ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 799

[OPPTS–42187; FRL–4869–1]

RIN 2070–AC76

Proposed Test Rule for Hazardous Air Pollutants

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: EPA is proposing a test rule under section 4(a) of the Toxic Substances Control Act (TSCA) to require manufacturers and processors of 21 hazardous air pollutants (HAPs) (biphenyl, carbonyl sulfide, chlorine, chlorobenzene, chloroprene, cresols [3 isomers], diethanolamine, ethylbenzene, ethylene dichloride, ethylene glycol, hydrochloric acid, hydrogen fluoride, maleic anhydride, methyl isobutyl ketone, methyl methacrylate, naphthalene, phenol, phthalic anhydride, 1,2,4-trichlorobenzene, 1,1,2-trichloroethane, and vinylidene chloride) to test these substances for certain health effects. EPA is also soliciting proposals for enforceable consent agreements (ECAs) regarding the performance of pharmacokinetics studies which would permit extrapolation from oral data to predict risk from inhalation exposure. EPA is also withdrawing the oncogenicity testing proposed for vinylidene chloride on August 12, 1986 (51 FR 28840).

DATES: Written comments on this proposed HAPs test rule must be received by EPA on or before December 23, 1996. Proposals for pharmacokinetics studies must be received by EPA on or before October 24, 1996. EPA will hold a public meeting in Washington, DC prior to the close of the comment period. If any person requests an additional public meeting by November 25, 1996, EPA will hold a second public meeting in Washington, DC.

ADDRESSES: Submit three copies of written comments on this proposed HAPs test rule, identified by document control number (OPPTS–42187A; FRL–4869–1) and three copies of proposals for pharmacokinetics studies, identified by document control number (OPPTS–42187B; FRL–4869–1) to: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (OPPT), Document Control Office (7407), Rm. G–099, 401 M St., SW., Washington, DC, 20460.

A public version of the rulemaking record supporting this action, excluding confidential business information (CBI), is available for inspection at the TSCA Nonconfidential Information Center, Rm. NE–B607, 401 M St., SW., Washington, DC 20460, from 12 noon to 4 p.m., Monday through Friday, except on legal holidays.

All comments which contain information claimed as CBI must be clearly marked as such. Three additional sanitized copies of any comments containing information claimed as CBI must also be submitted. Nonconfidential versions of comments on this proposed rule will be placed in the rulemaking record and will be available for public inspection at the TSCA Nonconfidential Information Center. Unit IX of this preamble contains additional information on submitting comments containing information claimed as CBI.

Comments and data may also be submitted in electronic form by sending electronic mail (e-mail) to: ncic@epamail.epa.gov. Such comments and data must be submitted in an ASCII file avoiding the use of special characters and any form of encryption. Comments and data will also be accepted on disks in WordPerfect in 5.1 file format or ASCII file format. All comments and data in electronic form must be identified by (OPPTS–42187A) (FRL–4869–1). No information claimed as CBI should be submitted through e-mail. Comments in electronic form may be filed online at many federal depository libraries. Additional information on electronic submissions can be found under Unit X of this preamble.

FOR FURTHER INFORMATION CONTACT: Susan B. Hazen, Director, Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Room E–543B, 401 M St., SW., Washington, DC 20460; telephone: (202) 554–1404; TDD: (202) 554–0551; e-mail: TSCA-Hotline@epamail.epa.gov. For specific information regarding this action or related activities, contact Gary E. Timm, Chemical Control Division, OPPT; telephone: (202) 260–1859; e-mail: timm.gary@epamail.epa.gov.

SUPPLEMENTARY INFORMATION:

Regulated persons. Potentially regulated persons are manufacturers (including importers) and processors of the chemical substances included in this proposed test rule. Processors, small-quantity manufacturers, and manufacturers of small quantities of these substances solely for research and development purposes, while legally subject to the rule, would be required to comply with the rule only if directed to do so in a subsequent notice.

Category	Examples of regulated persons
Manufacturers	Persons who manufacture or import 500 kg (1,100 lbs) or more of a subject chemical per year. Persons who produce a subject chemical as a byproduct.
Processors	Persons who process one or more subject chemicals.
Small-quantity manufacturers	Persons who manufacture or import less than 500 kg(1,100 lbs) per year of a subject chemical.
Manufacturers of small quantities of these substances solely for research and development purposes	Persons who manufacture quantities of these substances no greater than those necessary for purposes of scientific experimentation or analysis for research and development purposes.

This table is not intended to be exhaustive, but, rather, provides a guide for readers regarding entities likely to be regulated by this action. This table lists the types of persons of which EPA is now aware that potentially could be regulated by this action. To determine whether you would be subject to this rule, you should examine Unit IV.F. of the preamble entitled ''Persons Required to Test'' and consult 40 CFR 790.42.

I. Statutory Authority

This notice proposes a test rule under section 4 of the Toxic Substances Control Act (TSCA), 15 U.S.C. 2603 *et seq.*, that would require certain health effects testing for 21 chemical substances listed as hazardous air pollutants (HAPs) in section 112 of the Clean Air Act (CAA), 42 U.S.C. 7412.

Section 2(b)(1) of TSCA, 15 U.S.C. 2601(b)(1), states that it is the policy of the United States that ''adequate data should be developed with respect to the effect of chemical substances and mixtures on health and the environment and that the development of such data should be the responsibility of those who manufacture and those who process such chemical substances and mixtures[.]'' To implement this policy, section 4(a) of TSCA authorizes EPA to require by rule that manufacturers and processors of chemical substances conduct testing if the Administrator finds that:

(1)(A)(i) the manufacture, distribution in commerce, processing, use, or disposal of a chemical substance or mixture, or that any combination of such activities, may present an unreasonable risk of injury to health or the environment, [or]

(1)(B)(i) a chemical substance or mixture is or will be produced in substantial quantities, and (I) it enters or may reasonably be anticipated to enter the environment in substantial quantities or (II) there is or may be significant or substantial human exposure to such substance or mixture, [and]

(1)(A)(ii) and (1)(B)(ii) there are insufficient data and experience upon which the effects of the manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted, and

(1)(A)(iii) and (1)(B)(iii) testing of such substance or mixture with respect to such effects is necessary to develop such data[.]

Thus once the Administrator has made a finding under TSCA section 4(a)(1)(A)(i) that a chemical substance may present an unreasonable risk of injury to health or the environment or a finding under section 4(a)(1)(B)(i) that a chemical substance is or will be produced in substantial quantities and either it may enter the environment in substantial quantities or there may be significant substantial human exposure to the chemical substance, EPA may require any type of health effects or environmental testing necessary to address unanswered questions about the effects of the chemical substance. EPA need not limit the scope of testing required to the factual basis for the section 4(a)(1)(A)(i) or (B)(i) findings as long as EPA finds that data relevant to a determination of whether a substance does or does not present an unreasonable risk of injury to health or the environment are insufficient and that testing is necessary to develop such data. This concept is explained in more detail in EPA's statement of policy for making findings under TSCA section 4(a)(1)(B) (frequently described as the ''B policy'') in the Federal Register of May 14, 1993 (58 FR 28736). Unit V of this preamble also describes the B policy. Moreover, EPA need not limit the scope of the requirement only to testing needed to support regulatory action under TSCA. For further discussion of findings under TSCA section 4, see Unit V of this preamble and the document entitled ''TSCA Section 4 Findings for 21 Hazardous Air Pollutants'' in the record for this rulemaking.

In this proposed rule, EPA intends to use its TSCA section 4 authority to obtain data necessary to implement section 112 of the CAA, which provides a detailed strategy for the assessment and management of HAPs. EPA has used this broad TSCA section 4 authority in the past to support regulatory programs requiring health and environmental effects testing data. See, e.g., final test rule for the Office of Solid Waste chemicals (53 FR 22300, June 15, 1988); final test rule for the Office of Water Chemicals (58 FR 59667, November 10, 1993). Additional users of information collected under this test rule would include other federal agencies (e.g. the Agency for Toxic Substances and Disease Registry (ATSDR), the National Institute for Occupational Safety and Health (NIOSH), the Occupational Safety and Health Administration (OSHA), the Consumer Product Safety Commission (CPSC), other program areas within EPA (such as the hazardous waste program under the Resource Conservation and Recovery Act (RCRA), the Toxics Release Inventory (TRI), the Integrated Risk Information System database (IRIS), and the Office of Pesticide Programs (OPP)), and state and local environmental authorities.

Supporting statutory authority for this proposed rule is provided by section 112(b)(4) of the CAA, 42 U.S.C. 7412(b)(4), which specifically authorizes EPA to use any authority available to EPA to obtain the information needed to make determinations regarding the addition or deletion of substances to the statutory list of HAPs in CAA section 112(b)(1), 42 U.S.C. 7412(b)(1). If the data collected under this proposed test rule show that a chemical substance is not a concern to human health, this information would be helpful in making decisions concerning delisting the substance from the Clean Air Act HAPs list.

This toxicity testing program is also intended to fulfill in part EPA's statutory obligation under section 103(d) of the CAA, 42 U.S.C. 7403(d), to conduct a research program on the health effects of HAPs. This preamble, along with the supporting material in the record, provides information that would be used in the research program under CAA section 103(d) for the HAPs proposed for testing in this rule.

II. Uses for Data

EPA will primarily use the data proposed to be collected under this rule to implement several provisions of section 112 of the CAA, including the determination of residual risk (see below), the estimation of the risks associated with accidental releases of chemicals, and determinations whether or not substances should be removed from the CAA section 112(b)(1) list of hazardous air pollutants (delisting). The acute toxicity test data and developmental toxicity test data will be useful in judging risks from accidental release. The term ''accidential release'' is used broadly in this proposal to include any short-term, relatively high-level chemical exposure lasting from several minutes to several hours. Such a release may result from various causes, including spills, transportation accidents, process-upset conditions, or short bursts during charging of reaction vessels. All data are relevant to delisting decisions and all non-acute data will be used by EPA in meeting its statutory obligation under CAA section 112(f), 42 U.S.C. 7412(f), to assess the risk remaining (i.e. residual risk) after the imposition of technology-based emission standards (maximum achievable control technology or MACT standards) required by CAA section 112(d), 42 U.S.C. 7412(d). Section 112(e) of the CAA, 42 U.S.C. 7412(e), directs EPA to promulgate these standards between 1992 and 2000.

Section 112(f)(1) of the CAA requires EPA to submit, by November 1996, a report to Congress that will describe the methods for assessing the risk remaining after the application of technology-based standards under section 112(d) of the CAA. These methods will be used to assess any residual risk for persons exposed to MACT-regulated emissions. The assessment will include an analysis of both cancer and noncancer endpoints. Data generated by the proposed test rule would be used in the analysis to determine the nature and magnitude of any residual risk.

Within eight years after the promulgation of technology-based standards, EPA may need to set additional standards (''post-MACT standards'') to protect public health with an ample margin of safety. Section 112(f)(2) of the CAA specifies that if MACT standards have not reduced lifetime cancer risk to the individual most exposed to known or suspected carcinogenic emissions from a source to a level of less than 1 in a million (1×10^{-6}), health-based emission standards must be promulgated in order to protect public health with an ample margin of safety. EPA, therefore, would use data obtained under this proposed rule to determine whether health-based post-MACT standards are needed and, if they are needed, to assist in establishing the appropriate level of these standards.

For noncancer health effects, EPA applies an appropriate mathematical model to toxicity data in order to determine the benchmark dose level. The benchmark dose or concentration (BMD/C) is defined as the statistical

lower confidence limit on the dose estimated to produce a predetermined level of change in response (the benchmark response—BMR) relative to controls. If the data are not amenable to modeling, a no-observed-adverse-effect level (NOAEL) or a lowest-observed-adverse-effect level (LOAEL) may be obtained from an evaluation of the toxicity database. ''Uncertainty factors'' are then applied to these levels to account for uncertainties in deriving a dose-response estimate for human exposure (reference concentration (RfC)) from experimental data. An RfC is defined as ''an estimate (with uncertainty perhaps spanning an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer health effects during the lifetime'' (Ref. 1).

Uncertainties due to the extrapolation of effects data between species and for individual susceptibility within a species are accounted for by uncertainty factors. Because RfCs are intended to characterize risk for lifetime exposures, an uncertainty factor may be applied if the effects data are extrapolated from a subchronic study. An additional uncertainty factor is applied if a LOAEL is used to derive the RfC rather than a NOAEL. To provide an accurate characterization of lifetime risk, the database for a chemical should be comprehensive and, in principle, should address all potential endpoints at critical life stages. Therefore, an uncertainty factor also may be applied if data for appropriate endpoints are not available. Thus while each uncertainty factor may range up to 10, the composite factor used to derive an RfC for a chemical with a limited database may be on the order of up to 3,000 for inhalation studies and up to 10,000 for oral studies. Five uncertainty factors are never applied at the same time (i.e. no composite uncertainty factor can be greater than 10,000) because such derivations are considered too inaccurate to be used.

Large composite uncertainty factors result in lower RfCs (higher risk estimates) than do smaller composite uncertainty factors. If the RfC is low, EPA may be required to promulgate more stringent emission standards. Industrial plants subject to these standards would, in turn, be required to meet such standards, perhaps necessitating the installation of more costly emission controls. Better and more complete health effects data, on the other hand, may permit EPA to use smaller composite uncertainty factors, resulting in higher RfCs and, as a consequence, less stringent emission standards. Thus the economic cost of using poor-quality health effects data to make residual risk determinations under CAA section 112(f) could be considerable.

In addition, secondary—though as important—uses of the data to be collected under this proposed rule would be:

(1) Helping to better inform communities and citizens of toxic chemical hazards in their own localities. Understanding health effects associated with these chemicals is integral to furthering the public's involvement in environmental decisionmaking, especially at the state and local level. To be an effective participant in this process, the public needs information on both the inherent toxicity (i.e., hazard) of a chemical and the potential sources of exposure to the chemical. This rule will provide valuable information on health effects related to the affected chemicals, and under TSCA, such health and safety data are available to the public. Taken together with such publicly available information sources such as the Toxics Release Inventory (TRI), which provides site-specific information on chemical releases into the environment, the health effects data generated under this rule will allow all segments of the public to better assess the risks associated with the releases of these chemicals. Taken as part of a comprehensive right-to-know program, these data will provide the basis for individuals, communities, governments, producers, and users to assess the nature and relative severity of toxicity among different chemicals, as well as to assess site-specific, individual chemical risk.

(2) Assisting other agencies (e.g., ATSDR, NIOSH, OSHA, CPSC) in assessing chemical risks and in taking appropriate action within their programs. For example, OSHA has expressed a need for the data that will be acquired under the proposed rule. Fifteen of the 21 HAPS are candidates for OSHA's Permissible Exposure Limit (PEL) update and an additional 3 have no corresponding PEL. OSHA does not have authority to require testing, and must rely on toxicology data collected by other agencies for their risk assessments (Ref. 2). Establishing an ongoing mechanism for updating its PELs continues to be a high priority for OSHA. Five of the HAPs are on ATSDR's list of hazardous substances found at National Priorities List sites and are the subject of toxicological profiles. CPSC noted that 11 of the 21 substances are found in or are emitted by consumer products (Ref. 3).

