

Federal Register

**Friday
April 17, 1987**

Part III

Department of Health and Human Services Environmental Protection Agency

**Notice of the First Priority List of
Hazardous Substances That Will Be the
Subject of Toxicological Profiles and
Guidelines for Development of
Toxicological Profiles**

CTL017901

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Environmental Protection Agency

(OPTS-400003; FRL-3174-9(a))

Notice of the First Priority List of Hazardous Substances That Will Be the Subject of Toxicological Profiles

AGENCY: Department of Health and Human Services (DHHS) and Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: The Superfund Amendments and Reauthorization Act (SARA) amends the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA or Superfund) by establishing certain requirements for EPA and the Agency for Toxic Substances and Disease Registry (ATSDR) of DHHS with regard to hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List (NPL). Among these statutory requirements is a mandate for the two agencies to prepare a list of at least 100 hazardous substances, in order of priority, which are most commonly found at NPL facilities and which the agencies determine are posing the most significant potential threat to human health. Section 110 of SARA requires that the list be prepared no later than April 17, 1987. This notice contains that priority list of 100 substances, and provides a brief summary of the methodology used to assemble the list.

ADDRESS: Comments on this notice should bear the docket control number OPTS-400003, and should be submitted to the following address: Document Control Officer (TS-790), Office of Toxic Substances, Environmental Protection Agency, Room NE-G004, 401 M Street SW., Washington, DC 20460.

Comments which contain confidential business information (CBI) should clearly note that they contain CBI and should be sent in triplicate to the address given above. For further information regarding the submission of comments containing CBI, see Unit V of this notice. Non-confidential versions of comments on this notice will be available for public inspection in Room NE-G004 at the address given above from 8 a.m. to 4 p.m., Monday through Friday except legal holidays.

FOR FURTHER INFORMATION CONTACT: Edward A. Klein, Director, TSCA Assistance Office (TS-79), Office of Toxic Substances, Environmental Protection Agency, Rm. E-543, 401 M St.,

SW., Washington, DC 20460, Telephone: (202-554-1404).

SUPPLEMENTARY INFORMATION:

I. Background

On October 17, 1986, the President signed the Superfund Amendments and Reauthorization Act of 1986 (Pub. L. 99-499), which extends and amends the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (42 U.S.C. 9601 et seq.).

Section 110 of SARA amends section 104(i) of CERCLA by establishing requirements for the preparation of: (1) A list of hazardous substances found at NPL sites (in order of priority), (2) toxicological profiles of those substances, and (3) a research program to fill data gaps associated with the substances. The purpose of this notice is to identify the first 100 priority list substances and to provide a short summary of the methodology used by ATSDR and EPA to compile that list. Although the new statutory provisions have been added to CERCLA, this notice will refer to them as the section 110 requirements of SARA, to maintain a clear distinction in the notice between the new provisions and the existing requirements of CERCLA.

With regard to the priority list requirement, section 110 of SARA states that ATSDR and EPA:

shall prepare a list, in order of priority, of at least 100 hazardous substances which are most commonly found at facilities on the [CERCLA] National Priorities List and which, in their sole discretion, they determine are posing the most significant potential threat to human health due to their known or suspected toxicity to human health due to their known or suspected toxicity to humans and the potential for human exposure to such substances at facilities on the National Priorities List or at facilities to which a response to a release or a threatened release under [CERCLA] is under consideration.

Section 110 further requires that the agencies prepare the first priority list within 6 months of the enactment of SARA (i.e., no later than April 17, 1987).

After compiling the first priority list, ATSDR must prepare toxicological profiles of the listed substances. Section 110 of SARA establishes a timetable for revising the priority list and preparing toxicological profiles of hazardous substances on the list; profiles of no fewer than 25 substances on the first priority list must be completed within 1 year of the enactment of SARA (by October 17, 1987). The profiles will be made available to the public, with a notice of availability and a request for public comment to be published in the Federal Register. The profiles will be revised as necessary in response to the

public comments and additional data that subsequently become available to ATSDR (but no less often than once every three years). The toxicological profile process is described in greater detail in a notice which is published elsewhere in today's issue of the Federal Register.

The first priority list of 100 hazardous substances was prepared within 6 months of the enactment of SARA, as required by section 110. Unfortunately, ATSDR and EPA have not been able to solicit public comments on the preparation of the first priority list, because the time-constraints of SARA section 110 require the agencies to take extraordinary steps to expedite policy development and preparation of the first list and profiles. However, ATSDR and EPA have been as thorough as possible in compiling the first priority list, given the tight statutory timetable within which the agencies had to operate.

The methodology used to prepare the first priority list is summarized below. The agencies solicit public comment on this approach; such comments should be submitted in accordance with the instructions given in this notice. The listing process will be refined as future revisions of the list are prepared under less severe time-constraints. Later changes in the listing methodology will be based on comments received in response to this notice and on further evaluation of the process by ATSDR and EPA. All nonconfidential comments will be placed in the public file for this notice. A more detailed description of the listing methodology is contained in support documents which have been placed in the public file and are available for public review (see Unit V of this notice).

II. Methodology for Selecting Substances on the First Priority List

A. General Approach Taken by ATSDR and EPA

The hazardous substances listed in this notice were drawn from a list of 717 hazardous substances currently identified under section 102 of CERCLA. ATSDR and EPA used the CERCLA list to create a subset of hazardous substances which EPA has identified at National Priority List (NPL) sites. The two agencies then began a process of prioritizing that subset of hazardous substances based on the following three criteria for determining the degree to which each substance poses a potential human health risk: (1) Chemical toxicity, (2) frequency-of-occurrence of subset substances at NPL sites or other facilities, and (3) potential for human

exposure to the substances. These criteria reflect the requirements of SARA section 110, as well as the general practice of defining human health risk in terms of the toxicity and human exposure potential of a chemical substance.

