the ten substances and categories of substances listed in the accompanying table should be given priority consideration by the Administrator of the Environmental Protection Agency for the promulgation of regulations under Section 4(a) requiring the conduct of the types of testing specified. Each of these substances and categories is designated by the Committee for consideration by EPA within the next 12 months.

SUMMARY OF TESTING RECOMMENDATIONS
BY THE
TSCA INTERAGENCY TESTING COMMITTEE

Substance or Category	Types of Testing Recommended					
	Carcinogenicity	Mutagenicity	Teratogenicity	Other Chronic Effects	Environmental Effects	Epidemiological Study
Alkyl Epoxides	X	X	X	X	X	X
Alkyl Phthalates					X	
Chlorinated Benzenes, (Mono- and Di-)	X	X	X	X	X	X
Chlorinated Paraffins	X	X	X	X	X	
Chloromethane	X	X	X	X		
Cresols	X	X	X	X	X	
Hexachloro-1,3-butadiene					X	
Nitrobenzene	X	X			X	
Toluene	X		X	X		X
Xylenes		X	X			X

Table 1

In listing and designating these ten substances and categories, the Committee has decided that all should be given equal priority by EPA in the development of test rules under Section 4(a) of TSCA. All are of high priority and should be included in the first applicable "effects rule" (e.g., carcinogenicity) developed by EPA.

In selecting categories of substances for inclusion in its recommendations, the Committee recognizes that some members of a category may have already been adequately tested for one or more of the effects listed; in such cases no additional testing would be required. The Committee also recognizes that the precise definition of each category will have to be considered and decided by EPA in developing its test rules.

The Committee's reasons for including each substance or category of substances on its list of recommendations, which are required by Section 4(e)(1)(B) to be submitted with the Committee's recommendations, are presented in the following section. In addition, the Committee will forward to EPA in the next few weeks a dossier on each substance or category included on the Committee's list of recommendations. These dossiers will summarize the information pertaining to each substance or category which was considered by the Committee in making its decision to recommend testing.

3.2 REASONS FOR RECOMMENDING TESTING OF THE SUBSTANCES AND CATEGORIES

The ten substances and categories which the Committee has designated for consideration by the EPA Administrator for development of test rules within twelve months are listed below with the Committee's reasons for recommending them.

3.2.A ALKYL EPOXIDES

TESTING RECOMMENDATIONS:

Carcinogenicity
Mutagenicity
Teratogenicity
Other Chronic Effects
Environmental Effects
Epidemiology

CATEGORY IDENTIFICATION: This category includes all noncyclic aliphatic hydrocarbons with one or more epoxy functional groups.

REASONS FOR RECOMMENDATIONS:

Production, Release and Exposure: Although these compounds are generally used as industrial intermediates, several alkyl epoxides are produced in very large quantities (e.g., ethylene oxide at over 4 billion pounds per year). The vast amounts produced thus raise concerns primarily with respect to workplace exposure. The reactivity of these compounds is such that environmental persistence is not anticipated; however, their reaction products may be of significance.

EFFECTS OF CONCERN: The epoxy structure is a relatively reactive functional group which is believed to be the source of the carcinogenic and mutagenic activity which is well characterized for several members reviewed (particularly the diepoxides). Thus, while some members of the group appear to be relatively well characterized as potential mutagens and/or carcinogens, these results and the presence of the epoxy functional group raise the need for testing other compounds in this group for these and other effects.

Carcinogenicity: Diepoxides are demonstrated carcinogens in animal studies. Ethylene oxide proved inactive while propylene oxide showed carcinogenic activity in mice. Other alkyl epoxides are less well tested. Because of the alkylating properties of these compounds it is recommended that alkyl epoxides be tested for carcinogenic potential. Mutagenicity of most members of this group tested provides further concern for carcinogenic potential.

Mutagenicity: Because most members of this group which have been tested proved to be mutagenic; other members of this group should be tested for this effect.

Teratogenicity: In general, these compounds have not been adequately tested for teratogenicity but should be, considering the reactivity of the epoxy group toward biological materials.

Other Chronic Effects: Because of the reactivity of epoxides with biological materials, they should be tested for specific chronic organ effects and behavioral changes.

Environment Effects: While the persistence of these compounds as epoxides is not great, concern is expressed for reaction products. In view of this possibility, the fate of epoxides in the environment should be determined through testing.

Epidemiology: Because of the large scale production of several of these compounds, and because of the strong toxicological evidence of possible carcinogenic and mutagenic effects, the Committee recommends that retrospective epidemiologic studies be required for two or three of the highest exposure compounds when suitable cohorts can be identified.

3.2.B ALKYL PHTHALATES

TESTING RECOMMENDATIONS:

Environmental Effects

CATEGORY IDENTIFICATION: This category consists of all high production (e.g., 10 million lbs/yr or greater) alkyl esters of 1,2-benzene dicarboxylic acid (orthophthalic acid).

REASONS FOR RECOMMENDATIONS:

Production, Release, and Exposure: Many of these compounds are produced in large volume, some of them over one hundred million pounds per year. Their use as plasticizers in a wide variety of products results in large volumes of alkyl phthalates reaching the aquatic environment either as wastes from formulating plants or from use and disposal of end products.

Effects of Concern:

Environmental Effects: Many of the alkyl phthalates are quite stable, breaking down only slowly to monophthalates or phthalic acid.

There has been a great deal of information published on their environmental fate and toxicity to aquatic organisms. Some are known to have considerable toxicity to fresh water fish. In view of the large volume in which they can be expected to reach the aquatic environment and persist and accumulate in aquatic organisms, it is important to have data on the toxicity to aquatic organisms of all high production alkyl phthalates. Each such compound should be tested for chronic toxicity to typical aquatic organisms, especially fish. Effects on reproduction (or population) should be included in this testing.