(3) Assisting EPA in evaluating delisting petitions received under the CAA and the Emergency Planning and Community Right-to-Know Act (EPCRA), 42 U.S.C. 1101 *et seq.*, in making better clean-up decisions under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), 42 U.S.C. 9601 *et seq.*, in assessing inert ingredients in pesticide products, in setting more appropriate standards for hazardous wastes under RCRA, and by providing support for chemical risk assessment activities under TSCA.

(4) Assisting state and local permitting authorities in setting standards within their programs.

(5) Supporting assessments of ''burst'' exposures (high-level releases of short duration), such as in the accidental release prevention program under section 112(r) of the CAA, 42 U.S.C. 7412(r), due to the inclusion of an acute testing protocol.

Many HAPs are of broad programmatic interest, and are included in the Agency's Integrated Risk Assessment System (IRIS) database. Thus, a secondary benefit of this rule is that the health effects data generated by the rule may result in improvement to the data and increased confidence in the RfCs contained in IRIS. Improvements to the IRIS data can result in considerable benefits to the public since IRIS is publicly available and is used by a wide variety of governmental and non-governmental entities to assess the safety of chemicals.

In some cases where EPA has had access to better data, the Agency has been able to revise standards to make them less stringent, thus mandating less economically costly levels of control. For example, EPA has revised the maximum contaminant levels (MCL) of barium (from 1 mg/L to 2 mg/L) and selenium (from 0.01 mg/L to 0.05 mg/L) in drinking water and withdrew the MCL for silver (0.05 mg/L) based on new data (Ref. 4).

Data have also been used to remove chemical substances from lists of regulatory significance. Acrylic acid was removed from a list of ''high-risk'' pollutants developed under section 112(i)(5) of the CAA, 42 U.S.C. 7412(i)(5), for the early reductions program. The high-risk listing for this chemical was based on its predicted environmental exposure being at least 10 times larger than its RfC. Designation of acrylic acid as ''high risk'' had the effect of limiting the use of offsetting reduction of other pollutants in meeting early reduction goals. Recent data,

including those related to reproductive effects, developmental toxicity, and bioavailability, resulted in a decrease in the uncertainty factor for database deficiency by a factor of three and an increase in the RfC by the same amount (i.e. from 0.0003 mg/m^3 to 0.001 mg/m^3). Consequently, acrylic acid no longer met the criteria for the high-risk list.

Serious deficiencies exist in the current toxicity database for the 189 HAPs listed in the CAA, in that no toxicity data exist for many HAPs regarding various endpoints of concern. This problem is expected to be especially serious because post-MACT residual risks will arise primarily from exposures to emissions that contain different combinations of HAPs in varying concentrations. In view of the large number of HAPs of concern and the much larger number of combinations of those HAPs found in the mixtures of emissions subject to residual risk evaluation, the toxicity database should provide consistent characterization of individual HAPs. Therefore, EPA is proposing to obtain an even, across-the-board database for the HAPs listed in this proposed rule.

In its report regarding the risk assessment of HAPs, the National Academy of Sciences (NAS) states that ''[a]vailability of requisite data varies widely among the 189 [HAPs] chemicals'' (Ref. 5). According to this report, ''the toxicity data are incomplete on almost all 189 chemicals'' (Ref. 5). For example, the level of carcinogenic risk for approximately 40% of the 189 HAPs cannot be classified under EPA's current cancer risk classification system (Ref. 6). Moreover, while quantitative estimates exist for 70% of the HAPs that have been classified for cancer risk, about 70% of these estimates are based only on oral data and thus may not reliably characterize the potential risk encountered through inhalation exposure.

In evaluating 124 of the 189 HAPs for noncancer risk, EPA found that the databases for about 62% of the 124 HAPs were not adequate for deriving an RfC (Ref. 7). Even for those HAPs that have an RfC, the level of uncertainty associated with such figures is often high. EPA would use data from the testing proposed in this rule to identify the critical health risks posed by many individual HAPs and to characterize the adverse impact posed by exposure to mixtures of HAPs. EPA anticipates that the test data produced in response to this rule would provide the consistent database that the National Academy says is lacking at this time.

III. Testing Approach and Selection of Chemical Substances for This Proposed Rule

A. Testing Approach Chosen by EPA

With respect to EPA's responsibilities for meeting the requirements under section 112 of the CAA, the central question is: How broad and deep a data set should EPA require on each HAP?

Regarding specific endpoints and routes of exposure, CAA section 112(b)(2), 42 U.S.C. 7412(b)(2), indicates that Congress intended that adverse effects from any endpoint by any route of exposure be taken into account in listing substances as HAPs. According to this subsection, substances added to the Clean Air Act HAPs list shall include:

> * * * pollutants which present, or may present, through inhalation or other routes of exposure, a threat of adverse human health effects (including, but not limited to, substances which are known to be, or may reasonably be anticipated to be, carcinogenic, mutagenic, teratogenic, neurotoxic, which cause reproductive dysfunction, or which are acutely or chronically toxic) * * * .

Thus the CAA indicates that Congress was very concerned about the wide variety of health risks attributable to HAPs and intended that data necessary for characterizing both cancer and noncancer health risks from exposure to HAPs be developed.

Faced with a broad range of options and little specific guidance from Congress, EPA decided that some provision should be made for evaluating the health effects endpoints listed in the CAA, including respiratory tract toxicity, systemic effects, reproductive toxicity, developmental toxicity, genotoxicity, neurotoxicity, and carcinogenicity. EPA's objective was to select endpoints representing serious health effects that could occur as a result of exposure to HAPs. Each endpoint represents a health effect of concern arising from one or more of the following exposures—local concentrations (e.g., hotspots and plumes), area-wide sources, or accidental releases of HAPs.

EPA believes that it is critical to evaluate the respiratory tract thoroughly in addition to examining extra-respiratory effects (i.e., systemic toxicity) because inhalation is an important exposure route of concern. Carcinogenicity testing is significant because cancer is a serious health effect that may be caused by long-term, low-level exposure to toxic substances. Developmental toxicity addresses the potential of chemical substances to interfere adversely with human development (i.e., to cause death, structural abnormalities, growth alterations, and/or functional deficits in the immature organism that may be more sensitive than the adult to many chemical substances). Reproductive testing is designed to assess the effects of an environmental agent on male and female fertility and general reproductive function to humans exposed prenatally as well as postnatally. There is general consensus among toxicologists regarding the assessment of cancer and reproductive and developmental effects, and further explanation can be found in EPA's risk assessment guidelines (Guidelines for Carcinogen Risk Assessment (51 FR 33992, September 24, 1986); Guidelines for Developmental Toxicity Risk Assessment (56 FR 63798, December 5, 1991); Guidelines for Reproductive Toxicity Risk Assessment (Pub. No. EPA/600/AP–94/001, February 1994). Finally, certain aspects of the neurotoxicity and immunotoxicity testing required in this proposed rule warrant more explanation, which is provided below. EPA recently published a proposed revision of the 1986 Guidelines for Carcinogen Risk Assessment (see ''Proposed Guidelines for Carcinogen Risk Assessment'' at 61 FR 17960, April 23, 1996 (FRL–5460–3)).

Neurotoxicity resulting from chemical exposure can affect an organism in many ways, causing, for example, functional and structural deficits as well as behavioral effects. To assess neurotoxicity, EPA is proposing a screening-level battery, consisting of the functional observational battery and motoractivity and neuropathology tests. At this time, EPA is not proposing to require additional, more specialized testing for cognitive functions such as learning, memory, and performance.

The interest in the potential toxic effects of chemicals on the immune system arises from the critical role that the immune system plays in maintaining health. EPA considers the field of immunotoxicity a promising, scientifically sound, and important area in public health protection. From time to time, the Agency has considered information on the effects of chemicals on the immune system in risk assessments. For example, in its draft report reassessing the effects of dioxin compounds on human health (Ref. 8), EPA considered the effects of dioxin on the immune system to serve as an important health endpoint that provides useful information in developing a hypothesis about toxicity. In the draft reassessment report, however, EPA arrived at the preliminary conclusion that ''the impact of dioxin and related compounds on the immune system and

implications for characterizing risks are largely unknown at this time.''

This rule calls for an immunotoxicity screening test which can be performed as a satellite test to either a 90-day subchronic test or a reproductive effects test. This immunotoxicity screen will help identify chemicals as potential immunotoxicants. EPA is not proposing more comprehensive immunotoxicity testing at present because the application of immunotoxicity data in risk assessment has not yet sufficiently matured. As EPA's science policy develops and the Agency's use of immunotoxicity data in risk assessment increases, EPA will reconsider this position. Meanwhile, EPA seeks comments on its proposed approach of using a minimal screen and its preliminary conclusion that it is premature at this time to include more comprehensive immunotoxicity testing in this proposed HAPs test rule.

In developing this proposed rule, EPA considered the following range of options to select the information needed to characterize health effects of concern to implement section 112 of the CAA.

Option 1. One-species 90-day inhalation subchronic plus follow-up for known or suspect toxicities. Under this option, a 90-day inhalation subchronic test would be required, as well as testing for endpoints that have already been identified as existing or potential concerns, including cancer, by previous test results of the HAP at issue or structurally similar agents. A one-species 90-day inhalation test is considered the minimum information for the development of an RfC. The inhalation RfC takes into account toxic effects both for the respiratory tract (portal-of-entry effects) and peripheral to the respiratory system (extra-respiratory effects). Well-defined and well-conducted inhalation subchronic toxicity studies—that provide for histopathologic evaluation of organ toxicities, including the respiratory tract—are considered to be reliable predictors of certain kinds of chronic toxicity. But such studies do not, or do not adequately, account for neurological, developmental and reproductive toxicities. An RfC based solely on a 90-day subchronic test is, thus, usually given a low confidence rating because some potentially important toxic endpoints are not characterized.

In addition, EPA believes that for 90-day inhalation subchronic testing to constitute a minimally credible option, such a test should at least be augmented by testing for adverse health effects that are suggested or indicated, but not adequately characterized, by existing information such as short-term test data, mechanistic information or structure-activity relationships (SAR). Even with this modification, however, Option 1 still provides no test data on those health endpoints of concern for which no current information exists. If such testing were included, these effects might become critical in evaluating dose-response relationships or in demonstrating that a standard uncertainty factor is inadequate or inappropriate.

EPA thus believes that Option 1 is insufficient to meet EPA's mandate under section 112 of the CAA because the endpoints listed in section 112(b)(2) of the CAA, in particular, reproductive, developmental, and neurological toxicities, would be considered for testing only if data already exist that indicate or suggest the potential for these adverse effects. Moreover, this option also does not adequately address health risks associated with acute or accidental releases.

EPA did not select Option 1 for the reasons stated above. EPA believes that the TSCA section 4 program adopted for testing HAPs must go further toward ensuring that no serious health threat exists from both long- and short-term exposure for endpoints of potential concern for which there are no existing data.

Option 2. Option 1 plus inhalation screening for untested toxicity endpoints. The second option considered by EPA would require the incorporation of screening level testing for certain untested toxicities into Option 1. Like Option 1, Option 2 would include testing for endpoints (including cancer) that have already been identified as existing or potential concerns. At a minimum Option 2 would consist of—a 90-day subchronic inhalation study, a screening test for reproductive effects (i.e., a one-generation reproductive effects study), a subchronic inhalation neurotoxicity screening battery (consisting of the functional observation battery and motor activity and neuropathology tests), an *E. coli* reverse mutation assay, gene mutation in somatic cells in culture detection, an *in vivo* cytogenetics test (chromosomal analysis or micronucleus assay), and an immunotoxicity screening test. Any toxicity suggested but not characterized by existing studies in the toxicological literature would still be followed up on through more rigorous protocols.

Although Option 2 would conserve resources while allowing for the testing of a broader range of endpoints, including cancer, it has serious shortcomings. First, a one-generation reproductive test does not adequately address reproductive and developmental risk. Two-generation tests (in which animals have been exposed prenatally as well as postnatally, including the prepubertal period) are generally needed to evaluate the effects on reproduction from most exposures to chemical substances (Ref. 9). Two-generation tests permit the evaluation of delayed or latent manifestations of some toxicities, detection of effects absent in the first generation, and the expression and detection of some effects that may have a heritable basis. Because the standard two-generation reproductive test would not detect internal malformations, however, developmental toxicity testing is also needed for an adequate assessment of developmental risk. The Agency's policy is to require developmental testing in two species to adequately characterize the risk because of species-specific differences.

EPA did not select Option 2 because this level of testing would not provide an adequate evaluation of developmental or reproductive toxicity. Additional follow-up testing would be required to confirm suggestive results obtained in screening studies and provide data adequate for risk assessment under this option. Such testing would require an additional rulemaking cycle, costing further resources and incurring so much delay that data would not be available to meet the deadlines for setting risk-based standards. Moreover, this option does not adequately address health risks, such as respiratory tract effects and neurotoxicity, associated with acute or accidental releases.

Option 3. Option 1 plus less than chronic testing for noncancer endpoints of concern. In addition to the 90-day inhalation subchronic testing specified in Option 1, this option would add inhalation testing to assess reproductive effects (i.e., two-generation reproductive test) and developmental effects (developmental toxicity tests in two mammalian species). Option 3 includes an acute toxicity testing guideline for histopathology of the respiratory tract, kidney, and liver and a bronchoalveolar lavage after four hours of exposure. EPA believes that it is necessary to characterize the acute effects associated with accidental releases of HAPs. In addition, a respiratory sensory irritation assay is included. Acute and subchronic inhalation neurotoxicity screening batteries consisting of the functional observation battery, and motor activity and neuropathology tests would also be conducted. As in Option 2, first-tier tests would be required for mutagenicity

(i.e., an *E. coli* reverse mutation assay, gene mutation in somatic cells in culture detection, an *in vivo* cytogenetics test (chromosomal analysis or micronucleus assay)), as well as immunotoxicity.

Option 3 would follow Options 1 and 2 in requiring a cancer bioassay where concern for cancer is indicated by short-term data, general toxicity data, mechanistic information or structure-activity relationships (SAR). Where no cancer bioassay data exist, testing two species in both sexes would be required. If cancer bioassay data exist but are found to be too uncertain for inhalation dose-response assessment, a modified test, such as testing of the opposite sex in two species, may be required (Ref. 10).

The Option 3 level of testing would enable EPA to better characterize risk associated with both acute and longer-term exposures by providing data to identify and evaluate all the health effects listed under section 112 of the CAA and by providing data for dose-response evaluation within the general time frame for risk-based standards under CAA section 112(f). Accordingly, EPA has selected the Option 3 level as its preferred option for testing under this proposed rule.

