

businesses. However, EPA expects to receive few SNUNs for the substances. Therefore, EPA believes that the number of small businesses affected by this rule would not be substantial, even if all of the SNUN submitters were small firms.

#### C. Paperwork Reduction Act.

The information collection requirements contained in this rule have been approved by OMB under the provisions of the Paperwork Reduction Act (44 U.S.C. 3501 *et seq.*), and have been assigned OMB control number 2070-0012.

Public reporting burden for this collection of information is estimated to vary from 30 to 170 hours per response, with an average of 100 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, (2131), U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460; and to the Office of Management and Budget, Paperwork Reduction Project (2070-0012), Washington, DC 20503.

#### List of Subjects in 40 CFR Part 721

Environmental protection, Chemicals, Hazardous materials, Reporting and recordkeeping requirements. Significant new uses.

Dated: November 15, 1993.

Victor J. Kimm,

Acting Assistant Administrator for Prevention, Pesticides and Toxic Substances.

Therefore, it is proposed that 40 CFR part 721 be amended as follows:

#### PART 721—[AMENDED]

1. The authority citation for part 721 would continue to read as follows:

Authority: 15 U.S.C. 2604, 2607, and 2625(c)

2. By adding new § 721.340 to subpart E to read as follows:

#### § 721.340 Acrylate esters.

(a) *Chemical substances and significant new uses subject to reporting.*

(1) Chemical substances falling within the acrylate ester category definition and not on the TSCA Inventory as of [insert proposed date of this rule] are subject to reporting under this section for the significant new uses described in paragraph (a)(2) of this section. The acrylate ester category shall include any

ester of an acrylate, as defined in paragraph (b)(3)(i) of this section having:

(i) A measured number-average molecular weight of 1,000 amu (amu is the unified atomic mass unit referenced to the mass of Carbon 12) or less.

(ii) A measured number-average molecular weight of over 1,000 amu and containing more than 2 percent by weight of any acrylate ester with a molecular weight of 500 amu or less.

(2) The significant new uses are:

(i) *Protection in the workplace.*

Requirements as specified in § 721.63(a)(1), (a)(2)(i), (a)(2)(iii), (a)(2)(iv), (a)(3), (a)(4), (a)(5)(xi), (a)(6)(i), (a)(6)(ii), (a)(6)(iv), (b) (concentration set at 0.1 percent), and (c).

(ii) *Hazard communication program.*

Requirements as specified in § 721.72(a), (b), (c), (d), (e) (concentration set at 0.1 percent), (f), (h)(1)(i)(A), (h)(1)(i)(B), (h)(1)(i)(C), (h)(1)(iii)(A), (h)(1)(vi), (h)(2)(i)(B), (h)(2)(i)(C), and (h)(2)(i)(D).

(iii) *Industrial, commercial, and consumer activities.* Requirements as specified in § 721.80(o).

(b) *Specific requirements.* The provisions of subpart A of this part apply to this section except as modified by this paragraph.

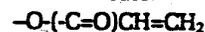
(1) *Recordkeeping requirements.*

Recordkeeping requirements as specified in § 721.125(a) through (i) are applicable to manufacturers, importers, and processors of these substances.

(2) *Limitations or revocation of certain notification requirements.* The provisions of § 721.185 apply to this section.

(3) *Definitions.* (i) *Acrylate* means those chemical substances (including combinations of chemical substances that are not mixtures) whose structures contain one or more covalently bound substructures which are described as terminal or pendant acrylate groups. Such chemical substances are considered to contain a functional acrylate moiety. The functional nature of these chemical substances is attributed to the conjugated carbon to carbon double bond present in the acrylate. Functional acrylate substructures may be produced from several types of reactions. Regardless of the synthetic route, the unsaturated bond of the acrylate group(s) remains present and unreacted. Functional acrylate substructures are typically but not always produced from reactions between mono- or polyhydric alcohols and acrylic acid in which the -OH radical(s) from the alcohol combines with the -COOH radical of the acrylic acid to form acrylate esters. This reaction mechanism ensures that the

double bond remains intact. The substructures produced from the possible chemical reaction types are diagramed below; the free valence is the location of covalent linkage to the rest of the molecule:



Acrylate Group (2-Propenoate Group)

(ii) [Reserved]

[FR Doc. 93-28611 Filed 11-19-93; 8:45 am]

BILLING CODE 6560-60-F

#### 40 CFR Part 799

[OPPTS-42150, FRL 4010-2]

RIN No. 2070-AB07

Acetophenone, Phenol, N,N-Dimethylaniline, Ethyl Acetate, and 2,6-Dimethylphenol; Proposed Test Rule, Notice of Opportunity to Initiate Negotiations for TSCA Section 4 Testing Consent Agreements

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) that would require manufacturers and processors of five chemicals (acetophenone, phenol, N,N-dimethylaniline, ethyl acetate, and 2,6-dimethylphenol) to conduct testing for certain chemical fate, health and environmental effects. This rule would require that testing be conducted to develop data with respect to chemical fate and health and environmental effects for which there is an insufficiency of data and experience and which are relevant to a determination that the manufacture, distribution in commerce, processing, use, or disposal of such chemicals, or that any combination of such activities, does or does not present an unreasonable risk of injury to health or the environment. In addition to the proposed test rule, EPA has negotiated a testing consent agreement development program under TSCA section 4 to allow the Agency to make greater use of enforceable consent agreements (ECAs). Therefore, EPA is soliciting interested parties for participation in or monitoring of consent agreement negotiations for the chemicals that are proposed for testing in this rulemaking. EPA is also inviting manufacturers and/or processors of chemical substances who wish to participate in consent agreement negotiations for the chemicals proposed for testing to develop and submit testing consent agreement proposals to EPA.

**DATES:** Written comments on the proposed rule must be received by EPA on or before January 21, 1994. If persons request an opportunity to submit oral comments by January 6, 1994, EPA will hold a public meeting on this proposed rule in Washington, DC. For further information on arranging to speak at the meeting see Unit VII of this preamble. Written ECA testing proposals must be received by January 21, 1994. Written notice of interest in being designated an "interested party" to the consent agreement negotiations for the chemicals proposed for testing in this rulemaking must be received by January 21, 1994. Those submitting written testing proposals will be considered "interested parties" and do not have to submit separate written notice of interest in being designated. EPA will contact all "interested parties" and advise them of meeting dates.

**ADDRESSES:** Submit written comments, identified by the document control number (OPPTS-42150) and the chemical-specific docket number, in triplicate to: TSCA Nonconfidential Information Center (7407), Office of Pollution Prevention and Toxics, Environmental Protection Agency, East Tower, Rm. G-99, 401 M St., SW., Washington, DC, 20460. A public version of the administrative record supporting this action, without confidential business information (CBI), is available for inspection at the above address in Room G-102, from 8 a.m. to 12 noon, and 1 p.m. to 4 p.m., Monday through Friday, except legal holidays.

**FOR FURTHER INFORMATION CONTACT:** Susan B. Hazen, Director, Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, Rm. E-543B, 401 M St., SW., Washington, DC 20460, (202) 554-1404, TDD (202) 554-0551.

**SUPPLEMENTARY INFORMATION:** This notice proposes a test rule under TSCA section 4(a)(1)(A) and (B) to require certain health, environmental, and chemical fate tests for acetophenone (CAS No. 98-86-2), phenol (CAS No. 108-95-2), *N,N*-dimethylaniline (CAS No. 121-69-7), ethyl acetate (CAS No. 141-78-6), and 2,6-dimethylphenol (CAS No. 576-26-1).

## I. Introduction

### A. ITC Recommendation

At the request of EPA, the ITC reviewed a subset of chemicals included on EPA's Integrated Risk Information System (IRIS) data base for which the Agency believed there is inadequate

data. EPA brought these chemicals to the ITC to foster interagency coordination and cooperation on testing needs. The ITC designated six chemicals included in IRIS (acrylic acid (addressed in a separate rulemaking at 57 FR 7656, March 4, 1992), acetophenone, phenol, *N,N*-dimethylaniline, ethyl acetate, and 2,6-dimethylphenol) for priority consideration as candidates for chemical fate, health effects and environmental effects testing.

IRIS is an electronic database prepared and maintained by EPA, containing both cancer and non-cancer chronic health hazard information on specific chemicals. IRIS provides hazard identification and dose-response assessment information. This information, when combined with specific exposure information, can be used to help characterize the public health risks posed by a chemical in a particular situation (Ref. 7).

In addition, as other agencies brought their testing needs and concerns for the chemicals to bear on the ITC deliberations, the ITC's testing recommendations expanded to include additional endpoints such as mutagenicity and neurotoxicity testing.

Besides health effects data, the ITC also recommended additional data to better characterize the environmental effects and chemical fate of two of these chemicals. The reasons for these particular testing recommendations by the ITC are further discussed in the Federal Register of March 6, 1991 (56 FR 9534), and in the chemical-specific sections of this notice.

### B. Test Rule Development Under TSCA

Under section 4(a) of TSCA, EPA shall, by rule, require testing of a chemical to develop appropriate test data if the Administrator makes certain findings as described in TSCA section 4(a)(1)(A) or (B). Discussions of the statutory section 4 findings are provided in EPA's first and second proposed test rules, which were published in the Federal Register of July 18, 1980 (45 FR 48510) and June 5, 1981 (46 FR 30300). EPA also proposed its policy for making findings under TSCA section 4(a)(1)(B) in the Federal Register of July 15, 1991 (55 FR 32294) and finalized this policy in the Federal Register of May 14, 1993 (58 FR 28736). This is referred to in this test rule as the "B policy." For further discussion of EPA's interpretation of its authority under sections 4(a)(1)(A) and (B) of TSCA, see Unit III of this preamble.

In evaluating the ITC's testing recommendations for these chemicals, EPA considered the information provided by the ITC, the on-line IRIS data base, and supplemental information developed by EPA in developing the testing requirements for this rule. EPA has also considered the status of acetophenone and phenol under the Clean Air Act Amendments of 1990 (Ref. 51). These considerations have influenced the proposed testing and routes of administration selected. From this evaluation, EPA is proposing health effects testing for five of these chemicals, and chemical fate and environmental effects testing for two of these chemicals under TSCA section 4(a)(1)(A) and/or (B). Either finding alone is sufficient to support a test rule. EPA has entered into an enforceable testing Consent Order for the sixth chemical—acrylic acid.

EPA did not require reporting for these chemicals under sections 8(a) or 8(d) of TSCA because production, use and exposure information and toxicity data for these chemical substances are available in the general literature and EPA expects that any unpublished studies will be submitted in response to the proposed rule. Where less is known about the toxicity and exposures to the chemical, section 8(a) and 8(d) information is needed and routinely required before EPA proposes a section 4 test rule.