B. Evaluation of Hazard Scoring Systems for Ranking Chemical Substances Under the Toxicity Criterion

The first step in prioritizing the subset of hazardous substances was the evaluation of existing hazard scoring systems and the selection of systems with the greatest applicability to the specific listing requirements in section 110 of SARA. In reviewing different hazard scoring systems, ATSDR and EPA focused on the evaluation of the toxicity ranking components of the systems; the exposure components of the scoring systems were not reviewed in detail, because they were considered more limited in their applicability to ranking of chemical risk under section 110. In addition, various approaches for characterizing frequency-of-occurrence and potential for human exposure were reviewed outside the context of the ranking schemes. These different approaches are discussed more fully in Units II.D. and II.E. of this notice.

ATSDR and EPA reviewed a number of hazard scoring systems for their degree of applicability to the ranking criterion of toxicity. Three general types of hazard scoring systems were identified:

1. Modeling schemes, which use a system of complex sub-models to combine the toxicological characteristics and environmental mobility and persistence of a substance into a single risk number, which takes into account chemical concentration at an exposure point (dose) and the probability of an effect as a function of dose.
2. Numerical schemes, which assign numerical sub-scores to the inherent toxicological and physical properties of a substance, and then combine the sub-scores into one or more hazard score(s).
3. General classification schemes, which assign chemical substances to hazard categories rather than assigning numerical sub-scores. The defining criteria for any hazard category can be quantitative or qualitative and, most often, can have a separate criteria component for toxicity, which could be used to provide a general grouping of chemical substances on the basis of toxicity.

The ATSDR and EPA review of potentially applicable scoring systems within these three categories was a two-tiered approach. Initially, scoring

systems were screened to eliminate those systems that were not feasible because of large, site-specific data requirements (as required with modeling schemes), or that addressed only one type of toxic effect (usually acute toxicity). Each of these screening elements was considered to be a critical limitation of a particular scheme for its use in the toxicity ranking of substances under section 110 of SARA. In addition, systems which address only one type of toxic effect were eliminated from consideration.

Hazard scoring systems not eliminated by the initial screen were then evaluated in greater detail, based on the degree to which a substance's toxicity was characterized by each system, data quality and availability, the relevance of the scoring scheme for the toxicity ranking of hazardous substances under section 110, and any methodological flaws in the approach used to combine toxicity data. An ideal toxicity criterion ranking scheme should evaluate a wide range of toxic responses, distinguish between mild and severe toxic responses, have a readily available data base containing peer reviewed toxicology information, and use a relevant and plausible approach to combine toxicity data.

C. Selection of Reportable Quantity as the Hazard Scoring System for Ranking Substances Under the Toxicity Criterion

Based upon a comparison of the strengths and limitations of each scoring system reviewed, ATSDR and EPA selected the Reportable Quantity (RQ) scoring scheme for the toxicity ranking of hazardous substances under section 110 of SARA. The RQ scheme is described in several Federal Register documents (50 FR 19456, 51 FR 34535, and 52 FR 8140).

CERCLA section 103(a) requires that the person in charge of a vessel or facility notify the National Response Center immediately when there is a release of a hazardous substance in an amount equal to or greater than the reportable quantity for that substance. Section 102(b) of CERCLA establishes RQs for releases of hazardous substances at 1 pound, unless other reportable quantities were assigned to the substances under the Clean Water Act. CERCLA section 102(s) authorizes EPA to adjust all reportable quantities by regulation, and the Agency has done so for most of the 717 CERCLA hazardous substances.

ATSDR and EPA selected the RQ approach as a hazard scoring system for several reasons. It provides the most complete characterization of toxicity of all hazard scoring systems reviewed by

the two agencies; all other schemes reviewed were more limited in either the consideration of different types of toxic effects, severity of effect, or potency. In addition, unlike most other ranking schemes, toxicity data used in the RQ approach are derived from primary, peer reviewed literature, and such data already are processed in a usable form for all hazardous substances frequently detected at NPL sites. Moreover, the determination of RQ health effect values utilizes weight-of-the-evidence considerations in the evaluation of data.

The RQ scoring system operates by correlating toxicity values to a tiered scale of RQ values (1, 10, 100, 1,000, and 5,000 pounds). For purposes of preparing the first priority list of hazardous substances, ATSDR and EPA used the lowest RQ value (representing the most severe human health hazard) for all candidate substances based upon acute mammalian toxicity, chronic mammalian toxicity, and carcinogenicity. The agencies did not use available RQ values for ignitability, reactivity, and aquatic toxicity of the substances, because these criteria were not considered relevant to the requirements and objectives of SARA section 110. Certain of the RQ health effect values were adjusted based on considerations of environmental persistence. The adjusted RQ value was the final figure for toxicity ranking under SARA section 110.

D. Selection of a Data Source Relating to the Criterion of Frequency-of-Occurrence

The second criterion used by ATSDR and EPA to prepare the first priority list of hazardous substances under section 110 of SARA was the frequency-of-occurrence of hazardous substances at NPL sites. The agencies evaluated various sources of data associated with this criterion. Ideally, frequency-of-occurrence data would include standardized monitoring data from sites on the NPL and would contain site-specific data on the frequency-of-detection and medium-specific location of hazardous substances at sites.

Using these data parameters for guidance, ATSDR and EPA decided to use Contract Laboratory Program (CLP) data for ranking substances under the frequency-of-occurrence criterion. The CLP is an EPA program which supports that Agency's hazardous waste activities by providing a range of state-of-the-art chemical analysis services of known quality. Many of the waste samples analyzed as part of site inspections and remedial investigations are part of the CLP. EPA's central

directive governing the structure and function of the CLP is to provide legally defensible analytical results. Therefore, a high level of quality assurance and documentation has been incorporated into all aspects of CLP activities.