Option 4. Option 3 plus chronic testing. Under this option, in the absence of existing adequate data, EPA would require chronic inhalation bioassays (for both cancer and noncancer effects) in two different mammalian species for each chemical substance. The balance of the test program would be the same as under Option 3 (developmental studies in two mammalian species, a two-generation reproductive study, acute and subchronic neurotoxicity screening batteries, first-tier mutagenicity tests, an immunotoxicity screening test, and acute testing). In general, cancer bioassay data in two species, a two-generation reproductive test, and a developmental study in two species are required to establish a high-confidence RfC. Because the RfC is intended to serve as a lifetime estimate, lifetime exposure studies to evaluate potential health endpoints at various critical life stages should be considered.

To a greater degree than under other options, the broad and deep database that would be produced by this comprehensive testing scheme could help defuse complaints that EPA frequently regulates industrial activities without sufficient data regarding either the need for an appropriate level of regulation or what such a level should be. EPA has decided, however, that the disadvantages of choosing this option outweigh its considerable benefits. The extensive chronic testing required under Option 4 would impose a significant cost on industry. In addition, as compared to Option 3, the strain that choosing this option would place on certain resources—such as inhalation testing facilities and supplies of laboratory animals—would significantly diminish the cost-effectiveness of compiling the data. For these reasons, EPA did not select this option. EPA is soliciting comments on the testing approach to the HAPs that it has selected in this proposal.

It should be noted that, regardless of the test option chosen, if adequate toxicity data on a HAP is produced by testing using a route of exposure other than inhalation, route-to-route extrapolation may be possible (see Unit IV.D. of this preamble).

B. National Academy of Sciences Approach

In section 112(o) of the CAA, 42 U.S.C. 7412(o), Congress directed EPA to arrange for the NAS to review EPA's risk assessment methodology relevant to HAPs subject to section 112. EPA has considered the recommendations of the NAS regarding the assessment of risks associated with HAPs. The NAS recommended that EPA ''* * * compile for each of the 189 chemicals an inventory of the existing and relevant chemical, toxicologic, clinical, and epidemiologic literature'' (Ref. 5). It also recommended that EPA ''screen the 189 chemicals for priorities for the assessment of health risks, identify the data gaps, and develop incentives to expedite generation of the needed data by other public agencies (such as the National Toxicology Program, the Agency for Toxic Substances and Disease Registry, and state agencies) and by other organizations (industry, academia, etc.)'' (Ref. 5). As discussed in Unit III.C. of this preamble, EPA agrees and has taken this approach. To identify testing needs and help prioritize HAPs testing, Syracuse Research Corporation, an EPA contractor, has identified and summarized the existing health and exposure literature on the HAPs, and has identified testing programs currently in progress (Refs. 11, 12).

The NAS report also discussed how a gradual, highly iterative testing approach to the generation of health effects data on HAPs might work. The report recommended that HAPs could be prioritized on the basis of their acute toxicity and chemical structure, and testing might proceed stepwise, on a case-by-case basis, from acute toxicity to studies of the uptake, distribution, retention, and excretion of the substance, to subchronic toxicity, and ultimately, if needed, to endpoint testing in animals. Depending on the animal toxicity data produced by this iterative testing scheme, according to the NAS, EPA might decide that further studies of human toxicity or mechanisms of toxicity are warranted.

Although EPA agrees with the need to prioritize testing, it has taken a different approach to prioritization that is based on consideration of exposure potential and the rulemaking schedule of section 112 of the CAA. The amount and type of existing data vary greatly among the chemical substances that Congress designated as HAPs. In practice, therefore, no single uniform iterative approach based on toxicity factors alone would apply to all chemical substances. For example, one HAP might have only acute and short-term test data, while longer-term studies might exist for another HAP. Nevertheless, both the NAS and EPA approaches recognize that existing data must be considered if EPA is to avoid requiring duplicative testing that previously produced adequate data.

An iterative testing approach based on toxicity factors alone would be time consuming and require multiple rulemakings. This process would take too long to collect useful data for making decisions needed to meet upcoming statutory deadlines established in the CAA. Furthermore, multiple iterative rulemakings to develop needed test data would be prohibitively costly to EPA and would not recognize limitations on EPA resources. For Option 3, EPA's preferred testing level, follow-up testing would rarely be required beyond that level proposed in this rule. Such testing, if necessary, would be required in a separate rulemaking.

To make the multichemical decisions required under section 112 of the CAA regarding, for example, residual risk and delisting HAPs, EPA believes that it needs a consistent, even database covering HAPs across the same broad set of endpoints. EPA believes that Option 3 will permit timely gathering of a consistent database on HAPs more efficiently and at less cost to industry and EPA than is possible with other approaches.

C. Review of Data and Selection of HAPs

In choosing candidates for this proposed test rule, EPA considered, consistent with TSCA section 4 requirements, the potential for a chemical substance to present an unreasonable risk of injury to health or the environment, the production

volume of the substance, the amount of emissions produced by the chemical substance entering or reasonably anticipated to enter the environment or become a source of exposure for humans, the sufficiency of the existing database, and the need for further testing to develop needed data. Consequently, as indicated in Unit IV of this preamble, and explained in a separate document in the record entitled ''TSCA Section 4 Findings for 21 Hazardous Air Pollutants'', each candidate listed for testing in this proposed rule is:

(1) Considered to have the potential of presenting an unreasonable risk of injury to health or the environment (except in the case of ethylene glycol, for which no A finding was made—see the table in Unit V of this preamble);

(2) Produced in quantities exceeding 1,000,000 pounds per year;

(3) Emitted (i.e., released into the atmosphere) in the amount of 50 tons (100,000 pounds) per year or more according to the 1993 Toxics Release Inventory (TRI);

(4) Considered to have health effects data needs not addressed in other testing and research programs;

(5) Considered to have health effects data that are insufficient under TSCA section 4 for determining effects of the HAP on health; and

(6) Considered to need further testing to develop the needed data.

The determination that data are insufficient to ascertain the effects of the HAPs on human health is based on several factors. First, EPA determined the effects of concern (toxicological endpoints) and the depth and quality of data which the Agency needs in order to make residual risk determinations. This decision and the range of options EPA considered are discussed in Unit III.A. of this preamble. Having made the decision that standard endpoint tests are appropriate, EPA reviewed existing studies and, for the purposes of this rule, compared such studies against the testing methodology used in the 1985 version of the EPA test guidelines for these endpoints. The 1985 test guidelines were the first test guidelines issued by EPA for its TSCA chemical testing program and represent widely accepted, peer-reviewed methods for characterizing chemical toxicity.

The reasons why existing studies were judged to be inadequate are explained in a separate document in the record entitled ''TSCA Section 4 Findings for 21 Hazardous Air Pollutants'', and summarized in the table in Unit V of this preamble. The reasons are varied but include the following examples—not studying the appropriate endpoint; too few dose levels; inappropriately high- or low-dose levels; and too few animals to have statistical confidence in the results. Nevertheless, in some cases, EPA toxicologists determined that data were adequate when the weight of evidence from several flawed studies, which, when considered individually were determined to be inadequate, gave an adequate characterization of the toxicity of the substance. Thus expert judgment must always play a role in determinations of data adequacy. Indeed, the determination of adequacy is so intimately connected to the unique characteristics of study design for each toxicological endpoint that EPA is unable to articulate a universal test of data adequacy that might be applied consistently in all situations. EPA is soliciting comments on its approach to determining data adequacy for the HAPs.

To select HAPs for testing, EPA initially reviewed the production data and TRI data for all 189 HAPs. EPA realizes that TRI data represent estimates of environmental emissions of the TRI-listed chemicals and do not account for all chemical substances in the United States. Nevertheless, TRI figures offer the most complete, readily available emissions data, and EPA has determined that this database is sufficient for the purpose of helping EPA select high-emission HAPs for consideration as potential test candidates. While publicly available sources of production data are cited in the analysis supporting this rule, data from these sources were checked against the TSCA chemical inventory update production data, most of which are claimed as CBI.

After reviewing TRI data for all HAPs, EPA decided to select a number of HAPs for initial consideration by focusing its attention on HAPs with TRI emissions of 50 tons or more per year. The 66 HAPs in this group constituted a reasonably sized group for further review. The selection of 50 tons per year or more as a cutoff is appropriate because this number captures high-emission HAPs and because section 112 (a)(1) of the CAA, 42 U.S.C. 7412(a)(1), defines ''major source'' as emitting ''* * * 10 tons per year or more of any hazardous air pollutant or 25 tons per year or more of any combination of hazardous air pollutants * * *.''

A survey of testing conducted by EPA under TSCA section 4, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and other testing programs supplemented a preliminary review of health findings from secondary source documents and the IRIS database. This initial survey revealed that certain HAPs having high emissions (50 tons or more) already have a large inhalation toxicology database or are subject to testing or research in existing programs. Therefore, EPA decided not to pursue additional testing under this rule for benzene, butadiene, carbon disulfide, chromium, cyanide, ethylene oxide, formaldehyde, lead, methanol, methyl tertiary butyl ether, methylene chloride, tetrachloroethylene, toluene, trichloroethylene, vinyl chloride, and vinyl acetate. Additional testing under TSCA for these chemicals may be considered at some time in the future.

EPA decided that the remaining group of 50 HAPs could be handled most efficiently by promulgating more than one rule. Consequently, 21 high-emission HAPs were scrutinized further and were selected as candidates for this proposed rule, and the remaining 29 HAPs were deferred for consideration in subsequent HAPs test rulemaking efforts. In the second HAPs test rule, EPA plans to focus on persistent HAPs that may bioaccumulate. EPA may, therefore, require ecological and environmental testing for these HAPs. EPA also may require testing in the second rule to collect data needed to implement the ''Great Waters'' program of section 112(m) of the CAA, 42 U.S.C. 7412(m).

During the selection process for this proposed rule, EPA's contractor undertook a comprehensive search of the toxicological, health, and exposure literature for the 21 HAPs proposed for testing in the current rule (Refs. 11, 12). EPA's contractor performed the literature search in a stepwise manner to save both time and expense. The first step was to review secondary source health effects documents. EPA's contractor identified documents published by EPA, the International Agency for Research on Cancer (IARC), and ATSDR and extracted relevant data. EPA performed online Environmental Mutagen Information Center (EMIC) searches for genetic toxicity information (Ref. 13). In addition, an article entitled ''Genetic Activity Profiles of 110 Hazardous Air Pollutants Listed Under Title III of the Clean Air Act'' (Ref. 14) and the International Commission for Protection against Environmental Mutagens and Carcinogens (ICPEMC) have provided useful summary information.

EPA realizes that using secondary sources of information is not ideal. For example, it is possible that a secondary source document could miss an important study or that the document could fail to properly interpret a study. Consequently, whenever essential

information appeared to be missing from the review documents or was not explained clearly, EPA's contractor consulted original articles.

Through its contractor, EPA next checked several sources for relevant published and unpublished studies. It obtained unpublished but publicly available studies submitted to EPA under TSCA, searched the Toxic Substances Control Act Test Submissions (TSCATS) database by CAS Registry number, and reviewed the National Toxicology Program (NTP) Results Report (generated from NTP's CHEMTRACK database) to locate completed but unpublished NTP studies. With the contractor's assistance, EPA next undertook an update search of the open literature to locate any as yet unidentified studies published either shortly before or after the review documents appeared. For this purpose, EPA's contractor searched the National Library of Medicine (NLM) TOXLINE database for studies published during a period of time beginning three years prior to the date of the review document initially used to obtain toxicity information and ending on the date of the search.

In addition, EPA's contractor consulted with representatives of NIOSH, OSHA, the Food and Drug Administration (FDA), the National Institute of Environmental Health Sciences (NIEHS), and various chemical companies. The purpose of these inquiries was to determine if these organizations had any information on completed or ongoing studies that might not be found in any readily available database. Through its contractor, EPA also contacted the Chemical Industry Institute of Toxicology (CIIT), as well as trade associations and allied organizations to determine whether these organizations were sponsoring or knew of any relevant studies currently in progress. Finally, EPA's contractor closely reviewed data sheets compiled by EPA's IRIS RfD/RfC Working Group to ascertain if the group had identified any additional, otherwise unlocated information.

Varied levels of scrutiny were applied to different types of toxicity testing information throughout the literature search. Because the primary focus of the review of acute, subchronic, and chronic systemic toxicity literature was inhalation exposure, only inhalation studies were reviewed for these endpoints. Although oral studies can provide important information on target organ toxicity and should be considered in the design of any testing protocol, these studies usually provide limited information on the effects of a compound on the respiratory tract. In addition, the systemic dose remote to the respiratory tract for many compounds is affected by modulation of uptake at the portal of entry into the body. This modulation is not only from first-pass effects but from other influences of anatomy and physiology (Ref. 15). Because EPA's literature search did not encompass oral acute and subchronic toxicity studies, the preliminary findings of risk that EPA is making below, under TSCA section 4(a)(1)(A), are not based on such studies. Thus, oral acute and subchronic studies may provide additional evidence of potential toxicity.

The contractor reviewed studies of carcinogenicity, neurotoxicity, and reproductive and developmental toxicity, regardless of the route of administration.

EPA took a different approach to identify HAP candidates for immunotoxicity testing. EPA relied on an EPA document ''Hazardous Air Pollutants: Profiles of Non-Cancer Toxicity from Inhalation Exposures'' (Ref. 16), containing a database that was developed from EPA and ATSDR documents and data files, and from the Hazardous Substances Data Bank (HSDB) of NLM. The contractor searched recent literature (i.e., 1989 to present) for immunotoxicity data on the 21 HAPs in both MEDLINE and TOXLINE. For chemicals with ATSDR Toxicological Profiles, the profile was used to identify immunotoxicity data. Much of the identified immunotoxicity literature used rather insensitive indicators of impact (e.g., organ weight changes, histopathology, leukocyte counts, and total serum protein determinations), that were judged to constitute an inadequate evaluation of suppression of immune system responsiveness (Ref. 17). Thus, an immunotoxicity screening test is being proposed in this rule for many of these HAPs.

Although EPA has made intense and thorough attempts to identify all relevant studies, EPA recognizes the limitations inherent in relying on secondary sources and realizes that its literature search may have failed to locate studies recently undertaken or completed. Therefore, EPA solicits comments bringing to its attention any valid studies not identified in its search efforts.

D. Previous TSCA Testing Actions Affecting These Chemical Substances

Eight of the substances included in this proposed rule have been the subject of previous testing under TSCA section 4. Testing by the inhalation route was not generally required, however, and acute effects—including respiratory tract effects—were not generally a target endpoint. This subunit will briefly summarize previous testing decisions and explain the relationship between those activities and this proposed rule.