3.2.C CHLORINATED BENZENES, MONO- AND DI-

TESTING RECOMMENDATIONS:

Carcinogenicity
Mutagenicity
Teratogenicity
Other Chronic Effects
Environmental Effects
Epidemiology

CATEGORY IDENTIFICATION: This category consists of four closely-related chemical substances: monochlorobenzene (CAS No. 108-90-7), and ortho-, meta-, and paradichlorobenzene (CAS Nos. 95-50-1, 541-73-1, and 106-46-7).

REASONS FOR RECOMMENDATIONS:

Production, Release and Exposure: The chlorobenzenes are produced in large quantities, monochlorobenzene over 300 million pounds/year and ortho- and para-dichlorobenzene approximately 50 million pounds each. These chemicals are widely used in industrial processes, as solvents, and in many consumer products. Therefore, the exposure and potential for hazard is great, particularly in light of their high release rate and anticipated persistence in the environment.

Effects of Concern:

Carcinogenicity: One very limited animal study suggested the induction of sarcomas following subcutaneous injections of para-dichlorobenzene. A possible association of several cases of leukemia with human exposure to mixtures of ortho- and para-dichlorobenzenes has also been reported. These studies, as well as other animal toxicity experiments, do not provide sufficient data on which to assess the carcinogenic potential of members of this class.

Mutagenicity: While a study has demonstrated back mutations in yeast exposed to ortho-dichlorobenzene, the data are inadequate to assess the potential mutagenic hazard. Additional testing is needed in view of the widespread release and exposure. The other chemicals in this class should also be tested for mutagenicity.

Teratogenicity: While teratogenic effects are suspected for certain higher chlorobenzenes, the mono- and dichlorobenzenes have not been adquately tested.

Other Chronic Effects: Liver, kidney, respiratory and neurological effects have been observed with high level exposures. Effects at lower levels cannot be characterized from existing data. Chronic studies should be undertaken.

Environmental Effects: The environmental fate of these compounds should be determined. Evidence exists for environmental pollution and bioaccumulation in aquatic life. The effects are unknown. Studies should be initiated to assess the impact of these chemicals on terrestrial and aquatic systems.

Epidemiology: A possible link has been made between exposure to ortho- and para-dichlorobenzene and leukemia. Further efforts to evaluate chronic effects should be made by the identification and evaluation of specific populations who are or have been exposed to either ortho- or paradichlorobenzene.

3.2.D CHLORINATED PARAFFINS, 35-64% CHLORINE

TESTING RECOMMENDATIONS:

Carcinogenicity
Mutagenicity
Teratogenicity
Other Chronic Effects
Environmental Effects

CATEGORY IDENTIFICATION: This category is comprised of a series of mixtures of chlorination products of materials known commercially as paraffin oils or paraffin waxes; those having a chlorine content of 35% through 64% by weight are included.

REASONS FOR RECOMMENDATIONS:

Production, Release, and Exposure: The 1972 annual production of chlorinated paraffins was about 80 million pounds. The use of these materials in a wide variety of household and paint products, as well as adhesives and flame retardants, results in an estimated release rate of about 50 million pounds per year.

Effects of Concern:

Human Health Effects: A chronic study in mice showed evidence of degenerative changes in the liver and spleen; no data are available on the carcinogenicity, mutagenicity, teratogenicity, or other chronic effects of these mixtures. The Committee recommends that commercial products in this category be tested for such effects.

Environmental Effects: The occurrence of residues of chlorinated paraffins in fish indicates the need for critical assessment of the biological significance of this contamination of the aquatic environment. The persistence, environmental fate, and chronic effects on aquatic organisms of the chlorinated paraffins should be determined by appropriate testing.

3.2.E CHLOROMETHANE

TESTING RECOMMENDATIONS:

Carcinogenicity
Mutagenicity
Teratogenicity
Other Chronic Effects

SUBSTANCE IDENTIFICATION: CAS No. 74-87-3

REASONS FOR RECOMMENDATIONS:

Production, Release, and Exposure: The 1974 U.S. production of chloromethane was over 350 million pounds, most of this being used as a synthetic intermediate. However, it is estimated that about 5% of the annual production (over 15 million pounds per year) is released into the environment. NIOSH estimates that the number of workers exposed to chloromethane numbers about 31,000.

Effects of Concern:

Carcinogenicity: To date, chloromethane has not been the subject of a carcinogenicity study, although it is structurally related to chloroform, carbon tetrachloride, and iodomethane, all of which have been reported as being carcinogenic. Moreover, chloromethane has recently been reported as exhibiting mutagenic properties in the Salmonella mutagenic test with microsomal activation.

Mutagenicity: The initial positive results in the Salmonella mutagenic test with microsomal activation should be supplemented with test data regarding chromosomal abberrations.

Teratogenicity: The absence of data in this area, coupled with known toxic effects, calls for the initiation of studies to determine the extent of the potential hazard to the reproductive system and the fetus.

Other Chronic Effects: Exposure to chloromethane has been implicated in damage to the central nervous sytem, liver, kidneys, bone marrow and cardiovascular systems. Effects on these systems should be examined in chronic toxicity tests.

3.2.F CRESOLS

TESTING RECOMMENDATIONS:

Carcinogenicity
Mutagenicity
Teratogenicity
Other Chronic Effects
Environmental Effects

CATEGORY IDENTIFICATION: This category consists of the three isomers of methyl phenol: ortho-cresol (CAS No. 95-48-7), meta-cresol (CAS No. 108-39-4), and para-cresol (CAS No. 106-44-5).

REASONS FOR RECOMMENDATIONS:

Production, Release, and Exposure: Cresols are produced in large quantities, having a combined U.S. production in 1975 of about 90 million pounds. An annual release rate of about 45 million pounds has been estimated. Their wide use as industrial solvents leads to substantial occupational exposure. NIOSH estimates that roughly two million workers are exposed to cresols. In addition, cresols are used in many consumer products, resulting in a large general exposure.