This action constitutes EPA's response to the ITC as required by TSCA section 4(e)(1)(B).

## II. Proposed Testing and Reporting Requirements

### A. Test Standards and Reporting Requirements

EPA is proposing that health effects, environmental effects, and/or chemical fate testing be conducted on acetophenone, phenol, *N,N*-dimethylaniline, ethyl acetate, and 2,6-dimethylphenol according to the specific test guidelines set forth in § 799.4450.

Data developed under the final rule must be reported in accordance with TSCA Good Laboratory Practice (GLP) Standards, 40 CFR part 792.

As required by section 4(b)(1) of TSCA, EPA is proposing specific testing and reporting requirements for each of the proposed tests for the five IRIS chemicals as specified in the following Table 1:

TABLE 1.—TESTING AND REPORTING FOR FIVE IRIS CHEMICALS

Chemical Name (CAS No.)	Test (Route of Administration)	Guideline	Minimum Percent Purity	Deadline for Final Report <sup>1</sup> (months)	Docket No.	
Acetophenone (98-86-2).	<b>Health effects testing:</b>					42150/42151
	Subchronic toxicity, Inhalation .....	§ 798.2450	99.0	18		
	Toxicokinetics <sup>2</sup> , Oral .....	OECD 417	99.0	15		
	Toxicokinetics <sup>2</sup> , Inhalation .....	OECD 417	99.0	15		
	Neurotoxicity, Acute and Subchronic, Inhalation.	§ 798.6050 and 798.6200	99.0	21		
	Neurotoxicity, Subchronic, Inhalation .....	§ 798.6400	99.0	21		
	Reproductive toxicity, Gavage .....	§ 798.4700	99.0	29		
	Developmental toxicity, Inhalation .....	§ 798.4900	99.0	12		
	<i>Salmonella</i> assay .....	§ 798.5265	99.0	9		
	<i>In vitro</i> gene mutation assay .....	§ 798.5300	99.0	10		
	<i>In vivo</i> cytogenetics assay .....	§ 798.5385 or 798.5395	99.0	14		
	Phenol (108-85-2) .....	<b>Health effects testing:</b>				
Subchronic toxicity, Inhalation .....		§ 798.2450	99.0	18		
Toxicokinetics <sup>2</sup> , Oral .....		OECD 417	99.0	15		
Toxicokinetics <sup>2</sup> , Inhalation .....		OECD 417	99.0	15		
Neurotoxicity, Acute and Subchronic, Inhalation.		§ 798.6050 and 798.6200	99.0	21		
Neurotoxicity, Subchronic, Inhalation .....		§ 798.6400	99.0	21		
Reproductive toxicity, Inhalation .....		§ 798.4700	99.0	29		
Developmental neurotoxicity, Gavage .....		§ 795.250	99.0	21		
<i>N,N</i> -Dimethylaniline (121-69-7).	<b>Health effects testing:</b>					42150/42153
	Subchronic toxicity, Inhalation .....	§ 798.2450	99.0	18		
	Toxicokinetics <sup>2</sup> , Oral .....	OECD 417	99.0	15		
	Toxicokinetics <sup>2</sup> , Inhalation .....	OECD 417	99.0	15		
	Neurotoxicity, Acute and Subchronic, Inhalation.	§ 798.6050 and 798.6200	99.0	21		
	Neurotoxicity, Subchronic, Inhalation .....	§ 798.6400	99.0	21		
	Reproductive toxicity, Gavage .....	§ 798.4700	99.0	29		
	Developmental toxicity, Gavage .....	§ 798.4900	99.0	12		
	<i>In vivo</i> cytogenetics assay .....	§ 798.5385 or 798.5395	99.0	14		
	<b>Environmental Effects Testing:</b>					
	Algal test .....	§ 797.1050	99.0	12		
	Daphnid acute test .....	§ 797.1300	99.0	12		
	Mysid shrimp acute test .....	§ 797.1930	99.0	12		
	Fathead minnow life stage test .....	§ 797.1600	99.0	12		
	Sheepshead minnow life stage test .....	§ 797.1600	99.0	12		
	Daphnid chronic test .....	§ 797.1330	99.0	18		
	Mysid shrimp chronic test .....	§ 797.1950	99.0	18		
	<b>Chemical Fate Testing:</b>					
	Activated sludge testing .....	§ 796.3340	99.0	12		
	Anaerobic biodegradation testing .....	§ 796.3140	99.0	12		
Ethyl Acetate (141-78-6).	<b>Health effects testing:</b>					42150/42141A

TABLE 1.—TESTING AND REPORTING FOR FIVE IRIS CHEMICALS—Continued

Chemical Name (CAS No.)	Test (Route of Administration)	Guideline	Minimum Percent Purity	Deadline for Final Report <sup>1</sup> (months)	Docket No.
2,6-Dimethylphenol (576-26-1).	Reproductive toxicity, Gavage .....	\$ 798.4700	99.0	29	42150/42154
	Developmental toxicity, Gavage .....	\$ 798.4900	99.0	12	
	<i>In vitro</i> gene mutation assay .....	\$ 798.5300	99.0	10	
	Health effects testing:				
	Toxicokinetics <sup>2</sup> , Oral .....	OECD 417	99.0	15	
	Toxicokinetics <sup>2</sup> , Inhalation .....	OECD 417	99.0	15	
	Neurotoxicity, Acute and Subchronic, Gavage.	\$ 798.6050 and 798.6200	99.0	21	
	Neurotoxicity, Subchronic, Gavage .....	\$ 798.6400	99.0	21	
	Reproductive toxicity, Gavage .....	\$ 798.4700	99.0	29	
	Developmental toxicity, Gavage .....	\$ 798.4900	99.0	12	
	<i>In vitro</i> gene mutation assay .....	\$ 798.5300	99.0	10	
	<i>In vivo</i> cytogenetics assay .....	\$ 798.5385 or 798.5395	99.0	14	
	Environmental Effects Testing:				
	Algal test .....	\$ 797.1050	99.0	12	
	Fathead minnow life stage test .....	\$ 797.1600	99.0	12	
	Daphnid chronic test .....	\$ 797.1330	99.0	18	
	Chemical Fate Testing:				
	River die-away testing .....	(incorporated by reference) ????	99.0	12	
Anaerobic biodegradation testing .....	\$ 796.3140	99.0	12		
Aqueous photolysis testing .....	\$ 795.70	99.0	12		

<sup>1</sup> Figure indicates the reporting deadline in months calculated from the effective date of the final rule or from the date of test sponsor notification by certified letter to initiate test where such notification is specified.

<sup>2</sup> The toxicokinetics (pharmacokinetics and metabolism) guideline was developed by the European Organization for Economic Cooperation and Development (OECD) and is proposed to be incorporated by reference in this rule.

All of the guidelines referenced in Table 1 are intended to be used as currently published in Title 40 of the Code of Federal Regulations, except for the neurotoxicity test guidelines, which are modified in the codified section of this rule. The neurotoxicity guideline modifications specify the duration and frequency of exposure and specify that lower exposure levels shall show a graded neurotoxic response or no neurotoxicity. Exceptions also are the toxicokinetics and biodegradation in natural surface water guidelines, which are proposed to be incorporated by reference and are available in the docket for this rule.

#### B. Interim Mutagenicity Testing Policy

The proposed health effects testing in this rule reflects EPA's current thinking in the area of mutagenicity testing, both as an endpoint and as it leads to oncogenicity testing. The science of mutagenicity testing has undergone considerable change since EPA first

required mutagenicity testing in a section 4 test rule (50 FR 20662, May 17, 1985). This new information, particularly data from EPA's Gene-tox Program related to the ability of short term tests to predict mutagenicity (Ref. 105), the National Toxicology Program's study of the ability of short term tests to predict carcinogenic potential (Ref. 90), and expert meetings, such as the 1987 Williamsburg conference, has led EPA to revise the TSCA section 4 mutagenicity testing scheme. This includes how EPA requires additional mutagenicity testing based on results from lower-tier mutagenicity tests and also how it requires oncogenicity testing based on mutagenicity test results. EPA believes the flexibility and opportunity to apply professional scientific judgment offered by the new approach afford considerable advantages over the prior scheme. EPA's rationale for these changes is discussed in the technical literature (Ref. 19) and will not be discussed here.

For purposes of this rule, in which only Tier I testing is being proposed, the changes are relatively minor. First, Tier I is redefined as a battery of two *in vitro* tests and one *in vivo* test. There is no longer a distinction as to gene mutations or chromosomal aberrations in Tier I, and the previously utilized *in vitro* cytogenetics test would be eliminated. The purpose of Tier I testing, however, continues to be to determine intrinsic mutagenic potential.

Subsequent mutagenicity testing, including Tier II testing, is not being proposed at this time. The test guidelines for several of the Tier II tests are still undergoing refinement. Thus, rather than delaying the Agency's response to the ITC until all of the details of the mutagenicity testing scheme have been completed, EPA has decided to propose only Tier I of the new mutagenicity testing scheme at this time. If appropriate, further mutagenicity testing, including triggers to oncogenicity testing, will be

addressed in a subsequent rulemaking after review of the Tier I results.

#### C. Persons Required to Test

Because of the findings in Unit III of this preamble, EPA is proposing that persons who manufacture (including import) or process, or who intend to manufacture or process, acetophenone, phenol, *N,N*-dimethylaniline, ethyl acetate, or 2,6-dimethylphenol, 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. Byproduct manufacturers and importers of acetophenone, phenol, *N,N*-dimethylaniline, ethyl acetate, and/or 2,6-dimethylphenol are considered manufacturers under this rule. As explained in 40 CFR 790.42, manufacturers of these substances would be required to submit letters of intent to conduct testing or exemption applications. However, small quantity manufacturers, research and development manufacturers and processors would not be required to submit letters of intent or exemption applications unless directed to do so in a subsequent notice as described in § 790.46(b).

EPA has specified relatively pure substances for testing (99 percent, or higher). EPA is not proposing to require submission of equivalence data as a condition for exemption from testing, since EPA is interested in evaluating the effects attributable to the substances themselves.

#### III. Findings

EPA interprets TSCA section 4(a) to mean that EPA's authority to require testing under TSCA section 4(a)(1)(A) and (B) is related to the "data insufficiency" and "testing is necessary" findings under TSCA section 4(a)(1)(A)(ii) and (iii) and (B)(ii) and (iii). Thus, once the Administrator has made a finding under TSCA section 4(a)(1)(A)(i) that a chemical may present an unreasonable risk, or under TSCA section 4(a)(1)(B)(i) that a chemical is or will be produced in substantial quantities and may either be released to the environment in substantial quantities or that there may be substantial or significant human exposure to the chemical, the Administrator may require any type of testing necessary to address unanswered questions about the effects of the chemical. EPA need not limit the scope of testing required to the factual bases for the section 4(a)(1)(A)(i) or (B)(i) findings. For a more detailed discussion of this interpretation, see EPA's final

"B-policy" rule (58 FR 28736, May 14, 1993).