1,1'-Biphenyl was recommended by the Interagency Testing Committee (ITC) in its 10th report for environmental effects and chemical fate testing (47 FR 22585, May 25, 1982). Focusing only on environmental testing, EPA found that 1,1'-biphenyl may present an unreasonable risk to the environment and issued a test rule requiring environmental effects and chemical fate testing of the chemical on September 12, 1985 (50 FR 37182). This proposed rule complements the earlier action by requiring health effects testing of 1,1'-biphenyl, namely, acute toxicity, respiratory sensory irritation, subchronic toxicity, developmental toxicity, reproductive toxicity, neurotoxicity and immunotoxicity.

Chlorobenzene was recommended to EPA for health and environmental effects testing in the first report of the ITC (42 FR 55026, October 12, 1977). Subsequently, EPA found that the chemical may present an unreasonable risk to human health (an A finding) and issued a rule requiring reproductive effects testing (51 FR 24657, July 8, 1986). Although the preamble of the proposed rule described specific neurotoxicity concerns, EPA stated that neurotoxicity testing requirements were not being proposed because it had not issued neurotoxicity test guidelines at that time. Instead EPA explained its then-current views on neurotoxicity testing in the preamble and solicited public comment on those views (45 FR 48524, July 18, 1980). Because a neurotoxicity screening battery guideline (OPPTS 870.6200) has since been proposed, this rule proposes the testing of chlorobenzene for neurotoxicity, acute toxicity, respiratory sensory irritation, subchronic toxicity, and immunotoxicity.

Cresols are members of a chemical category consisting of three isomers: *ortho-*, *para-*, and *meta-*cresol. Based on both A and B findings, a test rule proposed on July 11, 1983 (48 FR 31812) would have required testing of cresols for subchronic toxicity, mutagenicity, carcinogenicity, developmental toxicity, reproductive effects, neurotoxicity, and skin sensitization. The final rule, published on April 28, 1986 (51 FR 15771), which specified testing for all three isomers and provided a rationale for this decision, required testing for mutagenicity, developmental toxicity, and reproductive effects. Data received

under this test rule satisfy the HAPs data needs for these endpoints. Based on the results from this first tier of tests, a conditionally required cancer bioassay was not triggered. In addition, oral subchronic toxicity studies and subchronic neurotoxicity studies were conducted by EPA's Office of Solid Waste. In accordance with the need for data on respiratory tract effects, today's rule proposes acute and subchronic inhalation toxicity, respiratory sensory irritation, acute neurotoxicity, and immunotoxicity tests for all three cresol isomers (see Unit IV.B. of this preamble). For the purposes of this proposal, the three cresol isomers are counted as a single chemical.

Methyl isobutyl ketone was the subject of a negotiated testing agreement between EPA and industry for mutagenicity, developmental toxicity, and subchronic testing (47 FR 58025, December 29, 1982, and 48 FR 44905, September 30, 1983). Data received under the negotiated testing agreement satisfy the HAPs data needs for these endpoints. Methyl isobutyl ketone is also being tested for neurotoxicity under a TSCA enforceable consent agreement (ECA) with industry (announced at 60 FR 4514, January 23, 1995 (FRL–4924–8)). This rule proposes testing for reproductive toxicity, acute toxicity, respiratory sensory irritation, and immunotoxicity to complement ongoing testing and existing data.

Phenol is the subject of a test rule proposed on the basis of A and B findings on November 22, 1993 (58 FR 61654). That rule proposed subchronic toxicity, neurotoxicity, and reproductive and developmental toxicity testing and a study of phenol's pharmacokinetics. EPA has received a proposal for an ECA for this chemical substance that would cover the testing proposed in the 1993 rule. The rule proposed herein would add acute inhalation toxicity, respiratory sensory irritation, and immunotoxicity to the testing program for phenol. Under the procedures set forth at 40 CFR 790.22, members of the CMA Phenol Panel and EPA have negotiated an ECA which provides for the testing proposed in November 1993 as well as additional testing, including immunotoxicity. Such testing would meet the HAPs-related data needs for phenol. If the ECA is successfully concluded, EPA will drop the testing requirement for phenol from the final HAPs rule.

1,2,4-Trichlorobenzene has been tested for carcinogenicity under a test rule (51 FR 24657, July 8, 1986) based on an A finding. Data received under this test rule satisfy the HAPs data needs for this endpoint. Although the preamble of the proposed rule described specific neurotoxicity concerns, EPA stated that neurotoxicity testing requirements were not being proposed because it had not issued neurotoxicity test guidelines at that time (45 FR 48545, July 18, 1980). Because a neurotoxity screening battery guideline (OPPTS 870.6200) has since been proposed, this rule proposes the testing of 1,2,4-trichlorobenzene for acute toxicity, respiratory sensory irritation, neurotoxicity, immunotoxicity, and developmental toxicity.

Oncogenicity testing for *vinylidene chloride* was called for in a proposed test rule based on an A finding on August 12, 1986 (51 FR 28840). The rule proposed that distribution, metabolism, and excretion studies and an inhalation oncogenicity study be conducted in mice on behalf of EPA's Office of Air Quality Planning and Standards (OAQPS). EPA has not finalized the vinylidene chloride proposal and is hereby withdrawing it. EPA is not pursuing these studies because the Agency has concluded that, at this time, an oncogenicity bioassay would do little to add to EPA's understanding of the oncogenic potential of the substance. Today's rule proposes testing for acute toxicity, respiratory sensory irritation, and neurotoxicity.

IV. Proposed Testing

A. Testing and Reporting Requirements

EPA is proposing specific testing and reporting requirements for each of the 21 HAPs as specified in table 1 in § 799.5053(a)(5) of this proposed rule. EPA is proposing for the first time in a TSCA section 4 rule to require an immunotoxicity screen and an acute inhalation toxicity test that focuses on respiratory damage and sublethal systemic toxicity. These and other test guidelines are discussed below in Unit IV.C. of this preamble.

EPA is proposing to require a modified inhalation carcinogenicity bioassay using only the male rat and female mouse when existing oral carcinogenicity data and supporting information for a chemical substance are deemed too uncertain to determine its carcinogenicity via inhalation (Ref. 10). The reduced protocol is less expensive than a traditional bioassay. However, test sponsors would also have the alternative of performing pharmacokinetics studies and using route-to-route extrapolation from existing adequate oral toxicity data under enforceable consent agreements (EDAs) in lieu of this and other test requirements if the Agency decides to use this approach (see Units IV.D. and IV.E. of this preamble).

A total of 21 months would be given for the submission of final reports for acute toxicity testing because the acute inhalation toxicity with histopathology guideline proposes to make certain histopathology studies contingent upon the results of the 90-day subchronic studies. The time for the submission of immunotoxicity studies would vary as a function of the test with which they can be combined (e.g., subchronic and reproductive effects).

B. Test Substance

EPA is proposing that a substance of at least 97% purity be used as the test substance. EPA recognizes that exposure to HAPs will occur as exposure to complex mixtures and that ideally one would like data on the mixtures themselves. However, it is not practical to test mixtures due to the huge number of possible combinations. EPA will thus evaluate the toxicity of HAP mixtures using data on the relatively pure components in order to avoid the possible confounding effects of impurities that might be found in technical grade substances. These impurities, if substantial contributors to air pollution, should also be captured as separate entries on the CAA list of HAPs. EPA believes that a purity of 97% is available or readily achievable for all substances covered by this rule.

For cresols, the subject of the test rule is a mixture (CAS No. 1319–77–3) of three isomers: ortho- (CAS No. 95–48–7), para- (CAS No. 106–44–5) and meta- (CAS No. 108–39–4). The mixture and individual isomers are contained in the CAA section 112(b)(1) list of hazardous air pollutants. Most human exposure is to the mixture. However, because the mixture is of variable composition, EPA believes that it would be very burdensome to test every possible variation of the mixture, which would have different proportions of isomers. Therefore EPA is proposing to follow the approach taken in the final test rule for cresols (51 FR 15771, 15776, April 28, 1986) and test each isomer (see Unit III.D. of this preamble).

Another critical factor in study design for HAP testing is the low vapor pressure of several of these substances (diethanolamine, 1,1'-biphenyl, phthalic anhydride). This raises two questions. To which forms of the chemical are humans exposed—vapor, aerosol or particle? How does one design a valid toxicity study that can be used to assess human risk to such exposures? Given the reported TRI releases to the atmosphere for these substances, EPA has assumed that exposures are to

aerosols or particulates from the condensation of high temperature stack gases. EPA is proposing that diethanolamine, 1,1'-biphenyl and phthalic anhydride be tested via aerosol exposure. EPA invites manufacturers and processors to submit information about the forms of these substances that are encountered in ambient exposures and the forms that should be tested, and encourages the development of pharmacokinetics data that would permit testing by the less expensive oral route for HAPs with low vapor pressure.

C. Test Guidelines

The 11 guidelines being proposed for use in testing HAPs under this rule are included in the recently harmonized health effects test guidelines proposed by EPA's Office of Prevention, Pesticides, and Toxic Substances (OPPTS). When final, these harmonized guidelines will incorporate an updated version of the test guidelines previously developed for use under TSCA and FIFRA into a single set. A notice of availability and request for comments on the proposed guidelines was published in the Federal Register of June 20, 1996 (61 FR 31522).

The 11 guidelines proposed for use in testing HAPs are included in the public version of the record for this rulemaking at the address specified in the ''ADDRESSES'' section of this document. The complete set of proposed guidelines is available electronically from the EPA Public Access Gopher (gopher.epa.gov) under the heading: ''Environmental Test Methods and Guidelines''; by internet e-mail: guidelines@epamail.epa.gov; by mail: Public Docket and Freedom of Information Section, Field Operations Division (7506C), Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, DC 20460; or in person or for courier pick-up: Room 1132, CM #2, 1921 Jefferson Davis Highway, Arlington, VA; telephone: (703) 305–5805.

The 11 guidelines proposed to be used for testing HAPs are as follows:

(1) Acute Inhalation Toxicity with Histopathology, OPPTS 870.1350, EPA Pub. No. 712–C–96–291, June 1996;

(2) Subchronic Inhalation Toxicity, OPPTS 870.3465, EPA Pub. No. 712–C–96–204, June 1996;

(3) Inhalation Developmental Toxicity Study, OPPTS 870–3600, EPA Pub. No. 712–C–96–206, June 1996;

(4) Reproduction and Fertility Effects, OPPTS 870.3800, EPA Pub. No. 712–C–96–208, February 1996;

(5) Carcinogenicity, OPPTS 870.4200, EPA Pub. No. 712–C–96–211, June 1996;

(6) *Escherichia coli* WP2 and WP2 uvrA Reverse Mutation Assays, OPPTS 870.5100, EPA Pub. No. 712–C–96–247, June 1996;

(7) Detection of Gene Mutations in Somatic Cells in Culture, OPPTS 870.5300, EPA Pub. No. 712–C–96–221, June 1996;

(8) In Vivo Mammalian Cytogenetics Tests: Bone Marrow Chromosomal Analysis, OPPTS 870.5385, EPA Pub. No. 712–C–96–225, June 1996;

(9) In Vivo Mammalian Cytogenetics Tests: Erythrocyte Micronucleus Assay, OPPTS 870.5395, EPA Pub. No. 712–C–96–226, June 1996;

(10) Neurotoxicity Screening Battery, OPPTS 870.6200, EPA Pub. No. 712–C–96–238, June 1996; and

(11) Immunotoxicity, OPPTS 870.7800, EPA Pub. No. 712–C–96–351, June 1996.

To be considered in this rulemaking, comments on the 11 proposed test guidelines that are specific to HAPs testing must be submitted to the OPPT Document Control Office. The comments must be submitted in the manner specified in the ''DATES'' and ''ADDRESSES'' sections at the beginning of this document. Comments on the 11 proposed guidelines, which are not specific to the HAPs test rule must be submitted to the Office of Pesticide Programs by August 19, 1996, at the address identified in the Federal Register of June 20, 1996 (61 FR 31522).

The process of developing OPPTS harmonized guidelines described above is proceeding at the same time as the development of the HAPs test rule. The OPPTS harmonization process may result in the revision of the guidelines prior to the end of the ocmment period for this proposed rule. If so, EPA will announce the availability of those of the 11 guidelines used in the HAPs rule that have been revised in order to allow for public comment on the applicability of the revised guidelines to the HAPs rule. If any of these 11 guidelines has not been revised by the end of the comment period for this proposed rule, EPA may issue the corresponding HAPs-specific guideline independent of the OPPTS harmonization process.

EPA is proposing to modify the subchronic inhalation toxicity test guideline (OPPTS 870.3465) for the purposes of this rulemaking to include enhanced histopathology of the respiratory tract and an assay for cell damage via lung lavage. EPA is requesting comment on adding these parameters to the subchronic test guideline for testing HAPs.

As part of this rulemaking, EPA proposes to use the acute inhalation toxicity with histopathology test guideline (OPPTS 870.1350). As indicated in Unit III.A. of this preamble, the study of sublethal effects, especially effects on the respiratory system, associated with accidental release and acute exposures is necessary for the HAPs. The standard acute inhalation toxicity test guideline (OPPTS 870.1300) focuses on gross lesions, body weight changes, and effects on mortality. The acute inhalation toxicity with histopathology test guideline assesses two endpoints: (1) histopathology of the respiratory tract, kidney, liver, and other target organs; and (2) cell damage via lung lavage. The guideline takes a stepwise approach to the evaluation of acute toxicity and initially requires a 4-hour exposure at three concentration levels. If the 4-hour study shows positive results in histopathology or the bronchoalveolar lavage, a 1-hour study and an 8-hour study would be required to define better the time and concentration dependence of acute exposures. Histopathology is being proposed for the respiratory tract, liver, and kidney. Other target organs identified by either gross pathology in the 4-hour acute study or by histopathology in the 90-day study would also have to be examined by histopathology in the 4-hour acute study. If these results are positive in the 4-hour study, histopathology in the 1-hour and 8-hour studies would be required. The 4-hour acute testing may be combined with acute neurotoxicity testing.

A respiratory sensory irritation test using American Standard Test Method (ASTM) E 981–84 is also being proposed to provide a quantitative estimate of the sensory irritant potential of an inhaled chemical. Irritation is detected by a characteristic change in the breathing pattern of mice, which results in a reduction in the breathing rate during exposure to a test atmosphere.

For all testing proposed in this rule, test sponsors would have to conduct testing and generate data in accordance with the specified test guideline. Data developed under the final rule must be reported in accordance with TSCA Good Laboratory Practice (GLP) Standards, 40 CFR part 792.

EPA is considering three alternative procedures for handling these test guidelines in the context of the final HAPs test rule. The first alternative is for the final HAPs rule to incorporate the guidelines by reference. Under this alternative, the text of the guideline would not appear in the Code of Federal Regulations. Instead the rule would include a reference to the guideline which would be available on the internet and elsewhere, as noted above.

A copy of the applicable guideline would also be maintained in the public version of the rulemaking record.