A statistically constructed survey of a subset of the CLP data (CLP survey) was developed in 1984 from the program utilization records of the CLP. The CLP survey represents a random, stratified sample of sites and waste samples from those sites which were analyzed under the CLP from 1980 to 1984. The survey provides data on the percentage of sites at which a substance was detected at least once in any medium (i.e., frequency-of-occurrence) and the average and range of concentrations across media or matrices (e.g., soil, groundwater, drums, etc.). Data from 358 sites and 3,000 waste samples were extracted from hard-copy laboratory analysis records and then computerized to create the data base. In addition, survey data on volatile organics have been updated to include data from 1981 to 1987.

The CLP survey has a number of limitations for purposes of the priority list exercise. Although the survey provides a statistically representative sample of CLP sites, it does not necessarily provide a representative sample of all NPL sites or all hazardous waste sites. In addition, the agencies determined frequency-of-occurrence from data on NPL and non-NPL sites, while section 110 of SARA requires a determination of frequently occurring substances at NPL sites only.

However, the CLP survey information was selected by ATSDR and EPA to determine the frequency-of-occurrence for hazardous substances at NPL sites because it represents the most comprehensive data available for identification of hazardous substances most commonly found at those sites. The survey provides a representative sample of existing data that has been derived under quality-assured and standardized analytical methods. The system is automated and thus provides easily accessed data for application to chemical frequency determinations under SARA.

E. Selection of Data Sources Relating to the Criterion of Potential for Human Exposure

ATSDR and EPA considered a third criterion in preparing the first priority list of hazardous substances under section 110 of SARA: the potential for human exposure to those substances. The agencies evaluated various sources of data associated with this criterion. Ideally, data for the characterization of

exposure potential at hazardous waste sites would contain detailed, site-specific information on hazardous substance contaminants, as well as identification of known or potential human exposure pathways, characterization of potentially exposed populations, and a determination of expected exposure levels and duration at each exposure point.

Using these data parameters for guidance, ATSDR and EPA selected the following sources of data for use in ranking substances under the criterion of human exposure potential.

1. *Surface water data, groundwater data, and indicator chemical substances.* ATSDR and EPA used the CLP survey data to derive a rough estimate of potential for human exposure to hazardous substances at NPL facilities. The agencies considered 3 types of exposure-related data from the CLP survey in prioritizing the list of 100 hazardous substances under SARA: the average concentration of the candidate substances detected in groundwater and surface water across the 385 NPL sites included in the CLP survey; the frequency of detection of those substances in groundwater and surface water across the 385 sites; and whether the substances had been selected for detailed exposure and risk assessment at Superfund Remedial sites (i.e., indicator substances).

The agencies believe that these data are the best readily available measures of potential human exposure. Groundwater and surface water are considered to be measures of mobility from the site and indicators of drinking water exposures. Many of the Superfund remedial actions to date have focused on protection from human health risks associated with contaminated drinking water. In addition, EPA has focused on indicator substances identified under CERCLA as substances for which the potential for human exposure has been determined to exist; ATSDR and EPA therefore recognized that the list of indicator substances should be used for the preparation of the first priority list under section 110 of SARA.

The use of CLP survey data for exposure characterization necessarily excluded considerations of environmental fate and mobility, exposure pathways, and population characteristics. In addition, some estimates of concentration derived from the CLP survey data were made from only a limited number of samples. However, the agencies believe that these limitations are outweighed by the fact that no other available data provide as accurate a measure of the potential

for human exposure to hazardous substances at NPL sites.

2. *Adjusted RQ values.* As noted in Unit II.C. of this notice, RQ values may be adjusted for considerations of environmental persistence. This process involves adjusting the RQ values based on biodegradation, hydrolysis, and photolysis, collectively referred to as BHP. The BHP criteria are secondary to the primary RQ criteria of acute and chronic toxicity and carcinogenicity. The BHP criteria were used by ATSDR and EPA, where appropriate, to change the RQ value one level from the original value calculated with the primary criteria alone. The agencies based their use of these secondary criteria on the fact that substances which have a tendency to degrade to innocuous products pose a less serious health concern than equally toxic substances that have less tendency to degrade.

ATSDR and EPA also used other secondary criteria such as bioaccumulation, high reactivity, and hazardous degradation products to determine if an adjustment of RQ values was appropriate for a given substance. In cases where a degradation product was more toxic than the parent compound, the RQ value was adjusted downward.

The use of adjusted RQ values in the preparation of the first priority list ensured the consideration of a number of relevant exposure factors in this scoring exercise. However, the extent of this adjustment for each candidate substance was either "no change" or a one-level adjustment in the primary RQ value. The RQ adjustment thus served only as a crude indicator of the human exposure potential of those substances.

F. Generation of the Priority List

ATSDR and EPA used the ranking factors described above to represent the three criteria for determining the potential human health risk of the candidate substances. Toxicity was principally represented by RQ health effect values; frequency-of-occurrence was principally represented by CLP site percent data; the potential for human exposure was principally represented by data on groundwater, surface water, and indicator chemical substances. The agencies generated an algorithm to calculate a hazard index value for each candidate substance, for purposes of placing the substances on the first priority list.

The starting point for the hazard index calculation was the subset of hazardous substances which EPA had identified at NPL sites by means of site percent data from the CLP survey. The

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agencies divided the site percent data value for each substance (representing frequency-of-occurrence) by the lowest RQ value for the substance (based on acute toxicity, chronic toxicity, or potential carcinogenicity) to generate a site index for each substance. ATSDR and EPA ranked the candidate substances based on their site indices. The agencies then calculated an exposure index for each substance by ranking them based on the three exposure-related factors (with each factor receiving equal weight). The final step in the algorithm was to combine the site index rank and the exposure index value to obtain a hazard index for each substance. The substances were prioritized based on their hazard indices.

The algorithm for calculating the hazard index is described in greater detail in the support document for this notice, which is contained in the public file notice. Note that the hazard index as described in this notice is not the same as the hazard index described in the Guidelines for Health Risk Assessment of Chemical Mixtures (51 FR 34014, September 24, 1986).