The proposed chemical fate, health and environmental effects testing is based on the authority of section 4(a)(1)(A) and (B) of TSCA. EPA finds that available data indicate that three of the chemicals may present an unreasonable risk of injury to human health or the environment: all five of these chemicals are produced in substantial quantities; there is or may be significant or substantial human exposure to all five of these chemicals; there is or may be substantial environmental release of one of these chemicals; there are insufficient data and experience to determine or predict the effects from manufacturing, distribution, processing, use, and disposal of all of these chemicals; and testing is necessary to develop these data.

As noted earlier, a general discussion of the statutory section 4 findings is provided in EPA's first and second proposed test rules, which were published in the Federal Register of July 18, 1980 (45 FR 48510) and June 5, 1981 (46 FR 30300), in EPA's final "B" policy, published in the Federal Register of May 4, 1993 (58 FR 28736), and in Unit II. C. of this preamble.

#### A. Acetophenone

EPA is proposing testing of acetophenone under the authority of section 4(a)(1)(B) of TSCA.

1. *Substantial quantities produced finding.* EPA believes that acetophenone is or will be produced in substantial quantities. According to records available to EPA, acetophenone production exceeds 1 million pounds per year; actual production volumes are CBI. EPA believes that production of 1 million pounds or greater constitutes substantial production under TSCA section 4(a)(1)(B)(i).

2. *Substantial human exposure finding.* EPA believes that there is or may be substantial human exposure to acetophenone. This assessment is based on a National Occupational Exposure Survey (NOES) which indicates that 39,880 workers were potentially exposed to acetophenone in various industrial applications (Refs. 70 and 109). Of these workers, 97 percent were potentially exposed during the use of trade name products containing acetophenone. As explained in EPA's "B" policy, EPA believes that the potential exposure of 39,880 workers to acetophenone constitutes substantial human exposure under section 4(a)(1)(B) of TSCA. Acetophenone is used as a perfume base in the fragrance industry, as a process solvent for gums,

resins, and dyestuffs, as an intermediate for the synthesis of pharmaceuticals, in corrosion inhibitors, in rubber chemicals, in flavorings, as a polymerization catalyst, and as a photoinitiator (Refs. 14 and 81). The use of acetophenone as a fragrance in soaps and detergents also gives rise to widespread consumer exposure. EPA estimates an exposure of individual persons up to 3,783 mg/yr from use of hand soaps (Ref. 96).

EPA also believes that there is or may be general population exposure to acetophenone. Acetophenone has been detected in U.S. drinking water supplies. In a survey of 10 U.S. cities between 1969 and 1972, acetophenone was found in Philadelphia's drinking water, on 7 different occasions, at a concentration of approximately 1.0 µg/L (Refs. 54 and 89). This may result in the exposure of millions of people. For the reasons set forth in EPA's "B" policy, EPA believes that the potential exposure of 100,000 or more people in the general population to acetophenone constitutes substantial human exposure under TSCA section 4(a)(1)(B)(i).

3. *Insufficient data and experience finding.* EPA believes that there are insufficient data and experience to determine or predict the effects on human health or the environment from manufacturing, processing, distribution, use, and/or disposal of acetophenone. EPA believes that available studies are insufficient and other data are lacking to sufficiently evaluate the effects of acetophenone.

Inhalation data to assess the subchronic effects of exposure to acetophenone do not adequately address the concentration-response relationship for the portal-of-entry effects via the inhalation route. The primary study cited as providing the baseline RfC (for inhalation) indicated a no observed effect level (NOEL) of 0.007 mg/m<sup>3</sup> and a lowest observed effect level (LOEL) of 0.07 mg/m<sup>3</sup> based on congestion of cardiac vessels, liver dystrophy and changes in the ratios of blood proteins and muscle chronaxie (Ref. 49). This study exposed groups of 15 white male rats continuously to acetophenone vapor at 0, 0.007, or 0.07 mg/m<sup>3</sup> for 70 days. While a NOEL and LOEL were reported, this study is inadequate because only one sex of animals was examined, only five animals per group were used to study cholinesterase activity, and serum protein levels and the number of animals which underwent histopathological examination were unreported (Ref. 51).

Another inhalation study reported a specific pattern of degeneration of the olfactory bulb in groups of four Wistar

rats continuously exposed to acetophenone vapors from 1 week to 3 months (Ref. 78). However, other parameters of toxicity were not evaluated in this study.

EPA is also aware of two oral subchronic studies. These studies failed to identify adverse effects in groups of five male and five female albino rats fed diets containing acetophenone at levels of 0.003, 0.05, 0.125, or 0.2 percent for 30 days (Ref. 85) or in groups of 10 male and 10 female Osborne-Mendel rats fed diets containing 1,000, 2,500, or 10,000 ppm acetophenone for 17 weeks (Ref. 40). These studies were judged adequate to predict oral toxicity, but only marginally so, because no LOAEL was established (Ref. 51).

Developmental toxicity data on acetophenone are limited to a study that reported no effects on length of gestation or postnatal development in the offspring of rats exposed dermally at 0.48 mg/kg on days 10 - 15 of gestation (Ref. 57). The data are insufficient because key study parameters were not reported, apparently only a single dose was administered, and the critical period of organogenesis may have been missed.

Available mutagenicity data in *Salmonella* (Ames testing) are insufficient because only three strains of the test organism were used, rather than the usual four or five that EPA considers necessary to establish a negative response in this assay. EPA's mutagenicity testing scheme (described in more detail in Unit II.B. of this preamble) also includes *in vitro* gene mutation and *in vivo* cytogenetics in the lowest tier. As neither study is available for acetophenone, additional mutagenicity testing is necessary to assess acetophenone's mutagenic potential.

Available *in vitro* and *in vivo* pharmacokinetics and metabolism studies are inadequate because quantitative data on acetophenone's rates of absorption, distribution, and excretion are lacking in these studies (Refs. 33, 58, 60, 91, 92, 84 and 55).

Finally, no data were found for reproductive effects or neurotoxicity.

**4. Testing is necessary to develop data finding.** EPA believes that testing of acetophenone is necessary to develop data for subchronic effects, neurotoxicity, pharmacokinetics and metabolism, reproductive effects, developmental effects and mutagenic effects. EPA believes that these testing data are needed to determine if the manufacturing, processing, distribution, use, or disposal of acetophenone or any combination of such activities does or

does not present an unreasonable risk of injury to human health.

#### B. Phenol

EPA is proposing testing of phenol under the authority of section 4(a)(1)(A) and 4(a)(1)(B) of TSCA.

**1. Unreasonable risk of injury to human health or environment finding.** EPA believes that the manufacture, processing, distribution in commerce, use, or disposal, or any combination of such activities for phenol may present an unreasonable risk of injury to health or the environment. This finding is based on several studies that indicate that phenol is neurotoxic. After 20 exposures by inhalation to 100-200 mg/m<sup>3</sup>, hind limb paralysis was reported for guinea pigs (Ref. 23). Continuous exposure to phenol vapors at 100 mg/m<sup>3</sup> for 15 days affected the performance of rats in a test assessing central nervous system (CNS) effects (Ref. 18). A developmental toxicity screening test with a single gavage dose of 100, 333, 667 or 1,000 mg/kg given to groups of 12-13 Sprague-Dawley rats on day 11 of gestation (Ref. 53), produced a syndrome of effects involving the limbs, tail, and urogenital system, which provides evidence of developmental neurotoxicity. The limb effects consisted of paralysis and/or palsy. Although the effect is not evident in newborns, limb function matures postnatally and requires a week to 10 days for effects to appear. This delayed effect was seen in 21.4 percent and 27.3 percent of the litters at 667 and 1,000 mg/kg, respectively.

As discussed further below, over 320,000 workers may be exposed to phenol in numerous industrial settings, and the wide variety of uses of phenol may result in more widespread worker and consumer exposure. Furthermore, phenol is produced and released into the environment in substantial quantities which may result in general population exposures. Because of these concerns, EPA believes that phenol may present an unreasonable risk of injury to health.

**2. Substantial quantities produced finding.** EPA believes that phenol is or will be produced in substantial quantities. EPA records indicate that phenol is produced in excess of 1 million pounds per year. In 1989, 13 facilities were listed as manufacturing this compound (Ref. 86). EPA estimates the annual production for 1989 to be 3,512,000,000 pounds for 10 manufacturers at 11 sites. As explained in the "B" policy, EPA believes that production of 1 million pounds or greater of phenol constitutes substantial

production under section 4(a)(1)(B)(i) of TSCA.

**3. Substantial human exposure finding.** EPA believes that there is or will be substantial human exposure to phenol. This assessment is based on worker, general population and consumer exposure to phenol. The NOES conducted during 1981-1983 by NIOSH estimated that 320,914 workers were potentially exposed to phenol in 35 different industrial categories (Refs. 70 and 109). For the reasons set forth in the "B" policy, EPA believes that the potential exposure of 341,516 workers to phenol is sufficient to qualify as substantial human exposure under section 4(a)(1)(B)(i) of TSCA.

Phenol is used in a variety of commercial applications including phenolic resins - 38 percent; synthesis of bisphenol A - 23 percent; synthesis of caprolactam - 17 percent; synthesis of alkylphenols - 4 percent; synthesis of aniline - 3 percent; miscellaneous uses - 5 percent; exports - 6 percent (Ref. 16). The miscellaneous uses of phenol include: (1) The synthesis of adipic acid, salicylic acid, phenolphthalein, pentachlorophenol, acetophenetidine, picric acid, and pharmaceuticals; (2) as a selective solvent for refining lubricating oils, germicidal paints, laboratory reagent, dyes and indicators, slimicide, biocide, and (3) as a general disinfectant (Ref. 81). Many of these are uses that can lead to worker and consumer exposure.

In a compilation of air monitoring data collected between 1970 and 1987, the mean concentration of phenol in suburban and urban areas was reported as 0.015 and 8.883 ppb, respectively (Ref. 83). The concentration of phenol in the air of Portland, OR, during seven rain events in 1984 was 56 to 105 ppt, while the concentration of phenol in the rain ranged from 75 to 1,200 ppt (Ref. 61). It has also been detected in U.S. drinking water supplies (Refs. 29 and 69).

Phenol is used in numerous consumer products indicating a potential for exposure to consumers (Ref. 100).