The second alternative would be for the final HAPs rule to refer to the guideline, the text of which would be available on the internet and elsewhere, as the pre-approved protocol. However, test sponsors may use other protocols after such protocols have been approved by EPA (''previously approved equivalents''). If EPA decides on this course of action, the Agency may issue a supplemental notice proposing specific implementation procedures if they are significantly different from the following procedures. A test sponsor would be required to submit to EPA for review and approval each test protocol that such sponsor believes is equivalent to the corresponding OPPTS test guideline. A submission would have to demonstrate equivalency, include a description of the differences between the sponsor's protocol and the corresponding OPPTS guideline, and indicate the rationale for changing the guideline. The deadline for these submissions would be 90 days after the effective date of the final HAPs rule. In the case of a study where the design depends upon the results of an earlier test (such as carcinogenicity where the dose level is contingent upon the results of a subchronic study), the deadline is 90 days following the date of submission of the final report for that study.

The third alternative is for the final HAPs rule to reference the guidelines currently in part 798 of title 40 of the Code of Federal Regulations and modify these guidelines to make them as nearly identical as possible to the harmonized OPPTS guidelines. The modifications that the Agency currently believes would be appropriate are set forth in a separate document in the record entitled ''Modifications to Health Effects Test Guidelines Currently in 40 CFR Part 798 for Use in the HAPs Test Rule''. EPA is soliciting comment on these three alternative procedures.

D. Route-to-Route Extrapolation

EPA would consider route-to-route extrapolation of toxicity data from routes other than inhalation when it is scientifically defensible to empirically derive the inhalation risk. Derivation of the inhalation risk is generally only reasonable when portal-of-entry effects (toxic effects on the respiratory tract from inhalation exposure) and/or first-pass effects can be ruled out or adequately characterized.

''First-pass'' effects refer to the metabolism that can take place in portal-of-entry tissue, prior to a chemical's entry into the systemic circulation. For example, after oral administration, many chemicals are delivered to the liver via the portal vein from the gastrointestinal (GI) tract before they enter into the systemic circulation. The respiratory tract can also exhibit a first-pass effect after inhalation due to its various cell types and metabolic enzyme systems. The first-pass action can alter the disposition of the parent and metabolites, thereby modulating the dose to remote or systemic target tissues in a route-dependent fashion. Therefore, unless this first-pass effect and dosimetry are adequately understood and taken into account, substantial error can be introduced in route-to-route extrapolation.

In the absence of data to determine dosimetry via inhalation, quantitative route-to-route extrapolation is subject to substantial error when a chemical is thought to be susceptible to first-pass effects (e.g., metabolized) or when a potential for portal-of-entry effects is indicated (e.g., skin irritation after dermal administration). There are situations where oral data should not be used for route extrapolation to inhalation. For example, chemicals with a short active half-life that were administered by gavage may result in high short-term blood concentrations and consequently much greater effects than the much lower constant blood levels that occur with inhalation exposure. Conversely, if a chemical requires metabolic activation via a rate-limited reaction, bolus dosing via gavage may underestimate the dose. Consideration of factors such as these is important in judging whether the oral study of interest qualifies for route extrapolation.

Regardless of the toxic endpoint considered, EPA's ability to perform quantitative route-to-route extrapolation is critically dependent on the amount and type of data available. The minimum information generally needed includes both the nature of the toxic effect and a description of the relationship between exposure and the toxic effect. The actual impact of exposure by different routes can best be estimated by taking account of factors that influence absorption at the portal of entry, such as:

(1) Physicochemical characteristics of the chemical (e.g., disassociation state, molecular weight, partition coefficient, reactivity, solubility);

(2) Exposure factors (e.g., concentration, duration, regimen); and

(3) Physiologic parameters (e.g., barrier capacity as related to variability in species, blood flow, cell types and morphology, metabolism, pH, specialized absorption sites, storage in cells) and those parameters that influence dose that are remote to the portal of entry including metabolism, clearance, tissue binding, tissue blood flows, tissue:blood partition coefficients, and tissue volumes.

Oral toxicity data are the most commonly available data as alternatives to inhalation data. Oral data are problematic for route-to-route extrapolation in the following instances:

(1) When groups of chemicals are expected to have different toxicities by the two routes, for example, metals, irritants, and sensitizers.

(2) When a first-pass effect by the liver is expected.

(3) When a respiratory tract effect is established but nodosimetry comparison can be clearly established between the two routes.

(4) When the respiratory tract was not adequately studied in the oral studies.

(5) When short-term inhalation studies, dermal irritation, or *in vitro* studies indicate potential portal-of-entry effects at the respiratory tract, but the studies themselves are not adequate for risk assessment.

Dose-response data from other routes of exposure, such as intravenous, intraperitoneal, subcutaneous, dermal, and intramuscular routes also may be available. Intravenous data can provide reliable information on blood levels, but such information should be supplemented by knowledge of the quantitative relationship between exposure concentration and blood levels in order to be useful. The other routes usually are less useful in route-to-route extrapolation because the pharmacokinetics are, in general, poorly characterized.

Methods for route-to-route extrapolation vary in accuracy and, therefore, in inherent uncertainty. The simplest approach is to use default absorption values for each exposure route dependent on the chemical class in question. Such values have only been developed for a few classes of organic chemicals. Because this approach entails increased uncertainty compared with those that use pharmacokinetics (PK) data and physiologically based pharmacokinetics (PBPK) modeling, use of default absorption values is generally considered highly uncertain for quantitative dose-response assessment.

EPA's optimal but most complex and data intensive method for performing route-to-route extrapolation involves the development of a PBPK model that describes the disposition (deposition, absorption, distribution, metabolism, and elimination) of the chemical for the routes of interest (Ref. 15). Such models

account for fundamental physiological and biochemical parameters and processes such as blood flows, ventilatory parameters, metabolic capacities, and renal clearance tailored by the physicochemical (e.g., blood:air and tissue:blood partitions) and biochemical properties (e.g., binding, depletion of cofactors) of the chemical in question. PBPK models should be used in conjunction with toxicity and mechanistic studies in order to relate the effective dose associated with an adverse effect for the test species and conditions to other scenarios. Although the development of a full PBPK model can involve greater effort than other methods using pharmacokinetics data, the application of pharmacokinetics modeling to determine health risk provides a considerable improvement in the reliability of an extrapolation across routes. The use of an existing model structure, essentially a template, can greatly reduce the effort required for model development of analogous chemicals.

More limited pharmacokinetics data such as measurement of bioavailability and disposition of an internal dose marker (e.g., blood cholinesterase activity, enzyme elevation, and amount of chemical bound to protein) may be used for route-to-route extrapolation in conjunction with a consideration of the uncertainties involved in each case. As above, if the portal of entry is affected by the agent, then more elaborate data may be required.

EPA realizes that the use of pharmacokinetics data for route-to-route extrapolation, as well as for the broader purpose of generally identifying the mechanisms by which exposure to a specific agent causes particular health effects, is a fast-developing and often controversial area of science at this time. However, under certain circumstances, as explained above, route-to-route extrapolation based on valid pharmacokinetics data can offer a useful and less expensive alternative to testing or retesting by another route of exposure.

E. Opportunity To Submit Proposals for Enforceable Consent Agreements for Pharmacokinetics Studies

Basic pharmacokinetics parameters provide information on a substance's absorption, distribution, biotransformation, and excretion which can aid in understanding the potential for accumulation of the substance in various tissues or organs and the mechanism of toxicity. Basic PK parameters can be determined through use of the OPPTS harmonized test guideline for pharmacokinetics studies (870.7485). EPA considered but rejected the option of requiring the use of this guideline in this proposed rule because the Agency is interested in a more sophisticated level of study that could potentially support PBPK modeling.

EPA believes that enforceable consent agreements (ECAs) and testing consent orders offer an opportunity to obtain this more in-depth understanding of the pharmacokinetics of HAPs. The Agency, therefore, is inviting manufacturers to submit proposals for pharmokinetics studies for HAPs to be used in the ECA process. Each study proposal should include the name of the chemical(s), a detailed description of the proposed pharmacokinetics study, and discussion of the application of the pharmacokinetics data in performing route-to-route extrapolations. Study proposals should reflect an understanding of the scientific reasoning presented in Unit IV.D. of this preamble, the existing database on the chemical and testing required under this proposed test rule. EPA expects to use a previously published decision tree (Ref. 15) as an element in the evaluation of these proposals. As noted in Unit IV.D., these data may be used for route-to-route extrapolation with a level of uncertainty in inverse proportion to their level of complexity and sophistication.

Each study proposal should be labeled: ''Proposal for Pharmacokinetics Study of (name of chemical),'' identified by document control number (OPPTS–42187B, FRL–4869–1), and sent to: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Document Control Office (7407), Room G–099, 401 M St., SW., Washington, DC 20460. Proposals for pharmacokinetics studies must be received by EPA no later than October 24, 1996. Enforceable consent agreements must be negotiated and signed no later than 12 months after the date of proposal of this rule in order to permit timely development of the final HAPs rule.

EPA will review the submissions and will select promising candidates for negotiation under the procedures in 40 CFR 790.22. If the Agency decides to proceed with the ECA process, it will publish a notice in the Federal Register soliciting persons interested in participating in or monitoring negotiations for the development of ECAs for PK studies to notify the Agency in writing.

EPA noted in Unit IV.D. that the development and use of a PBPK model represents the optimal approach to route-to-route extrapolation. The development of such models is often a complex and uncertain task that in most cases lies beyond the expectations of performance that could be embodied in an ECA. However, EPA would like to encourage extension of the data generated under the ECAs described above to the development of PBPK models. EPA envisions that PBPK models could be developed through voluntary cooperative arrangements and is interested in a dialogue with industry and others on ways to encourage and support PBPK model development.

F. Persons Required To Test

Based on the findings in Unit V of this preamble, EPA is proposing that persons who manufacture (including import) or process, or who intend to manufacture or process 1,1'-biphenyl, carbonyl sulfide, chlorine, chlorobenzene, chloroprene, cresols (all three isomers), diethanolamine, ethylbenzene, ethylene dichloride, ethylene glycol, hydrochloric acid, hydrogen fluoride, maleic anhydride, methyl isobutyl ketone, methyl methacrylate, naphthalene, phenol, phthalic anhydride, 1,2,4-trichlorobenzene, 1,1,2-trichloroethane, and vinylidene chloride, other than as an impurity, at any time from the effective date of the final test rule to the end of the reimbursement period, be subject to the testing requirements in this rule. Manufacturers would be required to submit letters of intent to conduct testing or exemption applications (40 CFR 790.45). However, under 40 CFR 790.42, processors, small-quantity manufacturers, and manufacturers of small quantities of these substances solely for research and development purposes would not be required to submit letters of intent or exemption applications unless directed to do so in a subsequent notice as described in 40 CFR 790.48(b).

EPA is proposing to exempt those manufacturers and processors that produce the chemical substances listed above only as an impurity, as defined in 40 CFR 790.3, because it would be difficult and prohibitively expensive for EPA, manufacturers, and processors to identify with complete assurance all chemical substances that contain the 21 substances solely as an impurity. In addition, EPA would find it difficult to apply both the exemption and reimbursement processes to those who manufacture and/or process these chemical substances solely as an impurity. EPA's reimbursement regulations, issued pursuant to TSCA section 4(c), 15 U.S.C. 2603(c), state that those persons who manufacture or process chemical substances as impurities are not subject to test

requirements unless a particular test rule specifically states otherwise (40 CFR 791.48(b)). EPA finds no basis to propose such a requirement in this rule.

Persons who manufacture these substances as byproducts, as defined in 40 CFR 791.3(c), would be subject to the testing requirements set forth in this proposed rule. The total amount of imports and domestic production of these chemical substances, including the amount produced as a byproduct, would be used in determining reimbursement shares under the TSCA section 4 data reimbursement regulations in 40 CFR part 791. In a previous multichemical test rule (undertaken for EPA's Office of Solid Waste) for which EPA had likewise proposed that byproducts be subject to the rule, an industry commenter objected to this inclusion based on historical grounds. The commenter said, ''The historical roots of section 4 in the Eckart Subcommittee work on TSCA were the sharing of the costs of test generation in direct proportion to the economic benefits which producers derived from the chemicals.'' In response to this comment, EPA explained that,

> EPA does not agree that the intention of Congress to have producers share the cost of testing should be interpreted to exclude producers of byproducts from TSCA section 4 testing requirements. While economic benefit is not derived directly from the production of the subject chemical, the production and disposal of the byproduct are a result of a production process by which the company does derive economic benefit (an indirect benefit). (53 FR 22300, 22305, June 15, 1988)

Carbonyl sulfide would be the first chemical substance subject to a TSCA section 4 test rule that is produced almost exclusively as a byproduct. Although some carbonyl sulfide is reported to be used in chemical synthesis, its large production and release, as reported in the TRI, is due to its creation as a byproduct which is unwanted. Consistent with EPA's position on byproducts testing, as explained above, all persons reporting the release of carbonyl sulfide in the TRI would be considered to be manufacturers of carbonyl sulfide and would be subject to the provisions of this proposed rule.

V. Findings

As explained in Unit I of this preamble, EPA is proposing findings under TSCA sections 4(a)(1)(A) and 4(a)(1)(B) for the 21 HAPs subject to this rule. The findings are summarized in the table below. The detailed discussion of the findings for each chemical substance included in this rule is contained in a separate document entitled ''TSCA Section 4 Findings for 21 Hazardous Air Pollutants'' that is available in the rulemaking record. Requirements for sections 4(a)(1)(A) and 4(a)(1)(B) findings appear in Unit I of this preamble.