For purposes of assessing hazardous substances in toxicity profiles, ATSDR and EPA combined some of the candidate substances into groups. If substances are stereoisomers of one another, are readily metabolized to other substances on the list, or generally are characterized as mixtures with respect to toxicity and/or frequency-of-occurrence, they were grouped together and occupy only one position on the priority list. Examples of these types of substances include: heptachlor and heptachlor epoxide; endrin and endrin aldehyde; aldrin and dieldrin; DDT, DDE, and DDD; isomers of lindane (BHC) and PCB's.

G. Prioritization Within the First List of 100 Hazardous Substances

The list of 100 prioritized substances has been separated into 4 priority groups of 25 substances each. ATSDR and EPA have listed the substances within each group in order of their Chemical Abstracts Services (CAS) Registry numbers, to reflect the somewhat inexact nature of the ranking algorithm and the uncertainties of the underlying data bases. The first (and highest) priority group of 25 hazardous substances is composed of the substances which will be the subject of the first toxicological profiles developed under section 110 of SARA.

III. List of Substances

The following 100 hazardous substances comprise the first priority list

of substances that will be the subject of toxicological profiles prepared by ATSDR. The substances are listed in 4 groups of 25 substances each. The four groups are listed in descending order of priority, with the first group having the highest priority substances of the first priority list. The substances within each group are listed in CAS number order.

PRIORITY GROUP 1

CAS No.	Substance name
50328	Benzo(a)pyrene
53703	Dibenzo(a,h)anthracene
58553	Benzo(a)anthracene
57125	Cyanide
60571	Dieldrin/aldrin
67663	Chloroform
71432	Benzene
75014	Vinyl chloride
75092	Methylene chloride
76448	Heptachlor/heptachlor epoxide
79016	Trichloroethene
86306	N-nitrosodiphenylamine
106467	1,4-Dichlorobenzene
117817	Bis(2-ethylhexyl)phthalate
127184	Tetrachloroethene
205992	Benzo(b)fluoranthene
218019	Chrysene
1745016	P-Dioxin
7439921	Lead
7440020	Nickel
7440382	Arsenic
7440417	Beryllium
7440439	Cadmium
7440473	Chromium
11196825	PCB-1260,54,48,42,32,21,1016

PRIORITY GROUP 2

CAS No.	Substance name
56235	Carbon tetrachloride
57749	Chlordane
62759	N-nitrosodimethylamine
72559	4,4'-DDE, DDT, DDD
75003	Chloroethane
75274	Bromodichloromethane
75354	1,1-Dichloroethene
78591	Isophorone
78875	1,2-Dichloropropane
79005	1,1,2-Trichloroethane
79435	1,1,2,2-Tetrachloroethane
87865	Pentachlorophenol
91941	3,3'-Dichlorobenzidine
92875	Benzidine
107062	1,2-Dichloroethane
108883	Toluene
108952	Phenol
111444	Bis(2-chloroethyl)ether
121142	2,4-Dinitrotoluene
319846	BHC-alpha, gamma, beta, delta
542881	Bis(chloromethyl)ether
621647	N-nitrosodi-n-propylamine
7439978	Mercury
7440666	Zinc
7782492	Selenium

PRIORITY GROUP 3

CAS No.	Substance name
71556	1,1,1-Trichloroethane
74873	Chloromethane
75218	Oxirane
75252	Bromoform
75343	1,1-Dichloroethane
84742	Di-N-butyl phthalate
88062	2,4,6-Trichlorophenol
91203	Napthalene
98953	Nitrobenzene
100414	Ethylbenzene
107028	Acrolein
107131	Acrylonitrile
108907	Chlorobenzene
118741	Hexachlorobenzene
122667	1,2-Diphenylhydrazine
124481	Chlorodibromomethane
156606	1,2-Trans-dichloroethene
193395	Indeno(1,2,3-cd)pyrene
606202	2,6-Dinitrotoluene
1330207	Total xylenes
7221934	Endrin aldehyde/endrin
7440224	Silver
7440508	Copper
7664417	Ammonia
8001352	Toxaphene

PRIORITY GROUP 4

CAS No.	Substance name
51285	2,4-Dinitrophenol
59507	p-Chloro-m-cresol
62533	Aniline
65850	Benzoic acid
67721	Hexachloroethane
74839	Bromomethane
75150	Carbonylsulfide
75694	Fluorotrichloromethane
75718	Dichlorodifluoromethane
78933	2-Butanone
84862	Diethyl phthalate
85018	Phenanthrene
87683	Hexachlorobutadiene
95487	Phenol,2-methyl
95501	1,2-Dichlorobenzene
105679	2,4-Dimethylphenol
108101	2-Pentanone, 4-Methyl
120821	1,2,4-Trichlorobenzene
120832	2,4-Dichlorophenol
123911	1,4-Dioxane
131113	Dimethyl phthalate
206440	Fluoranthene
534521	4,6-Dinitro-2-methylphenol
541731	1,8-Dichlorobenzene
7440280	Thallium

As stated in the notice describing the toxicological profile development process, published elsewhere in today's issue of the Federal Register, ATSDR and EPA will prepare profiles of the 25 substances in the first priority group later this year. That notice solicits comments on the toxicological profile development process; such comments

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should be submitted in accordance with the instructions given in that notice.

IV. Submission of Key Studies

The very tight timetable mandated by Congress for the preparation of the first 25 toxicological profiles prevents the consideration of studies or other data not already in the possession of EPA and ATSDR. By the time any other studies could be submitted, ATSDR and EPA already will have begun development and peer review of the first profiles. Persons wishing to submit studies or other data on the first 25 toxicological profiles should note that such data will only be considered by ATSDR and EPA for purposes of revising the initial profiles after those profiles are issued. However, ATSDR and EPA are committed to an expeditious review of any submitted studies and to making any necessary revisions of the first 25 profiles in a timely manner.