Effects of Concern:

Carcinogenicity: Cresols have not been evaluated for carcinogenicity. Because of widespread exposure and suggestive evidence of mutagenic effects in certain plants, cresols should be tested for carcinogenicity.

Mutagenicity: There is some suggestion of the mutagenic potential of cresols in certain plants, but its potential as a human mutagen has not been assessed. It is, therefore, recommended that further mutagenic studies be conducted.

Teratogenicity: The teratogenicity of the cresols has not been assessed, but such testing is needed in view of the evidence of biological activity of cresols (see Other Chronic Effects, below) and their widespread exposure.

Other Chronic Effects: Although toxic effects involving the central nervous system, lungs, kidneys, liver, pancreas, and spleen have been observed following acute exposure to cresol-containing products, adequate testing of cresols for chronic effects following prolonged exposure has not been reported and should be conducted.

Environmental Effects: There is evidence that creosote oils containing cresols are acutely toxic to fish and taint fish flesh at low concentrations. Because of their substantial release into the aquatic environment, cresols should be tested for chronic effects on fish and other aquatic organisms.

3.2.G HEXACHLORO-1,3-BUTADIENE

TESTING RECOMMENDATIONS:

Environmental Effects

SUBSTANCE IDENTIFICATION: CAS No. 87-68-3

REASONS FOR RECOMMENDATIONS:

Production, Release, and Exposure: Although the most recent (1974) data available indicate that this compound is no longer commercially manufactured in the U.S., it continues to be produced as a waste byproduct of various chlorination processes and is also imported into the U.S. for industrial solvent use. The release of hexachlorobutadiene into the environment has not been quantified, but there is good evidence of widespread distribution in the aquatic environment.

Effects of Concern:

Environmental Effects: Hexachlorobutadiene's human health effects are being studied in depth. It is a stable substance which is widely distributed in the aquatic environment and has been reported to bioaccumulate in fish and other aquatic organisms. These factors indicate that hexachlorobutadiene should be tested to determine its fate in aquatic systems and its effects on invertebrates, fish, higher vertebrates, and plant life in aquatic systems. Its appearance in some European agricultural products suggests that its uptake by plants and/or foraging species should also be studied.

3.2.H NITROBENZENE

TESTING RECOMMENDATIONS:

Carcinogenicity
Mutagenicity
Environmental Effects

SUBSTANCE IDENTIFICATION: CAS No. 98-95-3

REASONS FOR RECOMMENDATIONS:

Production, Release, and Exposure: U.S. production of nitrobenzene in 1975 was about 400 million pounds. Its release to the environment has been estimated to be about 20 million pounds annually. Although its predominant use (97 percent of production) is in closed systems in aniline manufacture, nitrobenzene is also an industrial solvent and dye intermediate. General population exposure can arise from environmental release, and from dispersive uses such as perfume in soap; cleaner for woodwork, wood flooring and paneling; ingredient of metal polishes and shoe blacking. Nitrobenzene liquid and vapor penetrate intact skin readily, and the efficiency of vapor absorption by inhalation is high.

Effects of Concern:

Carcinogenicity: No information is available on the carcinogenicity of nitrobenzene. Since it is biologically active, producing cellular changes,
nitrobenzene should be tested for
carcinogenicity.

Mutagenicity: Although there is evidence of its biological activity, no mutagenicity testing has been reported for nitrobenzene. Mutagenicity testing should be performed.

Environmental Effects: Nitrobenzene is a relatively persistent substance in the environment. Its low volatility, stability to light, and low water solubility indicate that bioaccumulation is possible. Acute effects have been demonstrated in fish. Nitrobenzene inhibits oxygen utilization and hydrogen sulfide production in sewage microorganisms, inhibits growth in yeast, and is toxic to various soil bacteria and microorganisms. Additional data are needed to adequately characterize the persistence and fate of nitrobenzene and its matabolites in the aquatic environment. Testing is needed for such characteristics as well as to determine the effects of chronic exposure to nitrobenzene on fish, aquatic invertebrates, aquatic plant life, and waterfowl.

3.2.I TOLUENE

TESTING RECOMMENDATIONS

Carcinogenicity
Teratogenicity
Other Chronic Effects
Epidemiology

SUBSTANCE IDENTIFICATION: CAS No. 108-88-3

REASONS FOR RECOMMENDATIONS:

Production, Release and Exposure: Toluene is produced in large quantities with an annual production rate in excess of 5 billion pounds. Because of its widespread use as a solvent, as well as a multiplicity of other uses, toluene has an unusually high occupational exposure (over 1 million workers). Its presence in many consumer products leads to a large general exposure. Toluene is currently being substituted for many benzene-uses and has an annual release rate exceeding 1 billion pounds.

Effects of Concern:

Carcinogenicity: Previous studies based solely on skin application techniques in animals have demonstrated a carcinogenic potential for toluene. Some of these studies were limited in design and prevented an appropriate appraisal of the carcinogenic hazard of toluene. It is, therefore, recommended that testing be conducted in long-term animal experiments taking into consideration the appropriate route of exposure.

Teratogenicity: Information is lacking on the teratogenic hazard of this chemical, thus necessitating the initiation of studies to determine if toluene is teratogenic.

Other Chronic Effects: Liver, central nervous system and hematopoietic effects have been observed at high level exposures. Effects at lower levels cannot be characterized from existing data. Chronic studies to evaluate the effects of prolonged exposures are recommended.

Epidemiology: Occupational studies have been conducted predominantly on the acute toxic effects of toluene. There is little information on chronic effects in humans from exposure to low levels of toluene over an extended period of time. Because of its long-term use, high human exposure, and demonstrated effects in animals, epidemiological studies may be particularly important in assessing the human health effects of toluene.