**4. Release to environment in substantial quantities finding.** EPA believes that phenol is released to the environment in substantial quantities. Over 1 million pounds of phenol is released into the environment each year. The Toxics Release Inventory (TRI) for 1987, indicates that 8,100,731 pounds of phenol was released to the air, 402,579 pounds to water, and 1,098,624 pounds to land (Ref. 93). For 1988, the TRI indicates that 10,155,101 pounds was released to air, 262,127 pounds to water, and 2,162,250 pounds to land (Ref. 93). As explained in EPA's "B" policy, EPA

believes that 1 million pounds of release to the environment each year is a sufficiently large amount of release for making a finding of substantial environmental release under section 4(a)(1)(B) of TSCA.

Phenol was detected in 738 samples obtained from 33 industries and publicly owned treatment works (POTWs) at a maximum concentration range of 7.5 ppb to 530 ppm (Ref. 82). Data from the STORET database indicate that phenol was found in 42.1 percent of industrial effluent samples obtained from 1980-83, at a median concentration of 10 ppb (Ref. 87). The STORET database also indicates that phenol was found in 13 percent of ambient surface water samples, and 9 percent of sediment samples (Ref. 87), and also in groundwater samples (Ref. 88). Phenol was detected in 4 percent of 86 samples obtained during the National Urban Runoff Program of 1982, at concentrations ranging from 3 to 10 ppb (Ref. 17).

**5. Insufficient data and experience finding.** EPA believes that there are insufficient data and experience to determine or predict the effects on human health or the environment from manufacturing, processing, distribution, use, and/or disposal of phenol. EPA believes that there are insufficient data and experience to reasonably determine or predict the potential subchronic effects, neurotoxicity, pharmacokinetics and metabolism, reproductive toxicity, and developmental neurotoxicity from the manufacturing, processing, distribution, use, and/or disposal of phenol. Although a number of studies describe the metabolism and pharmacokinetics of phenol (Refs. 13, 20, 22, 52, 62, 65, and 66), the information is insufficient to make comparisons and assumptions that would allow full use of the existing database for regulatory purposes. The Chemical Manufacturers Association's Phenol Panel is conducting pharmacokinetic studies and has consulted EPA on study design (Refs. 113, 114, and 115).

A number of subchronic and chronic tests have been conducted with phenol by the oral and inhalation routes (Refs. 6, 21, 23, 27, 67, and 80). None of these studies are adequate to characterize portal-of-entry effects via the inhalation route. Several of the inhalation subchronic studies did not use controls and tested too few animals of unspecified sex (Ref. 23). A one-dose-level study determined a NOEL of 19 mg/m<sup>3</sup> (Ref. 80), but the design of this study did not include establishing an effect level for phenol. In addition, the information available shows phenol to

be more toxic by inhalation exposure than by oral exposure, thereby precluding a high degree of reliance on conclusions based on route-to-route extrapolation. For these reasons, EPA is proposing to require testing to develop data on the effects of phenol by the inhalation route.

Anger and Johnson (1985), summarizing known neurotoxic effects of a number of chemicals, indicate motor and mental disturbances for phenol (Ref. 2). EPA has insufficient information to evaluate these effects. Deichmann et al. (1944) reported hind-limb paralysis in guinea pigs after 20 exposures by inhalation to 100-200 mg/m<sup>3</sup> phenol (Ref. 23). In addition, Dalin and Kristoffarsson (1974) found that continuous exposure to phenol vapors at 100 mg/m<sup>3</sup> for 15 days adversely affected the performance of rats in a test assessing CNS effects (Ref. 18). Furthermore, Kavlock (1990) noted neurologically significant effects in the pups of dams exposed to phenol in a screening test for developmental effects (Ref. 53). However, these studies did not extend long enough to adequately characterize these effects. Furthermore, the Deichmann et al. study (Ref. 23) did not include control animals; and the Dalin and Kristoffarsson study (Ref. 18) did not establish a NOAEL for the observed CNS effects.

The Kavlock study (Ref. 53) also supports concern for developmental neurotoxicity. When pregnant rats were given a single gavage dose of phenol, their offspring showed developmental toxicity affecting the limbs, tail, and urogenital systems. This study was a screening test, designed to help identify substances which may need additional developmental toxicity testing, and was not adequate to characterize these effects. In order to address the inadequacy of the data developed by these studies, EPA proposes to require both neurotoxicity and developmental neurotoxicity testing for phenol.

No additional testing for developmental effects is being proposed because NTP studies (Refs. 71 and 112) are adequate for this endpoint. Although these studies were conducted by the oral route, EPA expects that additional reproductive effects testing, which will be conducted by the inhalation route, will be an adequate complement to the existing database.

EPA believes a reproductive effects study on phenol by Heller and Pursell (1938) is inadequate for risk assessment purposes because the experimental methodology and test results reporting are inadequate and unreliable (Ref. 44). EPA is proposing to require reproductive effects testing. The

inhalation route was selected because information indicates that animals are more sensitive to phenol when exposed by the inhalation route.

**6. Testing is necessary to develop data findings.** EPA believes that the testing of phenol is necessary to develop data for oral and inhalation pharmacokinetics and metabolism, inhalation subchronic effects, reproductive effects, developmental neurotoxicity, and neurotoxicity. EPA believes that these testing data are needed to determine if the manufacture, distribution in commerce, processing, use, or disposal of phenol, or any combination of such activities, does or does not present an unreasonable risk of injury to health or the environment.

#### C. *N,N*-Dimethylaniline

EPA is proposing testing of *N,N*-dimethylaniline under the authority of sections 4(a)(1)(A) and 4(a)(1)(B) of TSCA.

**1. Unreasonable risk of injury to health or the environment finding.** EPA believes that the manufacture, processing, distribution in commerce, use, or disposal, or any combination of such activities for *N,N*-dimethylaniline, may present an unreasonable risk of injury to health or the environment.

**a. Evidence of potential for adverse human health effects.** The health portion of this assessment is based on *N,N*-dimethylaniline's toxicity in subchronic (13-week), chronic, oncogenicity, and mutagenicity studies.

A 2-year chronic toxicity-oncogenicity gavage study in groups of 50 male and 50 female F344/N rats treated with 3 or 30 mg/kg 5 days per week and similarly sized groups of B6C3F1 mice treated with 15 or 30 mg/kg 5 days per week reported some evidence of carcinogenicity in male rats (sarcomas and osteosarcomas of the spleen) and equivocal evidence of carcinogenicity in female mice (squamous cell papillomas of the forestomach) (Ref. 72). Mutagenicity data were negative for reverse mutation in four strains of *Salmonella*, but were positive for forward mutation in mouse lymphoma L5178Y cells and for sister chromatid exchange and chromosomal aberrations in Chinese hamster ovary cells (Ref. 72).

A 13-week gavage study (that included comprehensive histopathological examination) in groups of 10 male and 10 female F344/N rats and B6C3F1 mice treated with 31.25, 62.5, 125, 250, or 500 mg/kg for 5 days per week identified the erythrocytes and the spleen as the most sensitive targets in both species (Refs. 1 and 72). Compound-related clinical

signs included lethargy in rats and mice and cyanosis in rats. The National Toxicology Program (NTP) study identified the rat as more sensitive than the mouse to the noncarcinogenic effects of *N,N*-dimethylaniline on erythrocytes and the spleen; these effects were seen in rats even at the lowest dose level tested, while an NOAEL of 31.25 mg/kg was seen for the mice (Ref. 72). An inhalation study reported altered muscle chronaxie and evidence of hemolytic anemia in the high dose group of rats continuously exposed for 100 days to 0.04 or 0.3 mg/m<sup>3</sup> (Ref. 64). Anger and Johnson (1985), summarizing known neurotoxic effects of *N,N*-dimethylaniline, indicate vision disturbances and central nervous system depression (Ref. 2).

As discussed further elsewhere in this preamble, over 28,000 workers may be exposed to *N,N*-dimethylaniline in various industrial settings and there is also evidence of general population exposure.

b. *Evidence of potential environmental toxicity.* This assessment is based on probabilistic dilution modelling indicating that *N,N*-dimethylaniline is present in the environment at levels within a factor of 100 of its known acute toxicity to environmental organisms. EPA believes that there may be an unreasonable risk of injury to the environment from chronic effects when acute toxicity is observed at levels within a factor of 100 of predicted stream concentrations. Specifically, EPA has determined a concentration of concern of 300 ppb (based on *N,N*-dimethylaniline's predicted chronic toxicity to daphnids) and has estimated that this concentration is exceeded 144 to 198 days of the year in receiving streams (Ref. 108).

Furthermore, *N,N*-dimethylaniline, which is produced in substantial quantities, has been detected in soil and water. According to the TRI, 147,692 pounds of *N,N*-dimethylaniline were released to the environment in 1987 (Ref. 93). For 1988, the TRI indicates that 119,122 pounds were released (Ref. 93). The TRI also indicates that some of these releases would be to the marine or estuarine environment (Ref. 116).

From these concerns, EPA believes that *N,N*-dimethylaniline may present an unreasonable risk of injury to health and the environment.

2. *Substantial quantities produced finding.* EPA believes that *N,N*-dimethylaniline is or will be produced in substantial quantities. EPA records indicate that domestic production of *N,N*-dimethylaniline in 1979 was 13.7 million pounds (Ref. 102). Information

on current production volumes is CBI, but production is substantial (1 million pounds or greater). For the reasons set forth above, EPA believes that production of 1 million pounds or more per year of *N,N*-dimethylaniline is substantial production under section 4(a)(1)(B)(i) of TSCA.

3. *Substantial human exposure finding.* EPA believes that there is or may be substantial human exposure to *N,N*-dimethylaniline. This assessment is based on an NOES survey which estimated that 27,895 workers were potentially exposed to *N,N*-dimethylaniline in 9 different industrial classifications (Refs. 70 and 109). Of these workers, 39 percent were potentially exposed during the use of trade name products containing this compound. *N,N*-Dimethylaniline is used in dyes, as a synthetic intermediate for vanillin, pharmaceuticals, and other compounds, and as a solvent, stabilizer, and polymerization catalyst (Refs. 59, 81 and 99). For the reasons set forth in the "B" policy, EPA believes that the potential exposure of 28,048 workers to *N,N*-dimethylaniline constitutes substantial human exposure under TSCA section 4(a)(1)(B)(i).