Nevertheless, this Federal Register notice does solicit unpublished key studies on the first 100 priority list substances, particularly if the submitter believes that the data would substantially affect the determination of levels of significant human exposure or the identification of toxicological data needs. Such studies should be submitted to EPA in accordance with the instructions given in this notice. The voluntary submission of such data would aid in the revision of the first 25 profiles. In addition, for the remaining 75 hazardous substances on the first priority list, the supplementary data would help to ensure that ATSDR will have all key studies in its possession and peer reviewed by the time ATSDR begins to draft future toxicological profiles.

In order to be useful to ATSDR and EPA in the preparation of toxicological profiles, any studies that are submitted voluntarily must provide sufficient detail as to test materials, test methods, and results obtained to permit proper evaluation and peer review. If the study already has been peer reviewed, the submitter is requested to identify the peer reviewers and provide copies of their comments.

V. Administrative Record

Although both ATSDR and EPA are issuing this notice, the agencies are establishing a single administrative record for the notice. EPA has established a public version of this record with non-confidential materials pertaining to this notice (docket control number OPTS-400003). The public file is available for inspection from 8 a.m. to 4 p.m., Monday through Friday, except

legal holidays, in the OTS Reading Room, NE-G004, 401 M St., SW., Washington, DC 20460. At this time there are no confidential materials in the record.

The record includes support documents for the first priority list. Any non-confidential public comments on the listing methodology or other non-confidential data or studies will be available for public inspection.

If a person intends to submit comments, data, or studies which contain confidential business information (CBI), the person must submit the materials in triplicate and mark the submissions as "confidential," "trade secret," or a similar designation. Any material which is marked as CBI will be handled in accordance with the procedures in 40 CFR Part 2. Any material which is not marked as CBI at the time it is submitted to EPA will be placed in the public file for this notice. ATSDR and EPA request that persons who submit CBI in response to this notice also submit a sanitized version of the materials which can be placed in the public file.

For the Agency for Toxic Substances and Disease Registry.

Dated: April 10, 1987.

James O. Mason,
Administrator, Agency for Toxic Substances and Disease Registry.

For the Environmental Protection Agency.

Dated: April 14, 1987.

Lee M. Thomas,
Administrator, Environmental Protection Agency.

[FR Doc. 87-3753 Filed 4-16-87; 8:45 am]

BILLING CODE 5699-29-01

(ATSDR-1; FRL-3174-9(b))

Guidelines for Development of Toxicological Profiles

AGENCIES: Department of Health and Human Services (DHHS) and Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: Under section 110 of the Superfund Amendments and Reauthorization Act (SARA), EPA and the Agency for Toxic Substances and Disease Registry (ATSDR) of DHHS are required to prepare guidelines for the development of toxicological profiles of hazardous substances listed under that Act. This notice describes the procedures and criteria to be used by ATSDR and EPA in developing toxicological profiles, and solicits public comment on these guidelines.

DATE: Written comments on this notice should be submitted by July 18, 1987.

ADDRESS: Written comments and other data submitted in response to this notice should bear the docket control number ATSDR-1, and should be submitted to: Director, Office of External Affairs, Agency for Toxic Substances and Disease Registry, Chamblee 28 South, 1600 Clifton Rd., Atlanta, GA 30333.

All written comments on this notice will be available for public inspection at the Agency for Toxic Substances and Disease Registry, Building 28 South, Room 1103, 4770 Buford Highway, NE, Chamblee, GA, from 8 a.m. to 4:30 p.m., Monday through Friday, except legal holidays.

FOR FURTHER INFORMATION CONTACT: Ms. Georgi Jones, Director, Office of External Affairs, Agency for Toxic Substances and Disease Registry, Chamblee 28 South, 1600 Clifton, Rd., Atlanta, GA 30333, Telephone: (404-454-4620).

SUPPLEMENTARY INFORMATION:

I. Background

On October 17, 1986, the President signed the Superfund Amendments and Reauthorization Act of 1986 (Pub. L. 99-499), which extends and amends the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund, 42 U.S.C. 9601 et seq.).

Section 110 of SARA amends section 104(i) of CERCLA by establishing requirements for the preparation of: (1) Lists of hazardous substances in order of priority, (2) toxicological profiles of those substances, and (3) a research program to fill data gaps associated with the substances. Although the new statutory provisions are being added to CERCLA, this notice will refer to them as the section 110 requirements of SARA, to maintain a clear distinction in this notice between the new provisions and the existing requirements of CERCLA.

Section 110 requires ATSDR and EPA to prepare a priority-order list of the hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List (NPL) and which pose the most significant potential threat to human health. The agencies are required to revise the list on a periodic basis. The first priority list of 100 hazardous substances and a summary of the methodology used to prepare that list is published elsewhere in today's issue of the Federal Register.

After compiling the first priority list, ATSDR must prepare toxicological profiles of the listed substances. SARA

establishes a timetable for revising the priority list and preparing toxicological profiles of hazardous substances on the list; profiles of no fewer than 25 substances on the first priority list must be completed within 1 year of the enactment of SARA (by October 17, 1987). The toxicological profiles will be provided to the States and made available to the public, with a notice of availability and a request for public comment to be published in the Federal Register. The profiles will be revised as necessary in response to the public comments and additional data that subsequently become available to ATSDR.

SARA section 110 requires that the toxicological profiles be prepared in accordance with guidelines developed by ATSDR and EPA. This notice summarizes the guidelines being used for the development of the initial set of 25 profiles. The 2 agencies may modify these guidelines for purposes of preparing subsequent profiles, based on their experience in preparing the first 25 profiles and on public comments received in response to this notice.

