ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 799

[OPTS-42061A; FRL-3130-8(a)]

Oleylamine; Testing Requirements

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final Rule.

SUMMARY: EPA is issuing a final rule under section 4(a) of the Toxic Substances Control Act (TSCA) requiring manufacturers and processors of oleylamine (9-octadecenylamine or ODA, CAS Number 112-90-3) to test this chemical for developmental toxicity, and for mutagenicity using a two-tiered scheme. The need for third-tier mutagenicity and for oncogenicity testing will be determined by EPA following a public program review of data. EPA is terminating rulemaking for the proposed 90-day dermal subchronic testing which was to include neurobehavioral observations, emphasis on reproductive system histopathology, and a dermal absorption determination. The substance, 9-octadecenylamine, will be referred to in this document as "ODA", and the term "oleylamine" will refer to commercial fatty amine mixtures containing 65 to 76 percent ODA. Proposed standards for testing ODA appear elsewhere in this issue of the Federal Register.

DATES: In accordance with 40 CFR 23.5, this rule shall be promulgated for purposes of judicial review at 1 p.m. eastern ["daylight" or "standard" as appropriate] time on September 8, 1987. This rule shall become effective on October 7, 1987.

FOR FURTHER INFORMATION CONTACT: Edward Klein, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Rm. E-543, 401 M St., SW., Washington, DC 20460, (202-554-1404).

SUPPLEMENTARY INFORMATION: The EPA is promulgating a final rule to require the testing of ODA for developmental toxicity, mutagenicity, and oncogenicity if certain mutagenicity test results are positive. EPA will conduct a public program review before requiring initiation of the top-tier mutagenicity tests or oncogenicity test.

I. Introduction

This document is part of the overall implementation of section 4 of the Toxic Substances Control Act (TSCA, Pub. L. 94-469, 90 Stat. 2003 *et seq.*, 15 U.S.C. 2601 *et seq.*), which contains authority for EPA to require development of data relevant to assessing the risks to health and the environment posed by exposure to particular chemical substances or mixtures.

Under section 4(a)(1) of TSCA, EPA must require testing of a chemical substance to develop health or environmental data if the Agency finds that:

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

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

(iii) testing of such substance or mixture with respect to such effects is necessary to develop such data; or

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

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

(iii) testing of such substance or mixture with respect to such effects is necessary to develop such data.

For a more complete understanding of the statutory section 4 findings, the reader is directed to the Agency's first proposed testing rule package (chloromethane and chlorinated benzenes, published in the Federal Register of July 18, 1980 [45 FR 48510]) and to the second package (dichloromethane, nitrobenzene, and 1,1,1-trichloroethane, published in the Federal Register of June 5, 1981 [46 FR 30300]) for in-depth discussions of the general issues applicable to this section.

II. Background

A. Profile

ODA (CAS Number 112-90-3) is a yellow liquid with an ammoniacal odor. Typical fatty amine mixtures (67 percent ODA) have a boiling range of 275-334 °C at 760 mm Hg and a specific gravity of 0.819 at 39 °C. ODA's solubility in water is estimated to be 0.5×10^{-3} mg/l or less at 20 °C, its estimated vapor pressure is $0.5 \times^{-4}$ mm Hg at 10 °C and its esimated log P (octanol-water partition coefficient) ranges from 7.5 to 8.1 (Ref. 1). The formula of 9-octa-decenylamine is as follows:

$$CH_3(CH_2)_7CH=CH(CH_2)_7CH_2NH_2$$

The U.S. International Trade Commission (USITC) reported 1982 ODA production to be 4.952 million pounds (Ref. 2). This production figure is for fatty amine mixtures called oleylamine by the producers. EPA estimated that the ODA contained in all the fatty amine mixtures produced in 1982 amounted to between 18 and 29 million pounds (Ref. 21). In 1984, the USITC reported ODA production to be 6.643 million pounds (Ref. 3). ODA is produced at nine sites by six firms: Akzo Chemie America; Witco Chemical Corp.; Jetco Chemicals, Inc.; Sherex Chemical Company, Inc.; Borg-Warner Corp.; and Tomah Products, Inc. Akzo uses a continuous reaction process and the others use closed-batch reactors. Akzo produces over 50 percent of the total U.S. production. ODA's major use in which human exposure is probable is as an additive to petroleum lubricants or as an intermediate for such additives. It is also used in a collector agent in ore flotation, in asphalt preparation, in a concrete mold release agent, and in the manufacture of paper, paperboard, and glues. For a more detailed discussion of properties, production, uses, and exposure of oleylamine and other ODA-containing mixtures, see the oleylamine support document available from the TSCA Assistance Office (Ref. 1).

B. ITC Recommendations

In the Thirteenth Report of the Interagency Testing Committee (ITC), published in the Federal Register of December 14, 1983, the ITC designated ODA for priority consideration for a staged testing program, beginning with toxicokinetics and then testing for mutagenicity and teratogenicity if percutaneous absorption is demonstrated.

C. Proposed Rule

EPA issued a proposed rule published in the Federal Register of November 19, 1984 (49 FR 45610), requiring, for ODA, oral developmental toxicity testing, a tiered mutagenicity testing scheme with capacity to trigger oncogenicity testing, and a 90-day dermal subchronic test which would include neurobehavioral observations, emphasis on reproductive system histopathology, and a dermal absorption determination.

The test requirements based on the authority of section 4(a)(1)(A) and (B) of TSCA were proposed in 40 CFR 799.3300 and are being recodified as 40 CFR 799.3175.

Under the authority of section 4(a)(1)(A), EPA made a proposed finding that the use of ODA may present an unreasonable risk to human health from developmental toxicity. This was based on available animal studies (Refs. 4 through 9) suggesting that oleylamine may cause such effects and on the potential exposure of approximately 2.8 million mechanics and others in related trades (Ref. 10).

Under the authority of section 4(a)(1)(B), EPA made the proposed findings that oleylamine is produced in substantial quantitites (EPA estimate of 18 to 29 million pounds per year), and that there is substantial exposure to this substance (approximately 2.8 million workers) (Ref. 10).

EPA found that there were insufficient data available to resonably determine or predict the effects of this exposure in the above-mentioned areas and that testing of ODA was necessary to develop such data.

The analysis and findings on which the above determinations were based are presented in the Oleylamine Support Document (Ref. 1), which is available from the Office of Toxic Substances' TSCA Assistance Office and in the public record for this rulemaking.

EPA did not propose an oncogenicity bioassay based on the section 4(a)(1)(B) finding because EPA considered the required mutagenicity tests an appropriate first tier for oncogenicity for this substance. However, EPA found that if certain of the required mutagenicity tests produced positive results, this would be sufficient to indicate that ODA may present an unreasonable risk of oncogenic effects. In such circumstances, EPA found that without data from a 2-year bioassay there would be insufficient data to predict oncogenicity, and testing would be necessary to develop oncogenicity data.

III. Public Comments

The Agency received comments from one source, the Oleylamine Program Panel of the Chemical Manufacturers Association (CMA). The comments addressed the proposed health effects testing requirements, data interpretation, human exposure, test substance concentration, and economics.

A. Health Effects Testing

The Panel commented that a 28-day dermal toxicity test is adequate to screen for potential subchronic effects. The Panel also believes that associated neurobehavioral and reproductive system testing is not needed. EPA is no longer requiring these tests (see Unit IV.).

The Panel commented that there is no need for a developmental toxicity study because exposure is not as high as EPA initially indicated, only 2,000 mechanics are women (Ref. 10), and because animal studies by Eifinger and Koehler and Bio/dynamics (Refs. 4 through 9) do not support it. Although EPA has adjusted the ODA human exposure figure downward (some potential exposure groups were double counted) to approximately 2 million (Ref. 10), mechanics and people in related trades, of whom approximately 27,000 are women, are still potentially exposed. EPA still believes that there is sufficient information to indicate that oleylamine may produce developmentally toxic effects (see Unit V.A). However, the data are insufficient to adequately characterize this potential, and appropriate testing is needed to do so.