3.2.J XYLENES

TESTING RECOMMENDATIONS:

Mutagenicity
Teratogenicity
Epidemiology

CATEGORY IDENTIFICATION: This category consists of the three isomers of dimethyl benzene: ortho-xylene (CAS No. 95-47-6), meta-xylene (CAS No. 108-38-3), and para-xylene (CAS No. 106-42-3)

REASONS FOR RECOMMENDATIONS:

Production, Release, and Exposure: In the aggregate, approximately 8 billion pounds of xylenes are produced each year. Approximately 900 million pounds are released to the environment each year. Mixed xylenes were ranked by NIOSH 13th out of approximately 7000 agents in terms of the number of workers exposed. Xylenes are also used in a wide variety of consumer products, resulting in general population exposures.

Effects of Concern:

Mutagenicity: Mutagenesis tests have not been reported for any of the xylenes, but should be conducted in view of widespread exposure and evidence of toxic effects to several organ systems.

Teratogenicity: Xylenes cross the placental barrier and, according to two Russian studies, are embryotoxic. Therefore, they should be tested for teratogenicity.

Epidemiology: Because of their long-term use, high human exposure, and demonstrated effects in animals, epidemiological studies may be particularly important in assessing the human health effects of xylenes and should be conducted.

APPENDIX A

DATA SOURCES USED FOR PREPARATION OF THE INITIAL LIST

01 Toxic Pollutants in Point Source Water Effluent Discharge

This list of 120 chemicals and categories consists of Appendices A and C of the settlement agreement dated 7 June 1976 between the Environmental Defense Fund and EPA. It is a priority list of toxic pollutants subject to regulations through point source effluent limitations (Section 307(a)) under the Federal Water Pollution Control Act.

02 Scoring of Organic Air Compounds, June 1976, MITRE, MTR-6248

This list of 337 chemicals and categories was compiled and documented by MITRE (September 1976) under contract to EPA. The relevant factors in selecting chemicals for the list were: (1) quantity produced, (2) potential for atmospheric release, and (3) toxicological effects.

03 Final Report of NSF Workshop Panel to Select Organic Compounds Hazardous to the Environment, April 1975

This list of 80 chemicals and categories was compiled and documented by Stanford Research Institute under contract to the National Science Foundation. The list consists of those chemicals having the greatest potential for environmental release, selected from the universe of manufactured organic chemicals with the highest calculated release rates.

04 Potential Industrial Carcinogens and Mutagens

This list of 88 chemicals has been compiled by the National Center for Toxicological Research. The list is made up of industrial compounds which are potential carcinogens and/or mutagens, and which have been selected based upon available data concerning activity, use, production, and population at risk.

05 Occupational Carcinogens for Potential Regulatory Action

This list of 116 chemicals and categories was compiled by OSHA from suspected carcinogens. Selection was based primarily upon data available through the NIOSH Registry (Source List 13).

07 Chemicals Tested or Scheduled for Testing at the Fish-Pesticide Research Laboratory, Department of Interior

This list consists of 174 toxic chemicals which are suspected of being hazardous to fish and wildlife.

08 Substances with Chronic Effects other than Mutagenicity, Carcinogenicity, or Teratogenicity; A Subfile of the NIOSH Registry

A subfile of the NIOSH Registry (Source List 13)

09 Criteria Documents Prepared or Planned by NIOSH, February 24, 1977

This list of 127 chemicals and categories consists of substances for which criteria documents have been or will be prepared and delivered to the Department of Labor. In selecting these chemicals NIOSH considered: a) the number of workers exposed, b) known or suspected toxic effects, and c) physical and chemical properties.

10 Suspected Carcinogens; A Subfile of the NIOSH Registry

This is a list of 1,900 chemicals and categories which have been reported to have produced cancer in test animals. The list is included in Source List 13.

11 Suspected Mutagens; A subfile of the NIOSH Registry

This is a list of approximately 100 chemicals and categories which have been reported to have produced mutagenic effects in test systems. This list is included in Source List 13.

13 NIOSH Registry of Toxic Effects of Chemical Substances, 1976

This list of 21,543 chemicals and categories was compiled and documented in the NIOSH Registry. Only those substances which were on Source Lists 8, 10, 11, or 12 were included in the INITIAL LISTING.

17 The Ecological Impact of Synthetic Organic Compounds on Estuarine Ecosystems, September, 1976, EPA-1600/3-76-075

This list of 9 chemicals was compiled as part of a study of the impact of synthetic organic compounds on estuarine ecosystems. The effects of the 9 chemicals and a number of pesticides were analyzed and documented in the study.

18 Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1976, American Conference of Government Industrial Hygienists

This list of approximately 570 chemicals and categories was compiled by the ACGIH to give Threshold Limit Values for chemical substances and physical agents in the workroom environment.

19 National Occupational Hazard Survey (1972-1974)

This list of over 7,000 chemicals and other hazards has been compiled by NIOSH. These hazards are ranked according to the estimated number of workers exposed. Only the chemicals ranked among the top 500 hazards were included in the INITIAL LISTING.

20 Chemicals Being Tested for Carcinogenicity by the Bioassay Program, DCCP, National Cancer Institute, 1977

This list of 372 chemicals includes those which have been selected for bioassay by the National Cancer Institute.

21 EPA/Office of Toxic Substances List of Priority Toxic Chemicals, 1977

This list of 162 chemicals was compiled by EPA/OTS from the NIOSH list of carcinogens (Source List 10).

22 A Study of Industrial Data on Candidate Chemicals for Testing, EPA Contract # 68-01-4109, November, 1976

This list of 650 chemicals and categories was compiled by Stanford Research Institute as part of the contracted effort to produce Source List 03. Production and calculated release data are included.