In articulating its policy for making findings under TSCA section 4(a)(1)(B) (frequently described as the ''B policy'', see Unit I of this preamble), EPA has defined ''substantial production'' as aggregate annual production of 1 million pounds or more and ''substantial release'' as an annual release, from all sources, into the environment of 1 million pounds or 10% of production, whichever is lower (58 FR 28736, 28746, May 14, 1993). These definitions apply to the terms ''substantial production'' and ''substantial release'' as used in this preamble. (As explained in Unit III.C. of this preamble, all the chemical substances proposed for testing in this proposed rule are emitted into the atmosphere in the amount of 50 tons per year or more according to the TRI.) EPA also defined ''substantial human exposure'' as an annual exposure of 100,000 members of the general population, 10,000 consumers, or 1,000 workers. *Id.*

TSCA Section 4(a) Statutory Findings

Chemical substance	4(a)(1)(A)(i) Finding is based on:	4(a)(1)(B)(i) Finding[a] is based on:	4(a)(1)(A)(ii)/(iii) and 4(a)(1)(B)(ii)/(iii) Finding are for:
1,1'-Biphenyl (CAS No. 92-52-4)	Reproductive toxicity Respiratory toxicity	Substantial production: 53.5 million lbs Substantial human exposure: 20,351 workers Consumer exposure	Acute toxicity[6,9] Subchronic toxicity[5,9] Developmental toxicity[2] Reproductive toxicity[1] Neurotoxicity[7] Immunotoxicity[7] Respiratory sensory irritation[7]
Carbonyl Sulfide (CAS No. 463-58-1)	Oncogenicity Neurotoxicity	Substantial production: production is at least as much as environmental release (produced as a byproduct) Substantial environmental release: 16.7 million lbs	Acute toxicity[6] Subchronic toxicity[7] Developmental toxicity[7] Reproductive toxicity[5,6] Neurotoxicity[6,7] Oncogenicity[7] Immunotoxicity[7] Genetic toxicity[7] Respiratory sensory irritation[7]
Chlorine (CAS No. 7782-50-5)	Respiratory toxicity	Substantial production: 22.3 billion lbs Substantial human exposure: 170,000 workers Consumer exposure Substantial environmental release: 78,498 million lbs	Acute toxicity[5,8]

TSCA Section 4(a) Statutory Findings—Continued

Chemical substance	4(a)(1)(A)(i) Finding is based on:	4(a)(1)(B)(i) Finding[a] is based on:	4(a)(1)(A)(ii)/(iii) and 4(a)(1)(B)(ii)/(iii) Finding are for:
Chlorobenzene (CAS No. 108-90-7)	Respiratory toxicity Developmental toxicity Reproductive toxicity Liver toxicity Kidney toxicity Neurotoxicity	Substantial production: 210 million lbs Substantial human exposure: 17,056 workers General population Substantial environmental release: 2.58 million lbs	Acute toxicity[6] Subchronic toxicity[3,4,6,8] Neurotoxicity[7] Immunotoxicity[6,7]
Chloroprene (CAS No. 126-99-8)	Respiratory toxicity Reproductive toxicity Liver toxicity Neurotoxicity Hematotoxicity Developmental toxicity	Substantial production: 321 million lbs Substantial human exposure: 17,749 workers General population Substantial environmental release: 1.7 million lbs	Acute toxicity[3,6] Reproductive toxicity[7,8] Neurotoxicity[6,8] Immunotoxicity[7] Respiratory sensory irritation[7]
Cresols (CAS No. 1319-77-3) mixture of 3 isomers: ortho-isomer (CAS No. 95–48–7) para-isomer (CAS No. 106–445) meta-isomer (CAS No. 108–39–4)	Respiratory toxicity Developmental toxicity Neurotoxicity	Substantial production: 84.3 million lbs Substantial human exposure: 132,742 workers Consumer exposure General population Substantial environmental release: 1.5 million lbs	Acute toxicity[8] Subchronic toxicity[5,8] Acute neurotoxicity[5,6] Immunotoxicity[6,7] Respiratory sensory irritation[7]
Diethanolamine (CAS No. 111-42-2)	Reproductive toxicity Neurotoxicity	Substantial production: 198 million lbs Substantial human exposure: 573,025 workers Consumer exposure	Acute toxicity[8] Subchronic toxicity[5] Developmental toxicity[6] Reproductive toxicity[7] Neurotoxicity[5,6,7] Immunotoxicity[7] Respiratory sensory irritation[7]
Ethylbenzene (CAS No. 100-41-4)	Developmental toxicity Kidney toxicity Neurotoxicity	Substantial production: 11.4 billion lbs Substantial human exposure: 80,726 workers Consumer exposure General population Substantial environmental release: 8.8 million lbs	Acute toxicity[6] Developmental toxicity[2] Reproductive toxicity[7] Neurotoxicity[6,7] Immunotoxicity[6,7] Respiratory sensory irritation[7]
Ethylene dichloride (CAS No. 107-06-2)	Oncogenicity General systemic toxicity	Substantial production: 14.3 billion lbs General population Substantial human exposure: 77,111 workers Consumer exposure Substantial environmental release: 4 million lbs	Acute toxicity[1,4,5,6] Subchronic toxicity[4,5,8] Developmental toxicity[2] Reproductive toxicity[9] Neurotoxicity[6,7] Respiratory sensory irritation[7]
Ethylene glycol (CAS No. 107-21-1)		Substantial production: 7.2 billion lbs Substantial human exposure: 1,133,792 workers Consumer exposure Substantial environmental release: 17.5 million lbs	Acute toxicity[7] Subchronic toxicity[4,6] Neurotoxicity[7] Immunotoxicity[5] Respiratory sensory irritation[7]
Hydrochloric acid (CAS No. 7647-01-0)	Respiratory toxicity	Substantial production: 5.75 billion lbs Substantial human exposure: 1,131,879 workers Consumer exposure Substantial environmental release: 287.7 million lbs	Acute toxicity[5,6]

TSCA Section 4(a) Statutory Findings—Continued

Chemical substance	4(a)(1)(A)(i) Finding is based on:	4(a)(1)(B)(i) Finding[a] is based on:	4(a)(1)(A)(ii)/(iii) and 4(a)(1)(B)(ii)/(iii) Finding are for:
Hydrogen fluoride (CAS No. 7664-39-3)	Respiratory toxicity Liver toxicity Eye irritation	Substantial production: 322 million lbs Substantial human exposure: 182,589 workers Substantial environmental release: 9.2 million lbs	Acute toxicity[3,5,6,8] Subchronic toxicity[8,10] Developmental toxicity[7] Reproductive toxicity[7] Neurotoxicity[7] Immunotoxicity[7] Respiratory sensory irritation[7]
Maleic anhydride (CAS No. 108-31-6)	Respiratory toxicity Eye irritation	Substantial production: 382 million lbs Substantial human exposure: 37,897 workers	Acute toxicity[7] Developmental toxicity[2] Neurotoxicity[7] Oncogenicity[5,6] Immunotoxicity[7] Respiratory sensory irritation[7]
Methyl isobutyl ketone (CAS No. 108-10-1)	Developmental toxicity Neurotoxicity	Substantial production: 175 million lbs Substantial human exposure: 467,763 workers Consumer exposure General population Substantial environmental release: 27.7 million lbs	Acute toxicity[5,6] Reproductive toxicity[7] Immunotoxicity[7] Respiratory sensory irritation
Methyl methacrylate (CAS No. 80-62-6)	Respiratory toxicity Liver toxicity Kidney toxicity Neurotoxicity	Substantial production: 1,200 million lbs Substantial human exposure: 120,788 workers Consumer exposure Substantial environmental release: 2.8 million lbs	Acute toxicity[1,3,4,6] Developmental toxicity[2] Reproductive toxicity[7] Neurotoxicity[3,4,6,8] Immunotoxicity[6,7] Respiratory sensory irritation[7]
Naphthalene (CAS No. 91-20-3)	Respiratory toxicity Neurotoxicity	Substantial production: 235 million lbs Substantial human exposure: 23,092 workers Consumer exposure General population Substantial environmental release: 2.8 million lbs	Acute toxicity[5,6] Reproductive toxicity[5,6,7] Immunotoxicity[6,7] Respiratory sensory irritation[7]
Phenol[b] (CAS No. 108-95-2)	Respiratory toxicity	Substantial production: 3.9 billion lbs Substantial human exposure: 192,739 workers Consumer exposure General population Substantial environmental release: 10 million lbs	Acute toxicity[4,5,8] Immunotoxicity[4,5,6] Respiratory sensory irritation
Phthalic anhydride (CAS No. 85-44-9)	Respiratory sensitization	Substantial production: 874 million lbs Substantial human exposure: 62,644 workers	Acute toxicity[6,7] Subchronic toxicity[7] Developmental toxicity[5,8] Reproductive toxicity[7] Neurotoxicity[7] Oncogenicity[5] Immunotoxicity[7] Respiratory sensory irritation[7]
1,2,4-Trichlorobenzene (CAS No. 120-82-1)	Oncogenicity Developmental toxicity	Substantial production: CBI Substantial human exposure: 4,032 workers General population	Acute toxicity[1,3,6] Developmental toxicity[1,5,6] Neurotoxicity[6] Immunotoxicity[7] Respiratory sensory irritation[7]

TSCA Section 4(a) Statutory Findings—Continued

Chemical substance	4(a)(1)(A)(i) Finding is based on:	4(a)(1)(B)(i) Finding[a] is based on:	4(a)(1)(A)(ii)/(iii) and 4(a)(1)(B)(ii)/(iii) Finding are for:
1,1,2-Trichloroethane (CAS No. 79-00-5)	Oncogenicity Liver toxicity Kidney toxicity Neurotoxicity	Substantial production: estimated - 210 million lbs Substantial human exposure: 1,036 workers General population	Acute toxicity[7] Subchronic toxicity[7] Developmental toxicity[5,6] Reproductive toxicity[7] Neurotoxicity[6,7] Oncogenicity[5] In vivo cytogenicity[7] Immunotoxicity[6] Respiratory sensory irritation[7]
Vinylidene chloride (CAS No. 75-35-4)	Oncogenicity Respiratory toxicity Developmental toxicity Liver toxicity Kidney toxicity	Substantial production: 230 million lbs Substantial human exposure: 2,675 workers Consumer exposure	Acute toxicity[5,6] Neurotoxicity[7] Respiratory sensory irritation[7]

[1] Too few animals were tested.
[2] Only one species was adequately tested.
[3] Only one sex was tested.
[4] Too few exposure levels were tested.
[5] Inadequate exposure duration, schedule, or route.
[6] Only limited endpoints were assessed.
[7] No study addressing the specific endpoint was found.
[8] Insufficient reporting of data to make the study useful.
[9] No no-observed-adverse-effect level (NOAEL) was identified.
[10] No lowest-observed-adverse-effect level (LOAEL) was identified.

Notes to table:

a ''B'' findings are based on Ref. (10). It should be noted that all HAPs meet the 50 tons of emissions per year selection criteria discussed in Unit III.C. of this preamble.

b Findings made in 58 FR 61654, 61659-60, November 22, 1993.

VI. Economic Analysis of the Proposed Rule

EPA has prepared and placed in the record for this proposed rule an economic analysis that evaluates the potential for significant economic impacts as a result of the testing proposed in this notice. The total cost of this proposed rule is estimated to range up to $41.4 million. The total cost of testing for each chemical substance has been annualized and compared with annual revenues (defined as the product of sales price and total supply) as an indication of potential economic impact. Annualized test costs, calculated over 15 years using a 7% discount rate, represent the equivalent constant costs that would have to be recouped each year of the payback period to finance the testing expenditure in the first year. Annualized test costs are then divided by the total supply of the chemical substance to derive the annualized unit test costs. The percent price impact is calculated by dividing the annualized unit test costs by the sales price and multiplying by 100.

The upper-bound estimated total costs of testing (including both laboratory costs and administrative costs), annualized tests costs, and price impact for the chemicals in this proposed rule are as follows:

Chemical Substances	Total test cost ($)	Annualized test cost ($)	Price impact (%)
1,1'-Biphenyl	2,213,900	243,074	0.64
Carbonyl sulfide	5,509,163	609,876	NA
Chlorine	85,400	9,376	0.0003
Chlorobenzene	972,900	106,819	0.098
Chloroprene	1,603,488	176,054	0.076
Cresols (all 3 isomers)	2,139,600	234,917	0.39
Diethanolamine	2,327,838	255,584	0.23
Ethylbenzene	1,732,050	190,170	0.013
Ethylene dichloride	2,007,325	220,393	0.0071
Ethylene glycol	986,638	108,327	0.0097
Hydrochloric acid	85,400	9,376	0.0040
Hydrogen fluoride	2,135,888	234,509	0.094
Maleic anhydride	4,148,588	454,834	0.25
Methyl isobutyl ketone	1,228,913	134,928	0.16
Methyl methacrylate	1,732,050	190,170	0.023
Naphthalene	1,242,650	136,436	0.16
Phenol	85,400	9,376	0.0010

Chemical Substances	Total test cost ($)	Annualized test cost ($)	Price impact (%)
Phthalic anhydride	5,650,338	620,377	0.21
1,2,4-Trichlorobenzene	963,163	105,750	CBI
1,1,2-Trichloroethane	3,837,900	421,381	0.41
Vinylidene chloride	708,700	77,811	0.12

Note: The table shows the maximum costs and impacts estimated by EPA. The full range of estimates is given in the economic analysis document placed in the record for this proposed rule.

EPA believes, on the basis of these calculations, that the proposed testing of the HAPs presents a low potential for adverse economic impact. Because these chemical substances have relatively large production volumes, with the exception of carbonyl sulfide (to which this methodology does not apply) the annualized costs of testing, expressed as a percentage of annual revenue, are very small—ranging from 0.0003% to 0.64%. Costs of testing are therefore found to be insignificant relative to revenues for these chemical substances.

VII. Availability of Test Facilities and Personnel

Although earlier studies indicated that test facilities and personnel were available to perform the testing specified in this proposed rule (Ref. 18), the impact of this rule combined with other testing requirements may exceed capacity for inhalation testing facilities in the short term. While EPA believes that over the longer term, additional inhalation facilities will become available, any short-term effects can be dealt with by adjusting study due dates in response to comments on this rule or in response to a request for modification of reporting deadlines.

VIII. Public Meeting

EPA will hold a public meeting in Washington, DC prior to the close of the comment period. Announcemment of this meeting will be published in the Federal Register. If requested, EPA will hold an additional public meeting in Washington, DC.

IX. Comments Containing Confidential Business Information

All comments will be placed in the public version of the rulemaking record unless they are clearly labeled as containing information claimed as CBI when they are submitted. CBI claims will be deemed to have been waived if they are not made at the time of submission of the document containing the information claimed as CBI, and such document may be made public with no further notice to the submitter. While a part of the rulemaking record, comments claimed as CBI will be treated in accordance with 40 CFR part 2. A sanitized version of all comments containing information claimed as CBI must be submitted to EPA for inclusion in the public version of the rulemaking record.

It is the responsibility of the submitter to comply with 40 CFR part 2 so that all materials claimed as CBI may be properly protected. This includes, but is not limited to, clearly indicating on the face of the revelant section of the comment (as well as on any revelant associated correspondence) that information claimed as CBI is included and marking ''CONFIDENTIAL,'' ''TSCA CBI,'' or similar designation on the face of each section of any document or attachment in the comment that contains information claimed as CBI. Should putatively private information be put into the public file because of the submitter's failure to clearly claim and designate its confidential claim on the face of the comment, EPA will presume any such information that has been in the public file for more than 30 days to be in the public domain.

X. Rulemaking Record

EPA has established a record for this rulemaking (docket number OPPTS–42187) (including comments and data submitted electronically). This record contains the basic information considered by EPA in developing this proposal and appropriate Federal Register notices. EPA will supplement this record as necessary.

A public version of this record, including printed, paper versions of electronic comments, which does not include any information claimed as CBI is available for inspection from 12 noon to 4 p.m., Monday through Friday, except legal holidays. The public record is located in the TSCA Nonconfidential Information Center, Rm. NE–B607, 401 M St., SW., Washington, DC 20460.