Furthermore, there is or may be general population exposure to *N,N*-dimethylaniline. *N,N*-Dimethylaniline was detected in 8 samples obtained from three industries and POTWs at a maximum concentration of 3.1 ppm (Ref. 82). According to the TRI, 129,829 pounds of *N,N*-dimethylaniline was released to the air, 17,613 pounds to water, and 250 pounds to land in 1987 (Ref. 93). For 1988, the TRI indicates that 98,905 pounds was released to air, 19,967 pounds to water, and 250 pounds to land (Ref. 93). *N,N*-Dimethylaniline was detected in soil samples obtained near the bank of the Buffalo River, NY, at concentrations of 10 to 40 ppm (Ref. 68). *N,N*-Dimethylaniline was reported as being detected (no levels given) in water from Lake Ontario (Ref. 39).

4. *Insufficient data and experience finding.* EPA believes that there are insufficient data and experience to determine or predict the effects on human health or the environment from manufacturing, processing, distribution, use, and/or disposal of *N,N*-dimethylaniline. EPA believes that available studies are insufficient and other data are lacking to sufficiently evaluate the effects of *N,N*-dimethylaniline.

Data assessing the potential subchronic effects of inhalation exposure to *N,N*-dimethylaniline were not found in the literature. Available oral data are inadequate to estimate

inhalation risk because the dose levels selected did not give a NOAEL (for rats) and there are no data on comparative pharmacokinetics or portal-of-entry effects (Refs. 1 and 72). The only inhalation study report available was a brief abstract that indicated altered muscle chronaxie and evidence of hemolytic anemia in the high dose group (0.3 mg/m<sup>3</sup> of rats continuously exposed for 100 days to 0.04 or 0.3 mg/m<sup>3</sup>) (Ref. 64). This study cannot be used for risk assessment because it was reported in limited detail and histopathologic effects were not examined. Anger and Johnson (1985), summarizing known neurotoxic effects of a number of chemicals, cited visual disturbances and CNS depression for *N,N*-dimethylaniline (Ref. 2). EPA has insufficient information to evaluate these observations.

Developmental toxicity testing for *N,N*-dimethylaniline is limited to a screening study in 50 CD-1 albino mice treated with *N,N*-dimethylaniline in corn oil at 365 mg per kg per day on gestation days 7 to 14; maternal mortality, but no effects on body weight or viability of the neonatal offspring, was reported (Ref. 77). Although the test results are negative, EPA considers this test inadequate for risk assessment purposes because the exposure period did not cover the full period of major organogenesis (days 6 to 15 for the mouse), nor were sufficient dose groups used (only one versus the three required by EPA). EPA also specifies that two animal species be tested for a definitive developmental toxicity assessment. Therefore, developmental toxicity by gavage is proposed for two species, a rat and a non-rodent.

The available (negative) *Salmonella*/Ames data are adequate, as are the (positive) data in mouse lymphoma L51784 cells (Ref. 72). Available data also include positive results for sister chromatid exchange and chromosomal aberrations in Chinese hamster ovary cells (Ref. 72). Given these data, EPA believes that gene mutation data are adequate but that the chromosomal toxicity of *N,N*-dimethylaniline is insufficiently characterized.

Although numerous metabolism studies have been conducted for *N,N*-dimethylaniline, these are inadequate because quantitative pharmacokinetics data for absorption, distribution, or excretion are lacking (Refs. 5, 10, 11, 25, 26, 28, 37, 38, 41, 43, 45, 46, 47, 56, 73, 74, 75, 76, 79, 95 and 106).

No reproductive effects data were found for *N,N*-dimethylaniline.

Environmental effects data for *N,N*-dimethylaniline are limited. Algal toxicity data include a toxicity test in

bluegreen algae (Ref. 9) and a study on energy metabolism enzymes in marine algae (Ref. 4). The study by Batterton et al. (Ref. 9) is inadequate because the Agency needs data for a sensitive species of green algae such as *Selenastrum capricornutum*. Blue-green algae are not an acceptable substitute for green algae. The study by Armstrong et al. (Ref. 4) is inadequate because a rigorous measurement of growth inhibition such as a 96-hour EC50 value was not determined. The Agency believes that the 96-hour EC50 value for growth will be a more sensitive measure of effects on energy metabolism enzymes and will have more relevance in an environmental risk assessment. Acute aquatic toxicity studies are available for a ciliated protozoan and several species of fish (Ref. 3). While the acute toxicity studies for fish appear adequate, no chronic toxicity data for fish were found, nor were any relevant data found for the acute or chronic effects of *N,N*-dimethylaniline on aquatic invertebrates. The toxicity data for the ciliated protozoan are of unknown utility because little is known about how representative protozoa are as surrogate species for other aquatic invertebrates.

EPA found no data to determine anaerobic biodegradation or the biodegradation of *N,N*-dimethylaniline in systems which simulate *in situ* wastewater treatment.

**5. Testing is necessary to develop data finding.** EPA believes that testing of *N,N*-dimethylaniline is necessary to develop data for subchronic effects, neurotoxicity, pharmacokinetics and metabolism, reproductive effects, developmental effects, mutagenic effects, algal toxicity, daphnid acute and chronic toxicity, mysid shrimp acute and chronic toxicity, fathead minnow chronic toxicity, sheephead minnow chronic toxicity, anaerobic biodegradation, and activated sludge biodegradation. EPA believes that this testing is needed to determine if the manufacturing, processing, distribution, use, or disposal of *N,N*-dimethylaniline or any combination of such activities does or does not present an unreasonable risk of injury to health or the environment.

#### D. Ethyl Acetate

EPA is proposing testing of ethyl acetate under the authority of sections 4(a)(1)(A) and 4(a)(1)(B) of TSCA.

**1. Unreasonable risk of injury to health or the environment.** EPA believes that the manufacture, processing, distribution in commerce, use, or disposal, or any combination of such activities for ethyl acetate may present

an unreasonable risk of injury to health or the environment.

**a. Evidence of potential for adverse human health effects.** This finding is based on ethyl acetate's neurotoxic effects, as outlined and supported in previous rule-making for the testing of this chemical [cite final multi-substance rule for the testing of neurotoxicity].

**1. Substantial quantities produced finding.** EPA believes that ethyl acetate is or will be produced in substantial quantities. In 1988, 254.2 million pounds of ethyl acetate was produced in the United States (Ref. 103). EPA estimates the annual U.S. production for 1989 to be 292 million pounds for three manufacturers at five production sites (Ref. 101). For the reasons set forth in the "B" policy, EPA believes that production of 1 million pounds or greater of ethyl acetate constitutes substantial production under section 4(a)(1)(B)(i) of TSCA.

**2. Substantial human exposure finding.** EPA believes that there is or will be substantial human exposure to ethyl acetate. The NOES survey estimated that 419,180 workers were potentially exposed to ethyl acetate (Refs. 70 and 109). Of these workers, 87 percent were potentially exposed during the use of trade name products containing this compound. Potential exposure to ethyl acetate was associated with 34 different industrial classifications (Ref. 70). Ethyl acetate has the following uses: coatings—41 percent; exports—36 percent; solvents—13 percent; plastics—8 percent; chemical synthesis—2 percent (Ref. 15). In addition, ethyl acetate is used as a solvent in numerous consumer applications. For the reasons explained in the "B" policy, EPA believes that the potential exposure of 419,180 workers to ethyl acetate is substantial human exposure under TSCA section 4(a)(1)(B)(i).

Ethyl acetate is found in numerous consumer products including lacquers, varnishes, coatings, detergents and soaps. EPA estimates the highest exposure levels occur by the dermal (4,680 mg/yr from use of latex paints) and inhalation (901 mg/yr from use of lacquer thinner) routes (Ref. 98).

There may also be widespread general population exposure. Ethyl acetate was detected in 66 samples obtained from 17 industries and POTWs at a maximum concentration of 7.7 ppm (Ref. 82). In a compilation of air monitoring data collected between 1970 and 1987, the median concentration of ethyl acetate in urban sites was 0.733 ppb (Ref. 83). Ethyl acetate was also detected in industrialized and urban sites in Virginia and West Virginia at

concentrations ranging from <0.012 to 1.9 ppb (Ref. 30). The STORET database indicates that ethyl acetate has also been detected in groundwater (Ref. 88).

**3. Insufficient data and experience finding.** EPA believes that there are insufficient data and experience to determine or predict the effects on human health or the environment from manufacturing, processing, distribution, use, and/or disposal of ethyl acetate. Under section 4(a)(1)(B)(ii), EPA believes that there are insufficient data and experience to determine or predict the potential reproductive toxicity, developmental toxicity, and mutagenicity from the manufacturing, processing, distribution, use, and/or disposal of ethyl acetate.

EPA is proposing to test ethyl acetate for reproductive effects and developmental toxicity. EPA found no data for these effects.

EPA is also proposing mutagenicity testing for ethyl acetate. Ethyl acetate was negative for induction of reverse mutation in *Salmonella* when tested with and without metabolic activation (Refs. 24 and 50). Positive results were observed for mitotic aneuploidy but negative results were observed for point mutations and recombinations in yeast (Ref. 107).

In mammalian test systems, a positive response was reported for chromosomal aberrations in Chinese hamster fibroblasts *in vitro* (Ref. 50); however, these results do not support a concern or a finding for chromosomal effects under TSCA section 4(a)(1)(A) because, in a more definitive *in vivo* test system, a negative response was reported for micronucleus formation in Chinese hamsters (Ref. 8).

EPA considers the existing *Salmonella* data (negative) on ethyl acetate to be acceptable. However, these data in bacteria alone are insufficient to adequately characterize the gene mutation effects of ethyl acetate, and EPA is proposing an *in vitro* gene mutation assay for ethyl acetate in mammalian cells in culture.

**4. Testing is necessary to develop data finding.** EPA believes that the testing of ethyl acetate is necessary to develop data for reproductive effects, developmental toxicity, and mutagenicity. EPA believes that this testing is needed to determine if the manufacture, distribution in commerce, processing, use, or disposal of ethyl acetate, or any combination of such activities, does or does not present an unreasonable risk of injury to health or the environment.

**E. 2,6-Dimethylphenol**

EPA is proposing to test 2,6-dimethylphenol under the authority of sections 4(a)(1)(A) and (B) of TSCA.

**1. Unreasonable risk of injury to human health and environment finding.** EPA believes that the manufacture, processing, distribution in commerce, use, or disposal, or any combination of such activities for 2,6-dimethylphenol may present an unreasonable risk of injury to health or the environment.

**a. Evidence of potential for adverse human health effects.** This assessment is based on 2,6-dimethylphenol's toxicity in an 8-month rat gavage study, that showed histopathological changes in the liver, spleen, and kidneys and changes in body weight, blood pressure and levels of protein sulfhydryl groups in blood serum and internal organs in 53 male rats treated with 6 mg/kg/day (Refs. 63 and 104). Effects were not seen in rats dosed with 0.06 mg/kg/day. In another study, increased relative liver and spleen weights, decreased body weight gain and marked atrophy and parenchymatous dystrophy of liver cells were observed in 10 male albino rats treated by gavage with 29.5 mg/kg/day for 10 weeks (Ref. 63).