24 General List of Problem Substances, Environmental Contaminants Committee, Ottawa, Ontario, Canada, 1977

This list of 160 chemicals and categories of environmental concern was compiled by the Canadian government.

OTHER LISTS USED FOR REFERENCE BUT NOT USED AS SOURCE LISTS FOR THE INITIAL LISTING:

06 Survey of Compounds which have been Tested for Carcinogenic Activity (Index, 1970-1971), NIH/HEW

This list of 3,634 chemicals and categories is a cumulative index by CAS number of PHS 149 volumes through 1970-1971.

14 Research Project to Gather and Analyze Data and Information on Chemicals that Impact Man and the Environment

This list of 3,200 chemicals and categories was compiled and documented by Stanford Research Institute under contract to the National Cancer Institute. The documentation includes total production and calculated release data for each of the chemicals in nine hazard categories: (1) over-the-counter drugs, (2) prescription drugs, (3) cosmetics, (4) trade-sales paints, (5) water pollutants, (6) air pollutants, (7) soaps and detergents, (8) pesticide residues in food, and (9) intentional food additives.

16 Other Potential Modifiers of the Stratosphere, 1975

This list of 41 chemicals was compiled by the National Institute of Environmental Health Sciences from the universe of 275 manufactured chemicals ranked for release rate used by Stanford Research Institute in preparing Source List 03. This list identifies potential modifiers of the stratosphere and provides related information.

23 EPA/Office of Research and Development, Chemical Production

A set of production data compiled by EPA/ORD on approximately 140 chemicals.

APPENDIX B

PRODUCTION, RELEASE, AND EXPOSURE SCORES

A. The production, environmental release, occupational exposure, and general population exposure factors described in the text were scored in the following manner: in the following manner:

Factor 1: Production

Annual production data were collected from a number of sources:

a. Scoring of Organic Air Compounds (Source List 02 of Appendix A)

b. A Study of Industrial Data on Candidate Chemicals for Testing (Source List 22 of Appendix A)

c. EPA/OR&D Chemical Production (Source List 23 of Appendix A)

d. Synthetic Organic Chemicals, United States Production and Sale, 1975, United States International Trade Commission

e. Chemical Economics Handbook, 1975 Stanford Research Institute

f. Chemical and Engineering News: Vol. 52, No. 51, dated 12/23/74; Vol. 55, No. 18, dated 5/2/77; Vol. 55, No. 24, dated 6/13/77

The Factor 1 score assigned to a chemical was the common logarithm of the highest annual production value (in millions lbs/yr) found in any of the above sources. If an annual production value was not available for a chemical in any of these sources, a Factor 1 score of -0.5229 (corresponding to an assumed annual production of 300,000 pounds) was assigned.

Factor 2: Quantity Released into the Environment

The quantity of chemical released into the environment was scored on a scale from 0 to 3 as follows:

Score	Release Rate	Estimate Based on Uses
3	30 percent	Mostly dispersive uses
2	3 to 30 percent	Some dispersive uses
1	.3 to 3 percent	Few dispersive uses; or primarily industrial chemical with propensity for leaks
0	.3 percent	Well contained industrial chemical

Estimates of release rates for a number of chemicals are given in Source List 22 of Appendix A. For those chemicals for which no release rates were given, an estimate was made on the basis of the dispersive nature of the chemical's uses as indicated in the above table.

An estimate was also made of the chemical's persistence according to the following table:

Score	Lifetime	Example
3	Infinite (years or greater)	Compounds of metals, freons, CCl4, N2O, SF6, many polymers
2	Order of 1 year	Tetrachloroethylene, flame retardants, phthalate esters, silicones
1	Order of a few days	SO2
0	Hours or less	Reactive compounds

The sum of the scores of the two subfactors, release quantity and persistence, was taken as an indication of the environmental burden posed by the chemical.

Factor 3: Occupational Exposure

The source of data on occupational exposure to chemicals was the National Occupational Hazard Survey (NOHS) conducted by the National Institute for

Occupational Safety and Health. In this survey, the approximately 7000 most common hazards occurring in the working place were rank ordered. To achieve an occupational exposure score with a range and direction similar to those of the other factors, the Factor 3 score assigned to a chemical was 3.8451 minus the common logarithm of its rank on the NOHS list. (3.8451 is the logarithm of 7000.) Chemicals which did not appear on the NOHS list were given a score of zero, equivalent to having been ranked number 7000 on the survey.

Factor 4: Extent to Which the General Population is Exposed

Four individual subfactors were scored and then summed to measure the general population exposure. The four subfactors were scored as follows:

SUBFACTOR 1 Number of people exposed to the chemical (exclusive of a workplace environment)

Score	No. of People	Example
3	20 X 10	Widely used household products (e.g., wearing apparel, shoe polish, certain surface coatings, common paints and their solvents, common plastics and their additives, detergents, furnishings and carpets, wood cleaning products, refrigerants, natural gas, nonfood packaging materials, flame proofers)
		General air, food and water contaminants
		Automotive products (e.g., gasoline and additives, rubber, surface coatings, plasticizers, flame proofers)
		Products used widely in commercial buildings (mostly same as household, including commercial cleaners, disinfectants)

Score	No. of People	Example
2	2-20 X 10	Less widely used household products (e.g., uncommon paints, specialty apparel such as baby wear, hobby uses, arts and crafts, tools)
		Regional air and water pollutants, farm chemicals (exclusive of pesticides)
1	0.2-2 X 10	Specialty hobbies (e.g., photography), specialty products
		Neighborhood air and water pollutants from local industries
0	2 X 10	Chemical intermediates rarely found outside the workplace

SUBFACTOR 2 Frequency of exposure (to the typical person in ranking number of people exposed under Subfactor 1)