Comments in electronic form may be submitted directly to EPA at:

ncic@epamail.epa.gov

Comments in electronic form must be submitted in an ASCII file avoiding the use of special characters and any form of encryption.

The official record for this rulemaking, as well as the public version, will be kept in paper form. Accordingly, EPA will transfer all comments received electronically into printed, paper form as they are received and will place the paper copies in the official rulemaking record which will also include all comments submitted directly in writing.

The record includes the following information.

A. Supporting Documentation

(1) Federal Register notices/EPA documents pertaining to this proposed rule consisting of:

(a) ''TSCA Interagency Testing Committee; Initial Report to the Administrator, Environmental Protection Agency'' (42 FR 55026, October 12, 1977).

(b) ''Chloromethane and Chlorinated Benzenes Proposed Test Rule; Amendment to Proposed Health Effects Standards'' (45 FR 48524, July 18, 1980).

(c) ''Dichloromethane, Nitrobenzene and 1,1,1-Trichloroethane; Proposed Test Rule'' (46 FR 30300, June 5, 1981).

(d) ''Tenth Report of the Interagency Testing Committee to the Administrator; Receipt of Report and Request for Comments Regarding Priority List of Chemicals'' (47 FR 22585, May 12, 1982).

(e) ''Methyl Isobutyl Ketone and Methyl Ethyl Ketone; Response to the Interagency Testing Committee'' (47 FR 58025, December 29, 1982).

(f) ''Toxic Substances Control Act; Data Reimbursement'' (48 FR 31786, July 11, 1983).

(g) ''Cresols; Proposed Test Rule'' (48 FR 31813, July 11, 1983).

(h) ''Methyl Isobutyl Ketone and Methyl Ethyl Ketone Decision to Adopt Negotiated Testing Program'' (48 FR 44905, September 30, 1983).

(i) ''Toxic Substances; Biphenyl; Test Rule'' (50 FR 37182, September 12, 1985).

(j) ''Cresols; Testing Requirements'' (51 FR 15771, April 28, 1986).

(k) ''Chlorinated Benzenes; Final Test Rule'' (51 FR 24657, July 8, 1986).

(l) ''Toxic Substances, 1,1,-Dichloroethylene; Proposed Test Rule'' (51 FR 28840, August 12, 1986).

(m) ''Guidelines for Carcinogen Risk Assessment'' (51 FR 33992 (September 24, 1986).

(n) ''Office of Solid Waste Chemicals; Final Test Rule'' (53 FR 22300, June 15, 1988).

(o) ''Toxic Substances Control Act (TSCA); Good Laboratory Practice Standards'' (54 FR 34034, August 17, 1989).

(p) ''Metabolism and Pharmacokinetics Test Guideline'' (56 FR 32537, July 17, 1991).

(q) ''Guidelines for Developmental Toxicity Risk Assessment'' (56 FR 63798, December 5, 1991).

(r) ''TSCA section 4(a)(1)(B) Final Statement of Policy; Criteria for Evaluating Substantial Production, Substantial Release, and Substantial or Significant Human Exposure'' (58 FR 28736, May 14, 1993).

(s) ''Office of Water Chemicals; Final Test Rule'' (58 FR 59667, November 10, 1993).

(t) ''Acetophenone, Phenol, N,N-Dimethylaniline, Ethyl Acetate, and 2,6-Dimethylphenol; Proposes Test Rule, Notice of Opportunity to Initiate Negotiations for TSCA Section 4 Testing Consent Agreements'' (58 FR 61654, November 22, 1993).

(u) ''Testing Consent Orders for Acetone, n-Amyl Acetate, n-Butyl Acetate, Ethyl Acetate, Isobutyl Alcohol, Methyl Isobutyl Ketone, and Tetrahyrofuran'' (60 FR 4514, January 23, 1995).

(v) ''Executive Order 12866 of September 30, 1993; Regulatory Planning and Review'' (58 FR 51735, October 4, 1993).

(w) ''Executive Order 12898 of February 11, 1994; Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations'' (59 FR 7629, February 16, 1994).

(x) ''Guidelines for Reproductive Toxicity Risk Assessment'' (Pub. No. EPA/600/AP-94/001, February 1994).

(2) OPPTS test guidelines used in this proposed rule:

(a) Acute Inhalation Toxicity with Histopathology, OPPTS 870.1350, EPA Pub. No. 712–C–96–291, June 1996;

(b) Subchronic Inhalation Toxicity, OPPTS 870.3465, EPA Pub. No. 712–C–96–204, June 1996;

(c) Inhalation Developmental Toxicity Study, OPPTS 870–3600, EPA Pub. No. 712–C–96–206, June 1996;

(d) Reproduction and Fertility Effects, OPPTS 870.3800, EPA Pub. No. 712–C–96–208, February 1996;

(e) Carcinogenicity, OPPTS 870.4200, EPA Pub. No. 712–C–96–211, June 1996;

(f) *Escherichia coli* WP2 and WP2 uvrA Reverse Mutation Assays, OPPTS 870.5100, EPA Pub. No. 712–C–96–247, June 1996;

(g) Detection of Gene Mutations in Somatic Cells in Culture, OPPTS 870.5300, EPA Pub. No. 712–C–96–221, June 1996;

(h) In Vivo Mammalian Cytogenetics Tests: Bone Marrow Chromosomal Analysis, OPPTS 870.5385, EPA Pub. No. 712–C–96–225, June 1996;

(i) In Vivo Mammalian Cytogenetics Tests: Erythrocyte Micronucleus Assay, OPPTS 870.5395, EPA Pub. No. 712–C–96–226, June 1996;

(j) Neurotoxicity Screening Battery, OPPTS 870.6200, EPA Pub. No. 712–C–96–238, June 1996; and

(k) Immunotoxicity, OPPTS 870.7800, EPA Pub. No. 712–C–96–351, June 1996.

(3) Technical Support Documents consisting of:

(a) TSCA Section 4 Findings for 21 Hazardous Air Pollutants.

(b) Exposure Profiles for HAPs—Group 1.

(c) Summary Tables on the Health Effects Data for Hazardous Air Pollutants (HAPs)—Group 1.

(d) Economic Analysis of the Impact of the Test Rule.

(4) Communications consisting of:

(a) Written letters and memoranda.

(b) Contact reports of telephone conversations.

(c) Meeting summaries.

B. References

(1) U.S. Environmental Protection Agency. ''Methods for derivation of inhalation reference concentrations and application of inhalation dosimetry.'' p. xxviii. Prepared by the Office of Health and Environmental Assessment, Washington, DC. EPA/600/8–90/066F (1994).

(2) Letter from John F. Martonik, OSHA, to Susan B. Hazen, EPA, May 31, 1995.

(3) Letter from Val Schaeffer, CPSC, to Joe Carra, EPA, June 2, 1995.

(4) Orme-Zavaleta, J. ''OMB Question-Reply.'' Memorandum to Vicki Dellarco. May 9, 1996.

(5) NAS. National Academy of Sciences, Washington DC, ''Science and Judgment in Risk Assessment'' pp. 154, 157, 265 (1994).

(6) Siegel-Scott, C. ''Slope factors for hazardous air pollutants.'' Memorandum to Vicki Dellarco. September 7, 1994.

(7) Shoaf, C.R. ''Clean Air Act chemicals with adequate databases for development of RfC's.'' Memorandum to Vicki Dellarco. September 20, 1994.

(8) U.S. Environmental Protection Agency. Health assessment document for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds, Vol. III of III, pp. 9–48 to 9–50. Prepared by the Office of Health and Environmental Assessment, Washington, DC. EPA/600/PB–92/001C (1994).

(9) Francis, E.Z., and Kimmel, G.A. ''Proceedings of the workshop on one versus two-generation reproductive effects studies.'' *Journal of the American College of Toxicology.* 7:911–925 (1988).

(10) Lai, D.Y., Baetcke, K.P., Vu, V.T., Cotruvo, J.A., and Eustis, S.L. ''Evaluation of reduced protocols for carcinogenicity testing of chemicals: Report of a joint EPA/NIEHS workshop.'' *Regulatory Toxicology and Pharmacology.* 19:183–201 (1994).

(11) Syracuse Research Corporation. ''Summary tables on the health effects data for hazardous air pollutants (HARs)–Group 1.'' Syracuse, New York. (1995a).

(12) Syracuse Research Corporation. ''Exposure profiles for HAPs–Group 1.'' Syracuse, New York. (1995b).

(13) Valcovic, L.R. Memorandum: ''Genetic toxicity evaluation of HAPs'' to Vicki Dellarco, July 14, 1994.

(14) Waters, M.D., Stack, H.F., and Jackson, M.A. 1990. ''Genetic Activity Profiles of 110 Hazardous Air Pollutants Listed Under Title III of the Clean Air Act, as amended.'' U. S. Environmental Protection Agency. Internal Report. October 30, (1990).

(15) Gerrity, T.R., and Henry, C.J. ed. *Principles of Route-to-Route Extrapolation for Risk Assessment.* pp 1–12. Elsevier Science Publishing Co., Inc. New York, N.Y. (1990).

(16) U.S. Environmental Protection Agency. ''Hazardous Air Pollutants: Profiles of Non-Cancer Toxicity from Inhalation Exposures.'' Washington, DC. EPA/600/R-93/142. September 1993.

(17) Luster, M.I., Portier, C., Pait, D.G., White, K.L., Genings, C., Munson, A.E., and Rosenthal, G.J. ''Risk assessment in immunotoxicology. I. Sensitivity and predictability of immune tests.'' *Fundamental and Applied Toxicology.* 18:200–210 (1992).

(18) U.S. Environmental Protection Agency. ''EPA census of the toxicological testing industry final report.'' (1990).

XI. Regulatory Assessment Requirements

A. Executive Order 12866

Pursuant to Executive Order 12866 (58 FR 51735, October 4, 1993), it has been determined by OMB that this is a ''significant regulatory action.'' OMB was concerned that the amount of inhalation testing required by this rule may exceed the capacity of the testing industry, at least in the short run. This action was submitted to OMB for review, and any comments or changes made during that review have been documented in the public record.

In addition, EPA has prepared an economic analysis of the impact of this

action, which is contained in a document entitled ''Test Rule Support for 21 Hazardous Air Pollutants.'' This document is available as a part of the public record at the address listed in Unit X of this preamble and is briefly summarized in Unit VI of this preamble.

B. Regulatory Flexibility Act

Under the Regulatory Flexibility Act (5 U.S.C. 601 *et seq.*), EPA has determined that this test rule, if promulgated, would not have a significant impact on small businesses. EPA has identified the entities that currently manufacture or import the chemical substances required to be tested under this proposed rule and examined the practices that industry uses in carrying out chemical testing in response to EPA test rules. EPA believes that: (1) small businesses would not be expected to perform testing themselves, or to participate in the organization of the testing effort, because health effects testing of chemical substances is generally carried out by consortia of the large manufacturers or importers of the chemical substances; (2) small businesses would experience only very minor costs, if any, in securing exemption from testing requirements because exemption request requirements, described at 40 CFR 790.82, are minimal—particularly when, as in this proposed rule, EPA is not requiring exemption applicants to submit equivalence data (see Unit IV.F of this preamble)—and EPA does not charge a fee for filing such requests; and (3) small businesses are unlikely to be affected by reimbursement requirements because under the reimbursement rules (at 40 CFR 791.40 through 791.52), manufacturers or importers with a significant share of production or importation are the entities that must share testing costs under the reimbursement rules, and small businesses generally do not manufacture or import a significant portion of high-volume chemical substances.

C. Paperwork Reduction Act

OMB has approved the information collection requirements contained in this proposed rule under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3501 *et seq.*, and has assigned OMB control number 2070–0033.

The public reporting burden for this collection of information is estimated to average approximately the following number of hours per response for the chemicals listed below, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

Chemical substance	Total burden
1,1'-Biphenyl	20,620
Carbonyl sulfide	47,644
Chlorine	693
Chlorobenzene	7,707
Chloroprene	13,039
Cresols (all 3 isomers)	6,048
Diethanolamine	21,826
Ethylbenzene	14,400
Ethylene dichloride	16,707
Ethylene glycol	7,816
Hydrochloric acid	693
Hydrogen fluoride	18,068
Maleic anhydride	35,849
Methyl isobutyl ketone	10,471
Methyl methacrylate	14,400
Naphthalene	10,580
Phenol	693
Phthalic anhydride	51,032
1,2,4-Trichlorobenzene	8,091
1,1,2-Trichloroethane	33,133
Vinylidene chloride	5,439

The total public reporting burden is estimated to be 357,045 hours for all responses. The overall average per chemical is 15,524 hours.

Burden means the total time, effort, or financial resources expended by persons to generate, maintain, retain, or disclose or provide information to or for a Federal agency. This includes the time needed to review instructions; develop, acquire, install, and utilize technology and systems for the purposes of collecting, validating, and verifying information, processing and maintaining information, and disclosing and providing information; adjust the existing ways to comply with any previously applicable instructions and requirements; train personnel to be able to respond to a collection of information; search data sources; complete and review the collection of information; and transmit or otherwise disclose the information.

An Agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. The OMB control numbers for EPA's regulations are listed in 40 CFR part 9 and 48 CFR chapter 15.

Comments are requested on the Agency's need for this information, the accuracy of the provided burden estimates, and any suggested methods for minimizing respondent burden, including through the use of automated collection techniques. Send comments on the ICR to Sandy Farmer, OPPE Regulatory Information Division; U.S. Environmental Protection Agency (2136), 401 M St., SW., Washington, DC 20460, (202) 260–2740, or electronically by sending an e-mail message to: farmer.sandy@epamail.epa.gov. Send a copy of these comments to the Office of Information and Regulatory Affairs, Office of Management and Budget, 725 17th St., NW., Washington, DC 20503, marked ''Attention: Desk Officer for EPA.'' Please remember to include the ICR number in any correspondence. The final rule will respond to any comments on the information collection requirements contained in this proposal.

D. Unfunded Mandates Reform Act and Executive Order 12875

Pursuant to Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Pub. L. 104–4), EPA has determined that this action does not contain a Federal mandate that may result in expenditures of $100 million or more for State, local, and tribal governments, in the aggregate, or the private sector in any one year. (The analysis of the costs associated with this action is referenced in Unit XI.A. of this preamble.) Therefore, this action is not subject to the requirements of sections 202 and 205 of the UMRA.

E. Executive Order 12898

Pursuant to Executive Order 12898 (59 FR 7629, February 16, 1994), entitled ''Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations,'' the Agency has considered environmental justice-related issues with regard to the potential impacts of this action on the environmental and health conditions in low-income and minority communities. Because many sources of HAP emissions are located near populations of lower socioeconomic status and with a higher proportion of minorities, the improved health database that will be generated by this action will help to protect these individuals and communities.