The Panel commented that should EPA require a development toxicity study of ODA, the dermal rather than oral route should be used because human contact is expected to be dermal, however, if the oral route is required, ODA should be incorporated in the feed rather than given by gavage. The Panel maintained that a feeding study would decrease the effect of bolus administration by gavage and would also eliminate the additional stress factor which gavage introduces. EPA believes the oral route is the most appropriate because there is a sufficient data base by which to evaluate the results of oral developmental toxicity study and insufficient dermal data. Also, the corrosive effect of the dermal application of ODA may cause developmental toxicity because of stress thereby produced. The oral route via diet such as in the feed will be an acceptable means of exposure provided the test sponsor can accurately document the amount of ODA consumed daily.

The Panel commented that the National Institute for Occupational Safety and Health conducted a Health Hazard Evaluation in 1979 (Ref. 11) of one of Akzo's plants which showed no excessive number of deaths due to cance or heart disease. EPA does not agree with the Panel that the study alleviates concern for ODA's effects, but instead agrees with the author of the survey that serious limitations in the data, including few deaths and incompleness of personnel records, preclude any definitive conclusions.

The Panel commented that any question of oncogenicity testing should be deferred until after the results of the mutagenicity tests have been reviewed and discussed. EPA agrees that the decision to initiate the oncogenicity study (if triggered by positive results in one or more of the specified mutagenicity tests) should await the outcome of all of the second tier mutagenicity testing and a program review; EPA has included this step in the final rule.

The Panel commented that the developmental toxicity study should be conducted on only one species because some developmental effects data are available. EPA has reviewed the data referred to by the Panel and concludes they indicate the possibility of developmental effects as a result of exposure to oleylamine but are not adequate to characterize ODA's developmental toxicity in the species tested. The TSCA test guidelines require that the developmental toxicity study be performed on at least two mammalian species.

The Panel commented that a negative *in vitro* cytogenetics assay need not be followed by an *in vivo* mammalian bone marrow cytogenetics test to determine chromosomal aberration. This judgment is based on a review of the literature which the Panel contends shows that no chemical testing negatively in an *in vitro* mammalian cytogenetics assay has been found positive in *in vivo* cytogenetics tests. EPA has in past section 4 test rules included both *in vitro* and *in vivo* cytogenetics testing in its first tier of testing to maximize detection of potentially clastogenic agents, e.g., for cresols (51 FR 15771; April 28, 1986) and C_8 aromatic hydrocarbons (50 FR 20662; May 7, 1985). The Agency believes that the *in vitro* assay is subject to sufficient limitations, particularly in the use of *in vitro* metabolic activation systems, that a negative response, especially in cases of technical difficulties with the metabolic activation system or of erratic or narrowly-defined toxicity curves, should be confirmed in an *in vivo* test. The information presented by the Panel or otherwise available to the Agency is not sufficient to warrant a change in this view at this time.

The Panel commented that mouth rinse and toothpaste studies (Refs. 12 through 14) support their belief that ODA causes no long-term health effects. EPA believes that these human clinical trials, conducted to determine if mixtures of hydrofluorides of oleylamine and other amines could prevent the formation of caries and plaque, can not be used to determine ODA's toxic

potential. In general, toothpaste and/or mouthwash is in the mouth for relatively short periods of time whereupon the mouth is rinsed. The level of human exposure to oleylamine hydrofluoride in these clinical trials was possibly very low and in any case is unknown. Thus, even if these clinical trials were otherwise adequate, because of a lack of exposure data they can not be used to determine the toxicity that oleylamine may present.