II. Statutory Responsibilities of ATSDR and EPA

ATSDR and EPA jointly developed the first priority list of hazardous substances as well as the guidelines for the preparation of the first 25 toxicological profiles. ATSDR has sole responsibility under SARA for the development and publication of all toxicological profiles. However, given the short statutory time period for publishing the first 25 profiles, the 2 agencies have agreed to develop the initial profiles jointly, and will draw on the full range of available chemical data which have been submitted to EPA under that agency's various statutory mandates to support the development of the profiles.

An Interagency Agreement between ATSDR and EPA will provide the funding mechanism to support the contractors who will assist in the preparation of the first 25 profiles. The agencies will use approximately 5 contractors (for which contract mechanisms already are in place) to prepare and provide for peer review of the initial profiles. This joint effort between the 2 agencies is intended to ensure that the toxicological profile requirements of SARA section 110 will be met in a timely and cost-efficient manner. Competitive bids will be solicited for contractor assistance in the preparation of subsequent sets of toxicological profiles.

Both ATSDR and EPA will review and edit the products of the contractors'

efforts, as necessary, to ensure their scientific accuracy and their conformance to the requirements of SARA section 110 and the guidelines discussed in this notice. After the profiles are completed and made available for public comment, the agencies will jointly review the comments which are received and make necessary changes in the profiles with the assistance of the contractors.

III. General Principles for the Development of Toxicological Profiles

ATSDR and EPA have agreed that the following general principles will apply to the preparation of the first 25 toxicological profiles:

1. The principal audiences for the profiles will be health professionals at the Federal, State, and local levels and members of the public involved with Superfund sites; ATSDR and EPA will make a special effort to solicit comments from the States, because the agencies are required by section 110 of SARA to provide profiles to the States.

2. Each profile will have a summary, written in non-technical language, for distribution to interested professionals and the general public.

3. The profiles will be developed in sufficient detail to meet the needs of health officials for current toxicological information on individual hazardous substances.

4. A primary function of the profiles will be to present and interpret the available toxicological and human data on the substances being profiled; these data may be used to evaluate the significance to individuals and the public-at-large of current or potential exposures to the subject hazardous substances. The profiles also will review the adequacy of available data on the substances and will identify toxicological data needs for which research programs should be designed and initiated pursuant to the requirements of section 110 of SARA.

5. The profiles will use existing assessment documents to the fullest extent consistent with the intent of SARA, plus new studies which subsequently become available to ATSDR and EPA. Studies which are key to the profiles will be critically reviewed.

6. As part of the development of the profiles, each profile will be peer reviewed in a manner consistent with the definition of peer review given in section 110 of SARA.

7. Toxicity data that are used to support the principal conclusions of a profile and which have not previously been peer reviewed will be subject to an

independent peer review consistent with section 110 of SARA.

8. Generally, the level of detail in the profiles will be limited to summarizing the principal findings and conclusions of the studies which are found to be critical to evaluating the acute, subacute, and chronic health effects of the subject hazardous substances.

These general principles for the development of toxicological profiles are reflected in the discussion below of the content of the profiles and the procedures for their development.

IV. Content of the Toxicological Profiles

Under section 110 of SARA, the toxicological profiles must contain, at a minimum, the following information:

(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

Congress stated further that the development and implementation of a research program under section 110 of SARA must be coordinated "with the National Toxicology Program and with programs of toxicological testing established under the Toxic Substances Control Act and the Federal Insecticide, Fungicide, and Rodenticide Act. The purpose of such coordination shall be to avoid duplication of effort and to assure that the hazardous substances listed pursuant to [section 110 of SARA] are tested thoroughly at the earliest practicable date."

ATSDR and EPA have developed a detailed format which will serve as the guidelines for the content of the first 25 toxicological profiles. The format is presented in outline form in Appendix A to this notice. The agencies do not believe it is necessary for the initial profiles to include or refer to every major study of the first 25 substances, because such a comprehensive overview would repeat work that already has been done elsewhere and therefore is not necessary for the audience and purpose intended.

ATSDR and EPA have determined that the primary focus of the

toxicological profiles should be on the data most relevant for evaluating levels of significant human exposure and the acute, subacute, and chronic health effects of the subject hazardous substances (i.e., each profile will identify the quantity of a substance which represents a level of potential exposure that would constitute a public health concern based on available data). The agencies will consider multiple levels of exposure for each substance, and will evaluate more than one route of exposure (dermal, oral, and inhalation), and more than one exposure duration (short and long term). The profiles will discuss key studies which relate to the determination of significant levels of human exposure. There has been considerable discussion between ATSDR and EPA on how these determinations should be made, and it is clear that the concepts will evolve as the first toxicological profiles are developed in the coming months.

The toxicological profiles also must focus on important data needs that preclude the determination of significant levels of human exposure or contribute substantially to the uncertainty of such levels. With regard to the identification of these data needs, the agencies will assess the quality of the data which support the determination of significant human exposure levels and, where major gaps in the supporting data exist, identify those data needs in the toxicological profiles.

Since these discussions will be the core of the profiles, ATSDR and EPA expect most of the public comments on the first 25 toxicological profiles to focus on these subject areas. Each profile will include a non-technical summary of the document's principal findings and conclusions.

V. Support Data in the Profiles

The first 25 toxicological profiles will be based primarily on publicly available documents, studies, reports, and other data. The agencies and their contractors then will identify key studies which can appropriately serve as the basis for determining exposure levels which present a significant human health risk.

For many of the first 25 hazardous substances that are the subject of profiles, there have been recent chemical assessments done by EPA or other agencies which will assist ATSDR and EPA in identifying key studies for the purpose of drafting the toxicological profiles. In addition, there are extensive files of relevant studies within EPA and other Federal agencies which will be reviewed and evaluated.

The agencies and their contractors may identify key studies which support

the determination of significant human exposure levels or the identification of data needs, but which have not previously been peer reviewed. In the case of such studies, the contractors will arrange for expert peer review to evaluate the data in the studies and determine the validity of the studies. These expert panels also will evaluate the adequacy of the data for characterizing toxicity and serving as key data in toxicological profiles.