Score	Frequency	Exampless
3	Daily or more often	General air, food and water contaminants, household products in regular use, material used inside automobiles, clothing
2	Weekly	Hobby crafts, household products used intermittently (e.g., certain cleaners), bleaches, gardening products
1	Monthly	Dry cleaning, certain solvents, house maintenance (e.g., polishes, certain cleaning agents), automobile maintenance
0	Yearly or less frequently	Application of household paints, specialty products

SUBFACTOR 3 Exposure intensity. This is intended to reflect the total amount of material that comes into contact with the average or typical person whose exposure has been scored under subfactors 1 and 2. Scoring of this factor considered the number of grams of the material that makes contact with the average person in the course of one exposure (daily, weekly, monthly or yearly as scored in subfactor 2). Thus, for example, a trace pollutant may lead to exposure of a typical person of the order of micrograms per day every day; use of a specialty solvent might lead to exposure of a typical person of the order of grams per day once a year: these would be scored 3,0 and 0,3 respectively on subfactors 2 and 3.

Score	Intensity	Examples
3	High (10 or more grams per exposure)	Plastics, fabrics, surface coatings, volatile solvents in closed spaces, liquids contacting skin, high concentration gases
2	Medium (10 to 10 g per exposure)	Fabric additives, solvents in open spaces or outdoors, dusts, solutes, transitory exposures to vapors or aerosols
1	Low (10 to 10 g per exposure)	Low level indoor exposure, volatile substances from home furnishings and building materials (e.g., plasticizers, flame proofers), low volatility solvents, pigments
0	Very low (less 10 g per exposure	Environmental contaminants (low level air, food, and water contaminants), monomers in polymers

SUBFACTOR 4 Penetrability. This is a measure of the material that comes into contact with a person (whether by dermal, inhalation, or ingestion exposure) and that is expected to be absorbed into the body (even transitorily) with potential for interaction with cells.

Score	Penetrability	Examples
3	High (10 to 100% absorption)	Organic solvents in liquid, mist, or aerosol form, vapors and gases if likely to be soluble in body fluids, respirable-sized particles, surface active agents, materials known to have high dermal systemic toxicity
2	Medium (1 to 10% absorption)	Solvents with low volatility and/or larger molecules, organic materials in water solution, waxes and polishes, coarse dusts
1	Low (0.01 to 1% absorption)	Certain solids, dermal exposure to most inorganic materials in water solution
0	Neglegible (less than 0.01% absorption)	Polymers, metals

B. In making the judgments called for in scoring Factors 2 and 4 above, knowledge of the chemical's uses was necessary. Use information was collected from the following sources:

1. The Condensed Chemical Dictionary, Ninth Edition, Hawley, Van Nostrand Reinhold Company, New York, 1977.

2. The Merck Index, Ninth Edition, Merck and Company, Inc., Rahway, N.J., 1976.

3. Faith, Keyes, and Clark's Industrial Chemicals, Lowenheim and Moran, Fourth Edition, J. Wiley and Sons, Inc., New York, 1975.

4. Chemical Marketing Reporter, Schnell Publishing Company, Inc., New York.

5. Encyclopedia of Chemical Technology, Kirk-Othmer, Inter-Science Publishing Company, New York, 1972.

APPENDIX C

ORDERING THE CHEMICALS BASED ON PRODUCTION, RELEASE, AND EXPOSURE

A linear weighting scheme was used to rank order the chemicals. The rank of the j^{th} chemical, r_j, was computed by the formula:

$$r_j = \sum_{i=1}^{4} w_i \frac{f_{ij}}{s_i},$$

where w_i is the weight assigned to the i^{th} factor,

f_{ij} is the i^{th} factor score of the j^{th} chemical,

and s_i is a scaling factor chosen to normalize the assigned scores.

The four scaling factors employed were:

s_1 = log 20,850 - 4.3191; 20,850 million lb/yr being the maximum of all Factor 1 chemical production quantities.

s_2 = 6; 6 being the maximum of all Factor 2 environmental release scores.

s_3 = 3.8451 - log 3 = 3.3680; third being the highest NOHS rank among the scored chemicals. (Ranked first and second on the NOHS list were continuous noise and mineral oil, the former not being a chemical hazard and the latter not being among the scored chemicals.)

s_4 = 12; 12 being the maximum of all Factor 4 general population exposure scores.

This choice of s_1, s_2, s_3, s_4, guaranteed that $\left|\frac{f_{ij}}{s_i}\right| \leq 1$ for all i and j, and furthermore, that for each i,

$\left|\frac{f_{ij}}{s_i}\right| = 1$ for at least one chemical j.

Factor 3: Teratogenicity

a. Numerical Scores Assigned:

3 Confirmed teratogen in humans or in two appropriate animal species

2 Confirmed teratogen in 1 animal species

1 Insufficient or inadequate experimental data for definite conclusions, but either (a) no experimental or structural reason for suspicion, or (b) low biological activity

0 Adequately tested in two suitable animal species with negative findings for teratogenic activity

b. Letter Scores Assigned:

xxx Needs testing, strongly suspect (close structural relationship to known teratogen, inconclusive but suspicious positive animal tests, etc.)

xx Needs testing, suspect (equivocal result in animal test, etc.)

x Needs testing, some reason for suspicion

c. Criteria for Acceptance of Teratogenicity Tests

Accepted teratogenicity tests conformed reasonably to the recommendations and principles outlined in "Principles for Evaluating Chemicals in the Environment," National Academy of Sciences, pp. 173-182, 1975; and "The Testing of Chemicals for Carcinogenicity, Mutagenicity, Teratogenicity," Department of Health and Welfare, Canada, pp. 137-176, March 1973.