**b. Evidence of potential for environmental toxicity.** This assessment is based on probabilistic dilution modelling indicating that 2,6-dimethylphenol is present in the environment at levels within a factor of 100 of its known acute toxicity to environmental organisms (Ref. 108). EPA believes that there may be an unreasonable risk of injury to the environment from chronic effects when acute toxicity is observed at levels within a factor of 100 of predicted stream concentrations. Specifically, EPA has preliminarily determined a concentration of concern of 100 ppb (based on 2,6-dimethylphenol's predicted chronic toxicity to daphnids) and has estimated that this concentration is exceeded 260 days of the year in receiving streams (Ref. 108).

As discussed further below, over 1,900 workers may be exposed to 2,6-dimethylphenol in a variety of commercial applications. Furthermore, 2,6-dimethylphenol, which is produced in substantial quantities, has been detected in air, rain, wastewater, and groundwater samples, which may indicate general population and environmental exposures (Refs. 34, 36, 42, 61, 81 and 83). Because of these concerns, EPA believes that 2,6-dimethylphenol may present an unreasonable risk of injury to health and the environment.

**2. Substantial quantities produced finding.** EPA believes that 2,6-dimethylphenol is or will be produced in substantial quantities. Information available to EPA indicates that in 1977, from 2 to 20 million pounds of 2,6-dimethylphenol was produced at six different facilities in the United States (Ref. 94). There were two facilities that manufactured 2,6-dimethylphenol in the United States in 1989 (Ref. 86). EPA estimates production in 1989 to have been 130 million pounds (Ref. 101). For the reasons set forth in the "B" policy, EPA believes that production of 1 million pounds or greater of 2,6-dimethylphenol constitutes substantial production under section 4(a)(1)(B)(i) of TSCA.

**3. Substantial human exposure finding.** EPA believes that there is or may be substantial human exposure to 2,6-dimethylphenol. EPA finds that 2,6-dimethylphenol is used in a variety of commercial applications, many of which can lead to worker exposure. The NOES survey estimated that 1,941 workers were potentially exposed to 2,6-dimethylphenol (Refs. 70 and 109). Of these workers, 95 percent were potentially exposed during the use of trade name products containing this chemical. 2,6-Dimethylphenol is used primarily in the production of poly(phenylene oxide) resins (Ref. 31). 2,6-Dimethylphenol is also used in the manufacture of tetramethylbisphenol A, 2,6-dimethylaniline, bis(4-hydroxy-2,5-dimethylphenyl)methane, dyes, pharmaceuticals and fragrances, and as a mixture with other xylenols, in disinfectants, solvents, pharmaceuticals, insecticides, fungicides, plasticizers, rubber chemicals, lubricant and gasoline additives, and wetting agents (Ref. 81). As explained in the "B" policy, EPA believes that the potential exposure of 1,941 workers to 2,6-dimethylphenol is substantial human exposure under section 4(a)(1)(B)(i) of TSCA.

Furthermore, general population exposure to 2,6-dimethylphenol is also indicated. 2,6-Dimethylphenol was detected in 64 samples obtained from 33 industries and POTWs at a maximum concentration of 2,895 ppm (Ref. 81). Monitoring data indicate trace quantities of 2,6-dimethylphenol in air and rain (Refs. 61 and 83). 2,6-Dimethylphenol was detected in shale oil wastewater in the range 0.75 to 1.7 µg/L (Ref. 42) and at 12 mg/L in the wastewater from the gasification of coal (Ref. 34). In addition, it was detected in groundwater samples from a wood preserving facility in Florida at a concentration of 0.90 mg/L, while the concentration of 2,6-dimethylphenol in

groundwater 330 meters from the site was 0.29 mg/L (Ref. 36).

**4. Insufficient data and experience finding.** EPA believes that there are insufficient data and experience to determine or predict the effects on human health or the environment from manufacturing, processing, distribution, use, and/or disposal of 2,6-dimethylphenol. This assessment is based on the following information. EPA has adequate negative data evaluating the gene mutation effects of 2,6-dimethylphenol in *Salmonella* (Refs. 24 and 32). However, EPA has no data evaluating this chemical's potential as a gene toxicant in mammalian cells or as a chromosomal toxin. EPA found no data for neurotoxicity, pharmacokinetics and metabolism, reproductive effects, or developmental toxicity.

For environmental effects, acute aquatic toxicity studies are available for green algae, duckweed, daphnids, sea urchins, fathead minnows and Atlantic cod (Ref. 3). The study for green algae is inadequate because it lacks a rigorous measurement of growth inhibition as a 96-hour EC50 value. The effect measured was inhibition of chlorophyll synthesis and the lowest-observed-effect concentration (LOEC) was the only effective concentration reported. The Agency believes that the 96-hour EC50 value for growth will be a more sensitive effect than inhibition of chlorophyll synthesis and will be more relevant in an environmental risk assessment. While fish and invertebrate acute toxicity data are adequate, EPA found no available data for aquatic invertebrate chronic toxicity. An available 8-day study on fathead minnows for 2,6-dimethylphenol is of too short duration to be considered a chronic effects study, nor did it evaluate sensitive life stages, and, thus, this study is inadequate (Ref. 3).

Available chemical fate screening data for 2,6-dimethylphenol indicate that it may undergo substantial degradation under aerobic conditions; however, EPA found no available data to determine or reliably predict the half-life for the removal of 2,6-dimethylphenol by this process (Ref. 12). Data on the anaerobic degradation of 2,6-dimethylphenol are likewise limited. One screening study indicates that 2,6-dimethylphenol may not degrade under anaerobic conditions; another study indicated that this chemical undergoes anaerobic biodegradation in ground water and laboratory digestors (Refs. 12 and 35). These (contradictory) data are insufficient to adequately characterize this removal process. EPA also believes that the aqueous photolysis of 2,6-dimethylphenol is inadequately

characterized, with no data available which simulates this process under natural conditions (Ref. 12).

5. *Testing necessary to develop data finding.* EPA believes that testing of 2,6-dimethylphenol is necessary to develop data for neurotoxicity, pharmacokinetics and metabolism, reproductive effects, developmental effects, mutagenic effects, algal toxicity, fathead minnow chronic toxicity, daphnid chronic toxicity, aerobic biodegradation, anaerobic biodegradation, and aqueous photolysis. EPA believes that these testing data are needed to determine if the manufacturing, processing, distribution, use, or disposal of 2,6-dimethylphenol or any combination of such activities, does or does not present an unreasonable risk of injury to health or the environment.

#### IV. Issues for Comment

In addition to any relevant, general comments on the chemicals and proposed testing in this rulemaking, EPA would appreciate comments on the following specific issues:

1. EPA is proposing subchronic testing of acetophenone by the inhalation route of exposure. EPA is soliciting comment on the feasibility of inhalation testing given acetophenone's known irritant properties. If inhalation testing is not feasible, should EPA require subchronic testing by the oral route given the, at best, marginally acceptable nature of the existing oral studies?

2. In this rule, EPA is only proposing to require first tier mutagenicity testing at this time. For purposes of this rulemaking, EPA solicits comments on the appropriateness of these tests and its decision to defer higher tier mutagenicity testing and oncogenicity testing pending the receipt of first tier results.

3. EPA is also soliciting comments on the proposed toxicokinetics and biodegradation in natural surface water guidelines, which are proposed to be incorporated by reference.

#### V. Economic Analysis of the Proposed Rule

EPA has prepared an economic analysis that evaluates the potential for significant economic impacts as a result of the testing proposed in this notice (Ref. 101). Total costs of testing, including both laboratory costs and administrative costs, are as follows: acetophenone—\$1.3 to 2.0 million; phenol—\$1.5 to 2.4 million; *N,N*-dimethylaniline—\$1.4 to 2.2 million; ethyl acetate—\$0.8 to 1.2 million; and 2,6-dimethylphenol—\$1.2 to 1.7 million.

Total costs of testing for each chemical have been annualized and compared with annual revenues as an indication of potential economic impact. Annualized costs, calculated over 15 years using a 7 percent discount rate, represent the equivalent constant costs which would have to be recouped each year of the payback period to finance the testing expenditure in the first year.

On the basis of these calculations, EPA believes that for phenol, ethyl acetate and 2,6-dimethylphenol there is no potential for adverse economic impact. Because these three chemicals have relatively large production volumes, the annualized costs of testing, expressed as a percentage of annual revenue, are very small—ranging from 0.2- to 0.13 percent. Costs of testing are therefore found to be insignificant relative to revenues for these three chemicals.

For the remaining two chemicals—acetophenone and *N,N*-dimethylaniline—there may be some potential for adverse economic impacts due to the proposed testing. Because these two chemicals are produced in smaller quantities than the other three chemicals subject to this proposed rule, costs of testing as a percentage of revenues are higher—ranging from approximately 2- to 4 percent. Costs of testing may therefore be significant relative to revenues for acetophenone and *N,N*-dimethylaniline.

#### VI. Availability of Test Facilities and Personnel

EPA believes that test facilities and personnel are available to perform the testing specified in this proposed rule. (Ref. 111).

#### VII. Public Meeting

If requested, EPA will hold a public meeting in Washington, DC after the close of the public comment period. Persons who wish to attend or to present comments at the meeting should contact Mary Louise Hewlett, Chemical Testing Branch (202) 260-8162 by January 6, 1994. The meeting will be open to the public, but active participation will be limited to those who requested to comment and EPA representatives. Participants are requested to submit copies of their statements by the meeting date. These statements and a transcript of the meeting will become part of EPA's rulemaking record.

#### VIII. Comments Containing Confidential Business Information

All comments will be placed in the public file unless they are clearly

labeled as Confidential Business Information (CBI) when they are submitted. While a part of the record, CBI comments will be treated in accordance with 40 CFR part 2. A sanitized version of all CBI comments must be submitted to EPA for inclusion in the public file.

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

#### IX. Rulemaking Record

EPA has established a record for this rulemaking (docket number OPPTS-42150). 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 the record, from which all information claimed as CBI has been deleted, is available for inspection in the TSCA Nonconfidential Information Center, also known as the TSCA Public Docket Office, East Tower, Rm. G-102, 401 M St., SW., Washington, DC 20460, from 8 a.m. to noon, and 1 p.m. to 4 p.m., Monday through Friday, except legal holidays.

The record includes the following information:

##### A. Supporting Documentation

(1) Notice containing the ITC designation.

(2) Federal Register notices pertaining to this rule consisting of:

(a) "Twenty-seventh Report of the Interagency Testing Committee to the Administrator; receipt of report and request for comments regarding priority list of chemicals." (March 6, 1991, 56 FR 9534).