It is possible that there are unpublished studies, currently unknown to ATSDR and EPA, which could be key studies for the development of certain toxicological profiles. The Federal Register notice containing the first priority list of hazardous substances, published elsewhere in today's issue of the Federal Register, discusses the procedures for handling the voluntary submission of such data to support the development of toxicological profiles.

VI. Scientific Peer Review of Toxicological Profiles

In order to ensure that the toxicological profiles developed under section 110 of SARA are of high scientific and technical quality, ATSDR and EPA have taken steps to ensure that the toxicological profiles themselves are properly peer reviewed. The contractors responsible for the preparation of toxicological profiles will assemble a peer review panel for each hazardous substance which is the subject of a toxicological profile.

Each peer review panel will consist of no less than 3 and no more than 7 experts who collectively have knowledge of the substance's physical and chemical properties, toxicokinetics, key health end points in animals and humans, mechanisms of action, human exposure, and quantification of risk to humans. The experts will have distinguished themselves through research, publications, and peer recognition as being highly qualified to serve as peer reviewers of studies and evaluations of the substance in question. ATSDR and EPA will ensure that the chosen experts do not have a conflict of interest in their peer review of toxicological profiles of specific substances.

This contractor-conducted peer review, plus an internal review by scientific experts within ATSDR and EPA, will be conducted before the first 25 toxicological profiles are made available for public comment.

VII. Solicitation of Public Comments and Other Data

A. Comments on the Process in General

ATSDR and EPA solicit comments on their implementation of the entire toxicological profile process under section 110 of SARA, including the preparation of the priority lists of hazardous substances, the guidelines for preparing the profiles, and the content, format, and scope of the profiles. (For details on the methodology for preparing the priority lists of hazardous substances, see the joint notice published elsewhere in today's issue of the Federal Register.

Unfortunately, the agencies will not be able to make use of public comments in preparing the initial priority list of 100 substances and the first 25 toxicological profiles of substances on that list, because the time-constraints of SARA section 110 require ATSDR and EPA to take extraordinary steps to expedite policy development and preparation of the first list and profiles. However, public comments on the process will be used to revise the process, if necessary, prior to the preparation of subsequent lists and profiles. All public comments will be available for review in the public file for this notice.

B. Comments on the First 25 Profiles

The Federal Register notice announcing the availability of the first 25 toxicological profiles (scheduled to be published no later than October 17, 1987) will solicit public comments on those profiles, and is expected to establish a 90-day comment period to ensure that there will be adequate time for the public to review and comment on the initial toxicological profiles.

VIII. Administrative Record

Although both ATSDR and EPA are issuing this notice, the agencies are establishing a single administrative record for the notice. ATSDR has established the public record of materials pertaining to this notice (docket control number ATSDR-1). The record is available for public inspection from 8 a.m. to 4:30 p.m., Monday through Friday, except legal holidays, at the Agency for Toxic Substances and Disease Registry, Building 28 South, Room 1103, 4770 Buford Highway, NE, Chamblee, GA. The record includes support documents for the toxicological profile process.

For the Agency for Toxic Substances and Disease Registry:

Dated: April 10, 1987.

James O. Mason,
Administrator, Agency for Toxic Substances
and Disease Registry.

For the Environmental Protection Agency:
Dated: April 14, 1987.

Lee M. Thomas,
Administrator, Environmental Protection
Agency.

APPENDIX—TOXICOLOGICAL PROFILES OUTLINE

I. Introduction

A. *Purpose.* A description of the purpose/intent for this profile as outlined in SARA.

B. *Objectives.* Contains a brief discussion of the objectives for this profile, including the intended audience, as outlined in SARA.

C. *Responsible parties/agencies.*

II. Health Effects Statement

This section of the profile, if removed from the rest of the document, should still be capable of conveying to the general lay public the substantive public health concerns associated with this substance. This section should be a health effects summary, written in layman's terms, to address issues such as:

A. Whether the substance is naturally occurring, synthetic only, or both.

B. How it is commonly used and where it is commonly encountered.

C. What its toxicity and hazards are (signs and general symptoms; acute, chronic, carcinogenicity, birth defects, etc.).

D. The potential for exposure via water, air, foodstuffs, commercial products, etc.

E. General statement on persistence in the environment.

F. Whether the substance is essential to human health; i.e., an essential nutrient.

G. A discussion of the relative benefit to society versus the risk.

H. A discussion or explanation of certain areas that may affect the layman's interpretation of the risk imposed by that particular substance. For example, vinyl chloride in its pure gaseous or liquid form is an extremely toxic (acute and chronic) and carcinogenic agent. However, it is most commonly encountered in polymeric form in plastics and, as such, is relatively inert and therefore harmless. A brief explanation of such would be appropriate here to avoid any misconception by the general public regarding risk through the use of vinyl chloride-containing plastics.

I. General discussion. This subsection should serve as a fairly complete and

concise statement of the general health risks associated with the subject hazardous substance.

III. Chemical Identity

A. Structure

1. CAS Registry number.
2. Molecular formula.
3. Chemical structure.
4. Chemical name (using current Collective Index).
5. Synonyms.
6. Trade names: To include names and makeup of commercial preparations utilizing this particular substance.

B. Analytical Methods

Should include an up-to-date listing of analytical methods (with detection limits and degree of accuracy) available for analysis in the following:

1. Environmental media.
 - a. Air.
 - b. Water.
 - c. Soil.
 - d. Food/food products.
2. Biomedical samples.
 - a. Fluids/exudates:
 - i. Blood/serum/plasma.
 - ii. Urine.
 - iii. Saliva.
 - iv. Seminal fluid.
 - v. Sebaceous fluid.
 - vi. Cerebrospinal fluid (CSF).
 - b. Tissues:
 - i. Adipose.
 - ii. Muscle.
 - iii. Hair, nails, skin.
 - iv. Other biopsy material as available.