Factor 4: Acute Toxicity

a. Numerical Scores Assigned:

3	extremely toxic:	< 50 mg/kg
2	very toxic:	50-500 mg/kg
1	moderately toxic:	0.5-5 g/kg
0	very slightly toxic:	> 5 g/kg

b. Letter Scores Assigned:*

xx not tested, but suspected to be in range 2-3

x not tested, but suspected to be in range 0-1

*See factor 2 for normalized scored.

c. Criteria for Quantitation of Acute Toxicity

Standard systems of toxicity rating based on probably lethal dose in humans were used when available . Lowest lethal doses and LD50 values in various animal systems were also widely used.

Factor 5: Other Toxic Effects

a. Numerical Scores Assigned:

3 Effects at low doses (Guidelines: < 1 mg/kg/day)

2 Effects at moderate doses (Guidelines: 1-10 mg/kg/day)

1 Effects at high doses (Guidelines: >10 mg/kg/day)

0 Very low or negligible biological activity (e.g., nitrogen, argon, etc.)

b. Letter Scores Assigned:

xxx Needs testing (structural similarity to another chemical which rates 2 or 3, questionable reports of effects which need confirmation, etc.)

xx Needs testing, some reasons for suspicion

x Needs testing, inadequate information available to give high pirority

c. Criteria for Scoring

This factor includes both reversible and irreversible effects, delayed or cumulative toxicity, organ-specific effects, effects on reproduction, behavior, etc. The score entered reflects the toxic effects noted in animals (or in humans if data were available) at the lowest dose-range. If the chemical was reported or suspected to have more than one toxic effect, xxx or xx for one type of toxic effect superseded any numerical score for another. Also, x for one type of toxic effect superseded 2 or 1 for another. In many cases, reports of one type of effect at low doses engendered suspicion of the likelihood of others; in such cases the chemical was scored with the appropriate number of x's, unless thoroughly tested.

Factor 6: Bioaccumulation

a. Numerical Scores Assigned:

3 High ($>10^4$)*

2 Appreciable (10^2–10^4)

1 Low ($<10^2$)

0 Experimental evidence for non-accumulation (<1); water soluble compounds

*The degree of bioaccumulation (more precisely, the tissue-specific storage factor) is defined as the concentration of the chemical in the tissues (at "steady state" or after prolonged exposure) divided by the concentration of the chemical in the ambient medium.

b. Letter Scores Assigned:

xxx Testing important, judged likely to be high

xx Testing important, judged not likely to be high, but likely to be appreciable

x Needs testing, little or no experimental data

c. Criteria for Scoring

Bioaccumulation is used here in its broad sense of the accumulation of a chemical in one or more tissues of an animal (or plant) to levels higher than those in the ambient medium. For purposes of screening chemicals, it was considered significant primarily in cases in which the accumulation in tissues represented an enhanced probability of effects, either on the organ in which the chemical was concentrated, or on animals which feed on the organism which accumulated the chemical. High degrees of bioaccumulation are usually found only in aquatic organisms. For these organisms, bioaccumulation is known to be dependent primarily on water solubility and it is empirically predicted by the octanol/water partition coefficient. Zero scores were assigned to completely water soluble organic chemicals.

Substances which are easily metabolized will not be bioaccumulated even if they have a high partition coefficient (example, chloroform). Thus ease of metabolism was a factor considered in evaluating the potential for bioaccumulation.

Factor 7: Ecological Effects

a. Numerical Scores Assigned:

3 Effects at low concentrations (10^{-9} or less in air or water)*

2 Effects at moderate concentrations (10^{-7} - 10^{-9} in air or water)

1 Effects at high concentrations (10^{-6} or greater in air or water)

0 No reported effects that could justify priority for testing

*In air for gases or vapors: 1 part of chemical per billion parts air by volume (ppb). In water for liquids and solids: 10^{-9} gram per cubic meter (ng/m^3)

b. Letter Scores Assigned:*

xx Testing needed, possibility of major or widespread effects

x Testing needed, possibility of minor or local effects

*See factor 2 for normalized scores.

c. Criteria for Scoring:

Ecological effects considered included beside toxic effects on non-human animals and plants, ecosystem effects, effects on atmosphere and climate, ozone depletion, etc. Generally, numerical scores (established hazard) were assigned only to a limited number of thoroughly tested chemicals (e.g., pesticides, some metal containing compounds, or some specific chemicals). In other cases, the potential for ecological effects was judged according to availability of data on toxicity in particular, published information on specific tests, structural similarity to compounds of better known eco-toxicity, published data on depletion potential for stratospheric ozone. Zero scores were assigned only to compounds with low biological activity (LD50 > 1 g/kg or AQTR > 100 ppm).

B. An extra factor was scored if the presence of a contaminant in a commercial product was the major reason for concern, or if a trace degradation product was the major reason for concern (examples: dioxin, methyl mercury).

Factor 6: Bioaccumulation

a. Numerical Scores Assigned:

3 High ($>10^4$)*

2 Appreciable (10^2–10^4)

1 Low ($<10^2$)

0 Experimental evidence for non-accumulation (<1); water soluble compounds

*The degree of bioaccumulation (more precisely, the tissue-specific storage factor) is defined as the concentration of the chemical in the tissues (at "steady state" or after prolonged exposure) divided by the concentration of the chemical in the ambient medium.

b. Letter Scores Assigned:

xxx Testing important, judged likely to be high

xx Testing important, judged not likely to be high, but likely to be appreciable

x Needs testing, little or no experimental data

c. Criteria for Scoring

Bioaccumulation is used here in its broad sense of the accumulation of a chemical in one or more tissues of an animal (or plant) to levels higher than those in the ambient medium. For purposes of screening chemicals, it was considered significant primarily in cases in which the accumulation in tissues represented an enhanced probability of effects, either on the organ in which the chemical was concentrated, or on animals which feed on the organism which accumulated the chemical. High degrees of bioaccumulation are usually found only in aquatic organisms. For these organisms, bioaccumulation is known to be dependent primarily on water solubility and it is empirically predicted by the octanol/water partition coefficient. Zero scores were assigned to completely water soluble organic chemicals.