(b) Notice of final rule on EPA's TSCA Good Laboratory Practice Standards (54 FR 34034, August 17, 1989).

(c) Notice of final rule on data reimbursement policy and procedures (48 FR 31786, July 11, 1983).

- (d) Notice of proposed test rule on chloromethane and chlorinated benzenes (45 FR 48524, July 18, 1980).
- (e) Notice of proposed test rule on dichloromethane, nitrobenzene and 1,1,1 trichloroethane (46 FR 30300, June 5, 1981).
- (f) Notice of final test rule on the C9 aromatic hydrocarbon fraction (50 FR 20662, May 17, 1985).
- (g) Notice of proposed TSCA section 4(a)(1)(B) statement of policy (56 FR 32294, July 15, 1991).
- (h) Notice of final TSCA section 4(a)(1)(B) statement of policy (58 FR 28736, May 14, 1993).
- (i) Notice of proposed test rule on glycidol and its derivatives category (56 FR 57144, November 7, 1991).
- (j) Notice of testing consent order for acrylic acid (57 FR 7656, March 4, 1992).
- (3) TSCA test guidelines cited as test standards for this rule.
- (4) Communications consisting of:
- Written letters.
  - Contact reports of telephone conversations
  - Meeting summaries.
- B. References**
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- (112) NTP (National Toxicology Program). Teratologic evaluation of phenol in CD mice. Prepared by Research Triangle Institute, Research Triangle Park, NC. NTIS PB85-104461 (July 29, 1983).
- (113) USEPA. Memorandum from Andrea Blaschka and John Schaeffer to the Workgroup scheduling a meeting with the Phenol Panel to discuss pharmacokinetic testing for phenol. CMA's Phenol Panel comments to the ITC Report and a protocol for pharmacokinetic testing for phenol are attached. Washington, DC, Office of Pollution Prevention and Toxics, USEPA (April 24, 1991).
- (114) USEPA. Memorandum from Andrea Blaschka and John Schaeffer to the Workgroup summarizing the results of the meeting with the Phenol Panel on 4/24/91 and a request for comments on pharmacokinetic protocols. Washington, DC, Office of Pollution Prevention and Toxics, USEPA (May 9, 1991).
- (115) USEPA. Memorandum from Andrea Blaschka to the Workgroup summarizing the meeting held on 11/7/91 and requesting comments on further testing. Washington, DC, Office of Pollution Prevention and Toxics, USEPA (November 22, 1991).
- (116) USEPA. Discharge of N,N-dimethylaniline and 2,6-dimethylphenol to saline surface waters. Memorandum from Sid Abel, Exposure Evaluation Division to John Schaeffer, Chemical Testing Branch. Washington, DC, Office of Toxic Substances, USEPA (April 15, 1992).
- (117) Elliger, C.A., Henika, P.R., and MacGregor, J.T. "Mutagenicity of flavones, chromones and acetophenones in *Salmonella typhimurium*: New structure-activity relationships." *Mutation Research*. 135:77-86 (1984).

## X. Regulatory Assessment Requirements

### A. Executive Order 12291

Under Executive Order 12291, EPA must judge whether a rule is "major" and therefore subject to the requirement of a Regulatory Impact Analysis. EPA has determined that this proposed test rule would not be major because it does not meet any of the criteria set forth in section 1(b) of the Order; i.e., it would not have an annual effect on the economy of at least \$100 million, would not cause a major increase in prices, and would not have a significant adverse effect on competition or the ability of U. S. enterprises to compete with foreign enterprises.

This proposed rule was submitted to the Office of Management and Budget (OMB) for review as required by Executive Order 12291. Any written comments from OMB to EPA, and any EPA response to those comments, are included in the rulemaking record.

### B. Regulatory Flexibility Act

Under the Regulatory Flexibility Act (5 U.S.C. 601 et seq.) EPA is certifying that this test rule, if promulgated, would not have a significant impact on a substantial number of small businesses because: (1) They would not be expected to perform testing themselves, or to participate in the organization of the testing effort; (2) they would experience only very minor costs, if any, in securing exemption from testing requirements; and (3) they are unlikely to be affected by reimbursement requirements.

### C. Paperwork Reduction Act

OMB has approved the information collection requirements contained in this rule under the provisions of the Paperwork Reduction Act of 1980, 44 U.S.C. 3501 et seq., and has assigned OMB Control number 2070-0033.

Public reporting burden for this collection of information is estimated to average 10,100 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. The total public reporting burden is estimated to be 222,000 hours for all responses. Send comments regarding the burden estimate or any other aspect of this collection of information,

including suggestions for reducing this burden, to Chief, Information Policy Branch, 2131, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460; and to the Office of Management and Budget, Paperwork Reduction Project (2070-0033), Washington DC 20503. The final rule will respond to any OMB or public comments on the information collection requirements contained in this proposal.

#### List of Subjects in 40 CFR Part 799

Environmental protection, Chemicals, Hazardous substances, Reporting and recordkeeping requirements, Testing, Incorporation by reference.

Dated: November 15, 1993.

Victor J. Kimm,

Acting Assistant Administrator for Prevention, Pesticides and Toxic Substances.

Therefore, it is proposed that 40 CFR, chapter I, subchapter R, part 799 be amended as follows:

#### PART 799—[AMENDED]

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

Authority: 15 U.S.C. 2601, 2603, 2611, 2625.

b. By adding § 799.4450 to subpart B to read as follows:

#### § 799.4450 Designated IRIS chemicals.

##### (a) Identification of test substances.

(1) The IRIS chemicals subject to this test guideline were designated in the Twenty-Seventh ITC report. These chemicals include acetophenone (CAS No. 98-86-2), phenol (CAS No. 108-95-2), *N,N*-dimethylaniline (CAS No. 121-69-7), ethyl acetate (CAS No. 141-78-6), and 2,6-dimethylphenol (CAS No. 576-26-1).

(2) Acetophenone, phenol, *N,N*-dimethylaniline, ethyl acetate, and 2,6-dimethylphenol of at least 99 percent purity shall be used as the test substance.

##### (b) Persons required to submit study plans, conduct tests and submit data.

All persons who manufacture (including import) or process or intend to manufacture or process acetophenone, phenol, *N,N*-dimethylaniline, ethyl acetate, and 2,6-dimethylphenol other than as an impurity, after January 5, 1994, to 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 for single-phase rulemaking, for the substances they manufacture subject

to exclusions contained in § 790.42(a)(2), (a)(4) and (a)(5). These sections provide that processors, persons who manufacture less than 500 kg (1,100 lbs) annually, or persons who manufacture small quantities of the chemical solely for research and development as defined in § 790.42(a)(5) shall not be required to submit study plans, conduct tests and submit data, or submit exemption applications as specified in this section unless directed to do so in a subsequent notice as set forth in § 790.48(b).

##### (c) Health effects—(1) Subchronic toxicity—(i) Required testing.

Subchronic toxicity testing shall be conducted by inhalation with acetophenone, phenol, and *N,N*-dimethylaniline in accordance with § 798.2450 of this chapter.

(ii) Reporting requirements. (A) The required subchronic toxicity test shall be completed and the final reports submitted to EPA within 18 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

##### (2) Pharmacokinetics and metabolism—(i) Required testing. (A)

Pharmacokinetics and metabolism studies shall be conducted with acetophenone, phenol, *N,N*-dimethylaniline, and 2,6-dimethylphenol by the oral route of administration in accordance with OECD test guideline 417

“Toxicokinetics”, which is incorporated by reference. Copies of this guideline are available in the TSCA

Nonconfidential Information Center, East Tower, Rm. G-102, 401 M St., SW., Washington, DC 20460. This guideline is also available for public inspection at the Office of the Federal Register, 800 North Capital St., Suite 700, Washington, DC. 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 guideline is incorporated as it exists on the date of approval and a notice of any changes to the guideline will be published in the Federal Register.

(B) Pharmacokinetics and metabolism studies shall be conducted with acetophenone, phenol, *N,N*-dimethylaniline, and 2,6-dimethylphenol by the inhalation route of administration in accordance with OECD test guideline 417

“Toxicokinetics”, which is incorporated by reference. Copies of this guideline are available in the TSCA

Nonconfidential Information Center, East Tower, Rm. G-102, 401 M St., SW., Washington, DC 20460. This guideline is available for public inspection at the Office of the Federal Register, 800 North Capital St., Suite 700, Washington, DC. 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 guideline is incorporated as it exists on the date of approval and a notice of any changes to the guideline will be published in the Federal Register.

(ii) Reporting requirements. (A) The required pharmacokinetics and metabolism studies shall be completed and the final reports submitted to EPA within 15 months after the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(3) Neurotoxicity (Inhalation)—(i) Required testing—(A) Functional observational battery. (1) Functional observational battery tests shall be conducted with acetophenone, phenol, and *N,N*-dimethylaniline in accordance with § 798.6050 of this chapter except for the provisions in paragraphs (d)(4)(ii), (d)(5), and (d)(6) of § 798.6050.

(2) For the purpose of paragraph (c)(3)(i)(A) of this section, the following provisions also apply:

(i) Lower doses. Either the data from the lower doses shall show graded dose-dependent effects or there shall be no neurotoxic (behavioral) effects at any dose tested.

(ii) Duration and frequency of exposure. For the acute testing, animals shall be exposed for 6 hours per day for 1 day. For the subchronic testing, animals shall be exposed for 6 hours per day 5 consecutive days per week for a 90-day period.

(iii) Route of exposure. Animals shall be exposed to acetophenone, phenol, and *N,N*-dimethylaniline by inhalation administration.

(B) Motor activity. (1) Motor activity testing shall be conducted with acetophenone, phenol, and *N,N*-dimethylaniline in accordance with § 798.6200 of this chapter except for the provisions in paragraphs (d)(4)(ii), (d)(5), and (d)(6) of § 798.6200.

(2) For the purpose of paragraph (c)(3)(i)(B) of this section, the following provisions also apply:

(i) Lower doses. Either the data from the lower doses shall show graded dose-dependent effects or there shall be no neurotoxic (behavioral) effects at any dose tested.

(ii) *Duration and frequency of exposure.* For the acute testing, animals shall be treated for 6 hours per day for 1 day. For the subchronic testing, animals shall be exposed 6 hours per day 5 consecutive days per week for a 90-day period.

(iii) *Route of exposure.* Animals shall be exposed to acetophenone, phenol, and *N,N*-dimethylaniline by inhalation administration.

(C) *Neuropathology.* (1) Neuropathology testing shall be conducted with acetophenone, phenol, and *N,N*-dimethylaniline in accordance with § 798.6400 of this chapter except for the provisions in paragraphs (d)(4)(ii), (d)(5), (d)(6) and (d)(8)(iv)(C) of § 798.6400.