List of Subjects in 40 CFR Part 799

Environmental protection, Chemicals, Hazardous substances, and Reporting and recordkeeping requirements.

Dated: June 20, 1996.

Lynn R. Goldman,

Assistant Administrator for Prevention, Pesticides and Toxic Substances.

Therefore, it is proposed that 40 CFR, chapter I, subchapter R, be amended as follows:

PART 799—[AMENDED]

3. The authority citation for part 799 would continue to read as follows:

Authority: 15 U.S.C. 2603, 2611, 2625.

4. By adding § 799.5053 to Subpart D of part 799 to read as follows:

§ 799.5053 Chemical testing requirements for hazardous air pollutants.

(a) *General testing provisions*—(1) *Identification of test substances.* Table 1 in paragraph (a)(5) of this section identifies those chemical substances that shall be tested in accordance with this section. The purity of each test substance shall be 97 percent or greater unless otherwise specified.

(2) *Persons required to submit study plans, conduct tests, and submit data.* All persons who manufacture (including those who import the substance or manufacture it as a byproduct) or intend to manufacture one or more of the substances listed in table 1 after the effective date listed in table 1 until the end of the reimbursement period shall submit letters of intent to conduct testing, submit study plans, conduct tests and submit data, or submit exemption applications, as specified in this section, subpart A of this part and parts 790 and 792 of this chapter. Persons who manufacture or process these substances only as an impurity are not subject to these requirements. As explained in part 790 of this chapter, processors, small-quantity manufacturers, and manufacturers of small quantities of these substances solely for research and development purposes would become subject to these requirements only after notification in the Federal Register that no manufacturer had notified EPA of its intent to conduct testing.

(3) *Applicability of test guidelines.* The guidelines and other test methods cited in table 1 in paragraph (a)(5) of this section are referenced here as they exist on the effective date listed in table 1 for that specific test. Testing shall be conducted in accordance with the designated Series 870—Health Effects Test Guidelines and other test methods. This incorporation by reference was approved by the Director of the Federal Register in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from the Public Docket and Freedom of Information Section, Field Operations Division (7506C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20360. Copies may be inspected at the above address or at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC.

(4) *Interim reporting requirements.* All testing requirements in this section are subject to the submission of interim progress reports every 6 months beginning 6 months after the effective date for any specific test listed in table 1 in paragraph (a)(5) of this section. The date for the submission of final reports is specified as the number of months after the effective date for the specific test listed in table 1.

(5) *Testing and reporting requirements.* The substances identified by CAS Registry number and chemical name in the following table 1 shall be tested in accordance with the designated OPPTS Harmonized Guideline testing requirements and any additional requirements and limitations specified in the ''Specific requirements under this section'' column of table 1. The numbers and letters in this column refer to the specific requirements set forth in paragraph (b) of this section. Final reports shall be submitted by the deadlines indicated as the number of months after the effective date shown in table 1.

TABLE 1

CAS No.	Chemical substance/required testing	OPPTS harmonized guidelines	Specific requirements under this section	Final report	Effective date
75-35-4	Vinylidene chloride:				
	Acute	870.1350	(b)(2)	21 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
79-00-5	1,1,2-Trichloroethane:				
	Acute	870.1350	(b)(2)	21 mo	
	Subchronic	870.3465	(b)(3)	18 mo	
	Developmental	870.3600		12 mo	
	Reproductive	870.3800	(b)(1)(ii)(A), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Carcinogenicity	870.4200	(b)(1)(i)(D), (b)(1)(ii)(A)	60 mo	
	In vivo cytogenetics	870.5385 or 870.5395	(b)(1)(ii)(A)	14 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	18 mo	
80-62-6	Methyl methacrylate:				
	Acute	870.1350	(b)(2)	21 mo	
	Developmental	870.3600	(b)(1)(i)(A)	12 mo	
	Reproductive	870.3800	(b)(1)(ii)(A), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	21 mo	
85-44-9	Phthalic anhydride:				
	Acute	870.1350	(b)(2)	21 mo	
	Subchronic	870.3465	(b)(1)(ii)(B), (b)(3)	18 mo	
	Developmental	870.3600	(b)(1)(ii)(B)	12 mo	
	Reproductive	870.3800	(b)(1)(ii)(B), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(B), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Carcinogenicity	870.4200	(b)(1)(ii)(B)	60 mo	

TABLE 1—Continued

CAS No.	Chemical substance/required testing	OPPTS harmonized guidelines	Specific requirements under this section	Final report	Effective date
	Immunotoxicity	870.7800	(b)(1)(ii)(B)	18 mo	
91-20-3	Naphthalene:				
	Acute	870.1350	(b)(2)	21 mo	
	Reproductive	870.3800	(b)(1)(ii)(A), (b)(5)	29 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	21 mo	
92-52-4	1,1'-Biphenyl:				
	Acute	870.1350	(b)(2)	21 mo	
	Subchronic	870.3465	(b)(1)(ii)(B), (b)(3)	18 mo	
	Developmental	870.3600	(b)(1)(i)(A), (b)(1)(ii)(B)	12 mo	
	Reproductive	870.3800	(b)(1)(ii)(B), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(B), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(B)	18 mo	
95-48-7, 106-44-5, and 108-39-4	Cresols:				
	Acute	870.1350	(b)(2)	21 mo	
	Subchronic	870.3465	(b)(3)	18 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	18 mo	
100-41-4	Ethylbenzene:				
	Acute	870.1350	(b)(2)	21 mo	
	Developmental	870.3600	(b)(1)(i)(A)	12 mo	
	Reproductive	870.3800	(b)(1)(ii)(A), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	21 mo	
107-06-2	Ethylene dichloride:				
	Acute	870.1350	(b)(2)	21 mo	
	Subchronic	870.3465	(b)(3)	18 mo	
	Developmental	870.3600	(b)(1)(i)(C)	12 mo	
	Reproductive	870.3800	(b)(1)(ii)(A), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
107-21-1	Ethylene glycol:				
	Acute	870.1350	(b)(2)	21 mo	
	Subchronic	870.3465	(b)(3)	18 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	18 mo	
108-10-1	Methyl isobutyl ketone:				
	Acute	870.1350	(b)(2)	21 mo	
	Reproductive	870.3800	(b)(1)(ii)(A), (b)(5)	29 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	29 mo	
108-31-6	Maleic anhydride:				
	Acute	870.1350	(b)(2)	21 mo	
	Developmental	870.3600	(b)(1)(i)(A)	12 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Carcinogenicity	870.4200	(b)(1)(ii)(A)	60 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	21 mo	
108-90-7	Chlorobenzene:				
	Acute	870.1350		21 mo	
	Subchronic	870.3465	(b)(3)	18 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	18 mo	

TABLE 1—Continued

CAS No.	Chemical substance/required testing	OPPTS harmonized guidelines	Specific requirements under this section	Final report	Effective date
108-95-2	Phenol:				
	Acute	870.1350	(b)(2)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	12 mo	
111-42-2	Diethanolamine:				
	Acute	870.1350	(b)(2)	21 mo	
	Subchronic	870.3465	(b)(1)(ii)(B), (b)(3)	18 mo	
	Developmental	870.3600	(b)(1)(ii)(B)	12 mo	
	Reproductive	870.3800	(b)(1)(ii)(B), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(B), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(B)	18 mo	
120-82-1	1,2,4-Trichlorobenzene:				
	Acute	870.1350	(b)(2)	21 mo	
	Developmental	870.3600		12 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	21 mo	
126-99-8	Chloroprene:				
	Acute	870.1350	(b)(2)	21 mo	
	Reproductive	870.3800	(b)(1)(ii)(A), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	21 mo	
463-58-1	Carbonyl sulfide:				
	Acute	870.1350	(b)(2)	21 mo	
	Subchronic	870.3465	(b)(3)	18 mo	
	Developmental	870.3600		12 mo	
	Reproductive	870.3800	(b)(1)(ii)(A), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Carcinogenicity	870.4200	(b)(1)(ii)(A)	60 mo	
	E.coli reverse mutation	870.5100		6 mo	
	Gene mutation	870.5300		6 mo	
	In vivo cytogenetics	870.5385 or 870.5395	(b)(1)(ii)(A)	14 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	18 mo	
7647-01-0	Hydrochloric acid:				
	Acute	870.1350	(b)(2)	21 mo	
7664-39-3	Hydrogen fluoride:				
	Acute	870.1350	(b)(2)	21 mo	
	Subchronic	870.3465	(b)(3)	18 mo	
	Developmental	870.3600		12 mo	
	Reproductive	870.3800	(b)(1)(ii)(A), (b)(5)	29 mo	
	Neurotoxicity	870.6200	(b)(1)(ii)(A), (b)(1)(iii)(A), (b)(1)(iii)(B)	21 mo	
	Immunotoxicity	870.7800	(b)(1)(ii)(A)	18 mo	
7782-50-5	Chlorine:				
	Acute	870.1350	(b)(2)	21 mo	

(b) *Test-specific requirements*—(1) *General.* In addition to the testing requirements specified in table 1 in paragraph (a)(5) of this section and applicable test guideline-specific modifications listed therein, the following additional requirements and limitations also apply when specified for a particular chemical substance in table 1 under ''Specific requirements under this section''.

(i) *Test species.* The test animal shall be:

(A) A mammalian species other than the rat.

(B) A mammalian species other than the mouse.

(C) A mammalian species other than the rabbit.

(D) The male rat and the female mouse.

(ii) *Route of exposure.* Animals shall be exposed:

(A) Via vapor-phase inhalation.

(B) Via inhalation of aerosol.

(C) Orally in the diet.

(iii) *Duration and frequency of exposure.* (A) Animals shall be exposed for a 4-hour period in an acute study.

(B) Animals shall be exposed for 6 hours per day, 5 days per week for a 90-day period in a subchronic study.

(2) *Acute test modifications.* In addition to the acute testing requirements specified in table 1 in paragraph (a)(5) of this section, the following additional requirements and limitations also apply when specified for a particular chemical substance in table 1 under ''Specific requirements under this section''.

(i) The appraisal of pulmonary irritation shall be evaluated during exposure to the substance by the use of the mouse respiratory sensory irritation assay method as outlined in ASTM E 981–84 (see paragraph (b)(2)(iii)(C) of this section). This method assesses the breathing patterns of test animals. This incorporation by reference was approved by the Director of the Federal Register in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. This material is incorporated as it exists on the date of approval and notice of any change in this material will be published in the Federal Register. Copies of the incorporated materials may be obtained from the TSCA Nonconfidential Information Center, Rm. NE–B607, 401 M St., SW., Washington, DC, 20460 or from the American Society for Testing and Materials (ASTM), 1916 Race Street, Philadelphia, PA 10103. Copies may be inspected at the above address or at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC. For information on this test guideline, the references in paragraph (b)(2)(iii) should be consulted.

(ii) Results of respiratory sensory irritation assay. (A) Data shall be included in the final report and tabulated to show:

(*1*) The magnitude of change in respiratory rate with exposure concentration and with time for each animal.

(*2*) A response concentration, which indicates the concentration at which the respiration rate is decreased by 50% (RD_{50}), will be calculated, along with the 95% confidence limits.

(B) Time-effect curves shall be included in the final report to evaluate the onset and shape of the response.

(iii) References.

(A) Alarie, Y., and Luo, J.E. ''Sensory Irritation by Airborne Chemicals: A basis to establish acceptable levels of exposure.'' *Toxicology of the Nasal Passages.* Hemisphere Publishing Corporation: New York pp. 91–100 (1986).

(B) Alarie, Y., and Stokinger, H.E. ''Sensory Irritation by Airborne Chemicals.'' *CRC Critical Reviews in Toxicology.* pp. 299–363 (1973).

(C) ASTM. ''Standard Test Method for Estimating Sensory Irritancy of Airborne Chemicals.'' In: *1984 Annual Book of ASTM Standards. Water and Environmental Technology.* Section 11. Volume 11.04 Designation E 981–84 pp. 572–584 (1984).

(3) *Subchronic test modifications.* In addition to the subchronic testing requirements specified in table 1 in paragraph (a)(5) of this section, the following additional requirements and limitations also apply when specified for a particular chemical substance in table 1 under ''Specific requirements under this section''.

(i) *Respiratory tract pathology.* (A) Care shall be taken that the method used to kill the animal does not result in damage to the tissues of the upper or lower respiratory tract. The heart-lung, including the trachea, shall be removed in bloc.

(B) Representative sections of the lungs shall be examined histologically. This shall include trachea, major conducting airways, alveolar region, terminal and respiratory bronchioles, alveolar ducts and sacs, and interstitial tissues.

(C) The nasopharyngeal tissue shall be examined for histopathologic lesions. This shall include sections through the nasal cavity, and examination of the squamous, transitional, respiratory, and olfactory epithelia.

(D) The larynx mucosa shall be examined for histopathologic changes. Sections of the larynx to be examined include the epithelium covering the base of the epiglottis, the ventral pouch, and the medial surfaces of the vocal processes of the arytenoid cartilages.

(ii) *Bronchoalveolar lavage.* (A) The lungs shall be lavaged *in situ* or after sacrifice. If the study will not be compromised, one lobe of the lungs may be used for lung lavage while the other is fixed for histologic evaluation. The lungs shall be lavaged using physiological saline after cannulation of the trachea. The lavages shall consist of two washes each of which consists of approximately 80 percent (e.g., 5 ml in rats and 1 ml in mice) of total lung volume. Additional washes merely tend to reduce the concentrations of the material collected. The lung lavage fluid shall be stored on ice at approximately 5 °C until assayed.

(B) The following parameters shall be determined in the lavage fluid as indicators of cellular damage in the lungs: total protein, cell count and percent leukocytes. In addition, a phagocytosis assay using the procedure of Burleson (Burleson et al., 1987; Gilmour and Selgrade, 1993) shall be performed to determine macrophage activity. The following references may be consulted:

(*1*) Burleson, G.R. et al. ''Poly (I): poly (C)-enhanced alveolar peritoneal macrophage phagocytosis: Quantification by a new method utilizing fluorescent beads.'' *Proceedings of the Society for Experimental Biology and Medicine.* 184:468–476 (1987).

(*2*) Gilmour, G.I., and Selgrade, M.K. ''A Comparison of the Pulmonary Defenses against Streptococcal Infection in Rats and Mice Following O_3 Exposure: Differences in Disease Susceptibility and Neutrophil Recruitment.'' *Toxicology and Applied Pharmacology.* 123:211–218 (1993).

(4) [Reserved]

(5) *Reproductive toxicity and fertility study test modifications.* In addition to the reproductive toxicity and fertility testing requirements specified in table 1 in paragraph (a)(5) of this section, the following additional requirements and limitations also apply when specified for a particular chemical substance in table 1 under ''Specific requirements under this section''.

(i) *Administration of the test substance.* The test substance shall be administered by inhalation. The requirements of OPPTS 870.3800(e)(2)(iii) do not apply.

(ii) [Reserved]

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