Substances which are easily metabolized will not be bioaccumulated even if they have a high partition coefficient (example, chloroform). Thus ease of metabolism was a factor considered in evaluating the potential for bioaccumulation.

Factor 7: Ecological Effects

a. Numerical Scores Assigned:

3 Effects at low concentrations (10^{-9} or less in air or water)*

2 Effects at moderate concentrations (10^{-7} - 10^{-9} in air or water)

1 Effects at high concentrations (10^{-6} or greater in air or water)

0 No reported effects that could justify priority for testing

*In air for gases or vapors: 1 part of chemical per billion parts air by volume (ppb). In water for liquids and solids: 10^{-9} gram per cubic meter (ng/m^3)

b. Letter Scores Assigned:*

xx Testing needed, possibility of major or widespread effects

x Testing needed, possibility of minor or local effects

*See factor 2 for normalized scores.

c. Criteria for Scoring:

Ecological effects considered included beside toxic effects on non-human animals and plants, ecosystem effects, effects on atmosphere and climate, ozone depletion, etc. Generally, numerical scores (established hazard) were assigned only to a limited number of thoroughly tested chemicals (e.g., pesticides, some metal containing compounds, or some specific chemicals). In other cases, the potential for ecological effects was judged according to availability of data on toxicity in particular, published information on specific tests, structural similarity to compounds of better known eco-toxicity, published data on depletion potential for stratospheric ozone. Zero scores were assigned only to compounds with low biological activity (LD50 > 1 g/kg or AQTR > 100 ppm).

B. An extra factor was scored if the presence of a contaminant in a commercial product was the major reason for concern, or if a trace degradation product was the major reason for concern (examples: dioxin, methyl mercury).

Factor 8: Contaminants and Environmental Degradation or Conversion Products

a. Numerical or Letter Scores Assigned:

1 Contaminants, etc., known to be important

0 Contaminants, etc., not suspected, or known to be of no importance.

x Contaminants, etc., suspect, needs testing

b. Criteria for Scoring:

The scores for this factor were not averaged. A letter score took priority over a numerical score at any time; if no letter score was assigned to a chemical, the numerical score 1 was overriding. A zero score was assigned only if it was scored unanimously by all scorers. The score for this factor was not added: (1) if the principal breakdown product was the major problem and it was the basis for scores on other criteria such as persistence and toxicity (examples: DDE, PAN); (2) for in vivo metabolism of carcinogens to active forms (e.g., arene oxides, activated nitrosamines, etc. etc.).

C. It is of relevance for the scoring method to add that in order to facilitate the inclusion of a zero score in a letter score average, the zero score was changed into 0.1X. Also, in some instances fractional numerical or letter scores were assigned by scorers.

D. The following literature sources were extensively used by the scorers:

References of general interest

1. NIOSH Registry of Toxic Effects of Chemical Substances (1976)

2. Kirk-Othmer Encyclopedia of Chemical Technology. Edited by A. Standen, Interscience Publishers, New York (1963, 1972).

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4. The Merck Index, 9th ed. Merck & Co., Inc., Rahway, N.J. (1976).

5. Chemical Consumer Hazard Information System. Consumer Product Safety Commission, Washington, D.C. (1977).

6. A Study of Industrial Data on Candidate Chemicals for Testing. Stanford Research Institute, Palo Alto, California, (1976).

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8. Brown, S.L., et al. Research Program on Hazard Priority Ranking of Manufactured Chemicals, Phase II- Final Report to National Science Foundation. Stanford Research Institute Menlo Park, California (1975).

9. Dorigan, J., et al. Scoring of Organic Air Pollutants, Chemistry, Production and Toxicity of Selected Synthetic Organic Chemicals, MITRE, MTR-6248 (1976).

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C1. Survey of Compounds Which Have Been Tested for Carcinogenic Activity Through 1972-1973 DHEW Publication No. NIH 73-453, National Cancer Institute, Bethesda, Maryland

C2. Suspected Carcinogens - A subfile of the NIOSH Toxic Substances List.

C3. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Lyon, France. WHO, International Agency for Research on Cancer.

C4. Chemicals Being Tested for Carcinogenicity by the Bioassay Program, DCCP. National Cancer Institute (1977).

C5. Information Bulletin on the Survey of Chemicals Being Tested for Carcinogenicity, No. 6. WHO, Lyon, France (1976).

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A04. Debruin, A. Biochemical Toxicology of Environmental Agents. Elsevier/North Holland, Inc., New York (1976).

A05. Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1976. American Conference of Government Industrial Hygienists.

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A011. Chemical Safety Data Sheets. Manufacturing Chemists Association, Washington, D.C.

A012. Industrial Safety Data Sheets. National Safety Council, Chicago, Illinois.

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BE1. Applegate, V.C., J.H. Howell, A.E. Hall, Jr. & M.A. Smith, 1957 Toxicity of 4.346 Chemicals to Larval Lampreys and Fishes. U.S. Dept. Interior, Fish & Wildlife Service. Special Scientific Report-Fisheries No. 207. Wash., D.C.

BE2. Battelle Columbus Laboratories 1971, Effects of Chemicals on Aquatic Life: Selected Data from the Literature through 1968. Vol. 3 of Water Quality Criteria Data Book. U.S. Environmental Protection Agency, Washington, D.C.

BE3. Hahn, W., and P. Jensen, Water Quality Characteristics of Hazardous Materials; Texas A & M University, (1974) (Taken from the NIOSH Registry of Toxic Effects of Chemical Substances (1976).

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[FR Doc.77-29727 Filed 10-11-77;8:45 am]