(2) For the purpose of paragraph (c)(3)(i)(C) of this section, the following provisions also apply:

(i) *Lower doses.* Either the data from the lower doses shall show graded dose-dependent effects or there shall be no neurotoxic (behavioral) effects at any dose tested.

(ii) *Duration and frequency of exposure.* For the acute testing, animals shall be exposed for 6 hours per day for 1 day. For the subchronic testing, animals shall be exposed for 6 hours per day 5 consecutive days per week for a 90-day period.

(iii) *Route of exposure.* Animals shall be exposed to acetophenone, phenol, and *N,N*-dimethylaniline by inhalation administration.

(iv) *Clearing and embedding.* After dehydration, tissue specimens shall be cleared with xylene and embedded in wax or plastic medium, except for the sural nerve, which should be embedded in plastic. Multiple tissue specimens (e.g. brain, cord, ganglia) may be embedded together in one single block for sectioning. All tissue blocks shall be labelled to provide unequivocal identification. Plastic embedding should follow the method described by Spencer, et al., in § 798.6400(f) of this chapter, or an equivalent method.

(ii) *Reporting requirements.* (A) The functional observational battery, motor activity, and neuropathology testing with acetophenone, phenol, and *N,N*-dimethylaniline shall be completed and the final reports submitted to EPA within 21 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(4) *Neurotoxicity (Gavage)—(i) Required testing—(A) Functional observational battery.* (1) A functional observational battery test shall be

conducted with 2,6-dimethylphenol in accordance with § 798.6050 of this chapter except for the provisions in paragraphs (d)(4)(ii), (d)(5), and (d)(6) of § 798.6050.

(2) For the purpose of paragraph (c)(4)(i)(A) of this section the following provisions also apply:

(i) *Lower doses.* Either the data from the lower doses shall show graded dose-dependent effects or there shall be no neurotoxic (behavioral) effects at any dose tested.

(ii) *Duration and frequency of exposure.* For the acute testing, animals shall be treated once. For the subchronic testing, animals shall be treated 5 consecutive days per week for a 90-day period.

(iii) *Route of exposure.* Animals shall be exposed to 2,6-dimethylphenol by gavage administration.

(B) *Motor activity.* (1) Motor activity testing shall be conducted with 2,6-dimethylphenol in accordance with § 798.6200 of this chapter except for the provisions in paragraphs (d)(4)(ii), (d)(5), and (d)(6) of § 798.6200.

(2) For the purpose of paragraph (c)(4)(i)(B) of this section, the following provisions also apply:

(i) *Lower doses.* Either the data from the lower doses shall show graded dose-dependent effects or there shall be no neurotoxic (behavioral) effects at any dose tested.

(ii) *Duration and frequency of exposure.* For the acute testing, animals shall be treated once. For the subchronic testing, animals shall be treated 5 consecutive days per week for a 90-day period.

(iii) *Route of exposure.* Animals shall be exposed to 2,6-dimethylphenol by gavage administration.

(C) *Neuropathology.* (1) Neuropathology testing shall be conducted with 2,6-dimethylphenol in accordance with § 798.6400 of this chapter except for the provisions in paragraphs (d)(4)(ii), (d)(5), (d)(6) and (d)(8)(iv)(C) of § 798.6400.

(2) For the purpose of paragraph (c)(4)(i)(C) of this section, the following provisions also apply:

(i) *Lower doses.* Either the data from the lower doses shall show graded dose-dependent effects or there shall be no neurotoxic (behavioral) effects at any dose tested.

(ii) *Duration and frequency of exposure.* For the acute testing, animals shall be treated once. For the subchronic testing animals shall be treated 5 consecutive days per week for a 90-day period.

(iii) *Route of exposure.* Animals shall be exposed to 2,6-dimethylphenol by gavage administration.

(iv) *Clearing and embedding.* After dehydration, tissue specimens shall be cleared with xylene and embedded in wax or plastic medium, except for the sural nerve, which should be embedded in plastic. Multiple tissue specimens (e.g. brain, cord, ganglia) may be embedded together in one single block for sectioning. All tissue blocks shall be labelled to provide unequivocal identification. Plastic embedding should follow the method described by Spencer, et al., in paragraph (f) of § 798.6400 of this chapter, or an equivalent method.

(ii) *Reporting requirements.* (A) The functional observational battery, motor activity, and neuropathology testing with 2,6-dimethylphenol shall be completed and the final reports submitted to EPA within 21 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(5) *Reproductive toxicity—(i) Required testing.* Reproductive toxicity testing shall be conducted with acetophenone, *N,N*-dimethylaniline, ethyl acetate, and 2,6-dimethylphenol by gavage, and phenol by inhalation in accordance with § 798.4700 of this chapter.

(ii) *Reporting requirements.* (A) The reproductive toxicity tests shall be completed and the final reports submitted to EPA within 29 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section.

(6) *Developmental toxicity—(i) Required testing.* Developmental toxicity testing in two species, a rat and a non-rodent, shall be conducted with acetophenone by inhalation, and *N,N*-dimethylaniline, ethyl acetate, and 2,6-dimethylphenol by gavage in accordance with § 798.4900 of this chapter.

(ii) *Reporting requirements.* (A) The developmental toxicity testing shall be completed and the final reports submitted to EPA within 12 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(7) *Developmental neurotoxicity—(i) Required testing.* Developmental neurotoxicity testing in the rat shall be

conducted with phenol by gavage administration in accordance with § 795.250 of this chapter.

(ii) *Reporting requirements.* (A) The developmental toxicity testing shall be completed and the final report submitted to EPA within 21 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(8) *Mutagenic effects—gene mutation*—(i) *Required testing.* (A) Gene mutation assays in the *Salmonella typhimurium* histidine reversion system shall be conducted with acetophenone in accordance with § 798.5265 of this chapter.

(B) Gene mutation assays in somatic cells in culture shall be conducted with acetophenone, ethyl acetate, and 2,6-dimethylphenol in accordance with § 798.5300 of this chapter.

(ii) *Reporting requirements.* Mutagenic effects—gene mutation tests shall be conducted and the final reports submitted to EPA as follows:

(A) Gene mutation in *Salmonella*, 9 months after the effective date in paragraph (f) of this section.

(B) Gene mutation in somatic cells in culture, 10 months after the effective date in paragraph (f) of this section.

(9) *Mutagenic effects—chromosomal aberrations* — (i) *Required testing.* *In vivo* cytogenetic assays shall be conducted by gavage with acetophenone, *N,N*-dimethylaniline, and 2,6-dimethylphenol in accordance with §§ 798.5385 or 798.5395 of this chapter.

(ii) *Reporting requirements.* (A) Mutagenic effects - *In vivo* cytogenetics testing shall be completed and the final reports submitted to EPA within 14 months after the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section.

(d) *Environmental effects* —(1) *Algal toxicity testing* — (i) *Required testing.* Algal toxicity testing shall be conducted with *N,N*-dimethylaniline and 2,6-dimethylphenol in accordance with § 797.1050 of this chapter.

(ii) *Reporting requirements.* (A) The algal toxicity test for *N,N*-dimethylaniline and 2,6-dimethylphenol shall be completed and the final reports submitted to EPA within 12 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6

months after the effective date in paragraph (f) of this section until the final report is submitted.

(2) *Invertebrate acute toxicity* — (i) *Required testing.* (A) Daphnid acute toxicity tests shall be conducted with *N,N*-dimethylaniline and 2,6-dimethylphenol in accordance with § 797.1300 of this chapter.

(B) Mysid shrimp acute toxicity tests shall be conducted with *N,N*-dimethylaniline in accordance with § 797.1930 of this chapter.

(ii) *Reporting requirements.* (A) Invertebrate acute toxicity testing shall be conducted and the final reports submitted to EPA within 12 months after the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(3) *Invertebrate chronic toxicity testing* —(i) *Required testing.* (A) Daphnid chronic toxicity tests shall be conducted with *N,N*-dimethylaniline and 2,6-dimethylphenol in accordance with § 797.1330 of this chapter.

(B) Mysid shrimp chronic toxicity tests shall be conducted with *N,N*-dimethylaniline in accordance with § 797.1950 of this chapter.

(ii) *Reporting requirements.* (A) Invertebrate chronic toxicity testing shall be conducted and the final reports submitted to EPA within 24 months after the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(4) *Fish chronic toxicity* —(i) *Required testing.* Fish early life stage toxicity tests shall be conducted with fathead minnows with *N,N*-dimethylaniline and 2,6-dimethylphenol, and sheepshead minnows with *N,N*-dimethylaniline, in accordance with § 797.1600 of this chapter.

(ii) *Reporting requirements.* (A) Fish early life stage toxicity tests shall be completed and the final reports submitted to EPA within 12 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(e) *Chemical fate*—(1) *Biodegradation in natural surface waters* —(i) *Required testing.* (A) Biodegradation testing in natural surface waters shall be conducted with 2,6-dimethylphenol.

(B) The testing shall be conducted in accordance with the test procedure specified in the American Society for Testing and Materials (ASTM) test method, entitled "Standard Test Method for Biodegradation By a Shake-Flask DieAway Method, Designation: E 1279-89," published in the Annual Book of ASTM Standards, March 1989, Philadelphia, Pa., which is incorporated by reference. Copies of this test method are available in the TSCA Nonconfidential Information Center, East Tower, Rm. G-102, 401 M St., SW., Washington, DC 20460. This test method is also available for inspection at the Office of the Federal Register, 800 North Capital St., Suite 700, Washington, DC. 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 method is incorporated as it exists on the date of approval and a notice of any changes to the method will be published in the Federal Register.

(ii) *Reporting requirements.* (A) The biodegradation test in natural surface waters shall be completed and the final reports submitted to EPA within 12 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(2) *Biodegradation in activated sludge* — (i) *Required testing.* Biodegradation testing in activated sludge shall be conducted with *N,N*-dimethylaniline in accordance with § 796.3340 of this chapter.

(ii) *Reporting requirements.* (A) The biodegradation test in activated sludge shall be completed and the final report submitted to EPA within 12 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in paragraph (f) of this section until the final report is submitted.

(3) *Anaerobic biodegradation* — (i) *Required testing.* Anaerobic biodegradation testing shall be conducted with *N,N*-dimethylaniline and 2,6-dimethylphenol in accordance with § 796.3140 of this chapter.

(ii) *Reporting requirements.* (A) The required anaerobic biodegradation testing shall be completed and the final report submitted to EPA within 12 months of the effective date in paragraph (f) of this section.

(B) Progress reports shall be submitted to EPA every 6 months beginning 6 months after the effective date in