C. General Discussion

IV. Environmental Fate and Human Exposure Potential

A. Environmental Background Levels

1. Water.
2. Air.
3. Soil.
4. Foodstuffs.
5. Other products.

B. Release to Environment

1. Point source.
2. Non-point source.

C. Environmental Fate

1. Transport and partitioning.
 - a. Within media.
 - b. Between media.
2. Transformation and degradation.
 - a. Chemical degradation (or transformation).
 - b. Biodegradation (or biotransformation).
 - c. Bioaccumulation/bioconcentration.

D. Human Exposure

1. Normal background exposure.

2. Media-specific exposure (certain foodstuffs, water in certain areas, etc.).
3. Special risk populations.
4. Occupational exposures.

E. General Discussion

V. Toxicokinetics/Pharmacokinetics

A. Absorption

Various exposure routes; inhalation, oral, dermal.

1. Animal studies.
2. Human.

B. Distribution

Identifies specific storage sites and depots.

1. Animal studies.
2. Human.

C. Metabolism

Identifies biotransformation pathways, metabolic products.

1. Animal studies.
2. Human.

D. Excretion

Identifies routes, time, products.

1. Animal studies.
2. Human.

E. General Discussion

VI. Toxicity

A. In Vitro Toxicity

1. Enzyme systems (e.g., AChE, MAOI).
2. Biochemical alterations (e.g., free radical formation).
3. Cellular system (e.g., monolayer cell culture systems).
4. Toxicity of metabolic products.
5. Proposed mechanism(s) of toxicity.

B. Animal Toxicity

The following subsections should all include a listing and discussion of the various toxic effects produced, the relative potency (dose-effect), the target organs/systems, and the mechanism(s) of action, if known.

1. Acute toxicity.
2. Subacute/subchronic toxicity.
3. Chronic toxicity.
4. Mutagenicity.
5. Reproductive and developmental toxicity.
6. Carcinogenicity.
7. Toxicity of metabolic (biotransformation) products.
8. Mechanism(s) of toxicity.

C. Human Toxicity

1. Case reports.
 - a. Synopsis of findings.
 - b. Synopsis of conclusions.
2. Epidemiological studies.
 - a. Acute toxicity.

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- b. Subacute/subchronic toxicity.
 - c. Chronic toxicity.
 - d. Reproductive and developmental toxicity.
 - e. Carcinogenicity.
 - f. Toxicity of metabolic (biotransformation) products.
 - g. Mechanism(s) of toxicity.
3. Experimental exposure studies.
- a. Acute toxicity.
 - b. Subacute/subchronic toxicity.
 - c. Chronic toxicity.
 - d. Reproductive and developmental toxicity.
 - e. Carcinogenicity.
 - f. Toxicity of metabolic (biotransformation) products.
 - g. Mechanism(s) of toxicity.

D. General Discussion

- 1. Potential for human toxicity.
- 2. Comparison of long-term, low level exposure to short-term, high level exposure.
- 3. What is the relevance of these findings to the potential for human toxicity?

VII. Levels of Significant Human Exposure

Specific guidance for this section will be provided in a follow-up report.

A. Conclusions Regarding Levels of Significant Human Exposure.

- 1. Acute health effects.
- 2. Subacute/subchronic health effects.
- 3. Chronic health effects.

B. General Discussion

VIII. Adequacy of Available Information

Specific guidance for this section to be provided in a follow-up report.

A. Conclusions Regarding Adequacy/Inadequacy of Existing Information

B. Discussions Regarding Information Currently Under Development

C. General Discussion

IX. Physical Chemical Information

A. Physical/Chemical Properties

- 1. Molecular weight.
- 2. Color.
- 3. Physical state.
- 4. Odor/odor threshold.
- 5. Melting/boiling points.
- 6. Autoignition temperature.
- 7. Solubility; water, organic solvents.
- 8. Density; vapor density.
- 9. Specific gravity.
- 10. Partition coefficient(s).
- 11. Vapor pressure.
- 12. Henry's Law constant.
- 13. Refractive index.
- 14. Flashpoint.
- 15. Flammable limits.

B. General Discussion

X. Manufacture, Importation, and Use

A. Production

- 1. Process.
- 2. Volume.
- 3. Sites of production.
- 4. Disposal.

B. Importation

C. Uses

D. General Discussion

XI. Regulatory and Advisory Status

A. Regulatory (Enforceable) Standards

- 1. Definition.
- 2. Purpose and use.
- 3. Regulatory (promulgating) agency.
- 4. Definitive levels/quantity, units, media.

B. Advisory (Non-Enforceable) Guidance

- 1. Definition.

- 2. Purpose and use.
- 3. Advising agency.
- 4. Definitive levels/quantity, units, media.

C. General Discussion

XII. Summary and Recommendations

Provides a summary review and discussion of all the preceding "General discussion" subsections.

A. Synopsis

Of relevant *in vitro*, animal, and human research findings.

- 1. Includes a review of homologous, inter-species toxic mechanisms.
- 2. Includes an assessment of the potential for adverse human health effects based on *in vitro* and/or non-human *in vivo* toxicity evaluations.

B. Assessment

Of potential exposure scenarios.

C. Recommendations

For future research as deemed appropriate and necessary. Notes: Specific guidance for developing this subsection will be provided in a follow-up report.

XIII. Appendices to Toxicological Profiles

A. Data Bases Reviewed

B. Unpublished Documents Cited

C. Peer Review Process

- 1. A description of the peer review procedures followed.
- 2. Identification of peer review members (and their affiliation).
- 3. A listing of those peer review comments not incorporated into the profile, with a brief explanation of the rationale for their exclusion.

D. Reference Section

[FR Doc. 87-8754 Filed 4-16-87; 8:45 am]

BILLING CODE 5000-50-M

CTL017910