The Panel commented that EPA did not use all available data in arriving at its testing decisions for ODA, was inconsistent in drawing conclusions, and used data in a biased way which leads to more testing. EPA did review all available data and found that, in all but the Eifinger and Koehler study (Ref. 4), the test substances were other than oleylamine, although some of these tests substances were closely related to ODA. Indeed, the Panel was especially critical of EPA's use of data on ODA analogs (Refs. 5 through 9, 27, and 28). However, EPA has been careful to distinguish between the use of analog data to suggest a potential concern and their use to determine that data are adequate. For example, dodecyldimethylamine oxide (DDAO), which can be considered analogous to ODA only for the purpose of qualitatively estimating its skin penetrating potential, has undergone rather extensive pharmacokinetic studies (Ref. 17). As part of the absorption profile, topical, radiolabeled doses of DDAO were applied to humans, rats, mice, and rabbits. The results indicate a fair degree of absorbtion in the lower mammal skins and an extremely poor degree of absorption in the human skin. The study is flawed, however, since the human exposure periods were only 11 percent of the total exposure periods for the rats, mice and rabbits. Nevertheless, the study did demonstrate the ability of DDAO to penetrate the human skin albeit very poorly. This is particularly significant since, by virtue of its polar nature, DDAO is less likely than oleylamine to penetrate human skin. Data on DDAO are not adequate to make quantitative inferences about ODA. For a quantitative analysis, specific skin penetration testing of ODA would be necessary.

The Panel commented that EPA incorrectly used the dermal absorption method of Scheuplein and Blank (Ref. 15) to estimate ODA's potential skin absorption by mechanics because: (1) Decanol rather than octanol should have been used as the model compound; (2) an alcohol rather than a water vehicle should have been assumed; and (3) hydrated abdominal skin as used in this method overstates absorption conditions for mechanics. EPA believes that the dermal absorption rate of ODA cannot be conclusively determined by the use of octanol or decanol as a model. For example, their use ignores the contribution of ODA's amine group to the skin penetration properties. A reliable absorption rate for ODA can be determined only by the use of ODA as the test substance. In any case, EPA is withdrawing the requirement of a dermal absorption test. The Agency plans to propose that a comparative oral-dermal absorption, distribution, metabolism, excretion assay be carried out for ODA. This proposal will be finalized if the developmental toxicity test required in this notice is positive.

The Panel commented that a skin-irritation test on rats conducted with ODA produced perceptible well-defined erythema with 0.3 percent ODA concentrations and severe sloughing with 1.5 percent ODA (Ref. 16). Because ODA concentrations in petroleum lubricants are approximately 0.3 to 1.0 percent (49 FR 45610; November 19, 1984), the Panel believes that the expected irritation would constitute an "early warning system" which would cause a mechanic to wash his hands at intervals or take other precautions precluding long-term exposure. EPA disagrees. In the 14-day test, the application sites were covered by gauze dressings which could have accentuated the erythema of the rats. Also, rat skin has been considered to be more permeable than human skin and, therefore, more readily irritated (Refs. 20 and 22). The Panel has not demonstrated that automotive mechanics and others exposed to petroleum lubricants experience erythema or sloughing and find it necessary to take precautionary measures. Even though humans may absorb less ODA and experience no erythema at the doses tested in the 14-day study, it is impossible to determine the potential toxic effects of does to which humans are exposed without further testing. However, EPA does believe that the 14-day study results do indicate the need to change the route of ODA administration in the oncogenicity test from dermal, as proposed in the Federal Register of November 19, 1984 (49 FR 45610), to oral to eliminate skin irritation as a complicating factor.

B. Test Substance Concentration

The Panel commented that EPA's belief that 97 percent ODA was available was in error, and that the test substance should be 90 percent ODA because the attainment of a higher ODA concentration is extremely difficult given the similarity of boiling points of the C_{18} alkylamines of which ODA is a member. EPA accepts the comment and agrees that not only would further concentration of ODA be extremely difficult, but 90 percent ODA is of sufficient purity to adequately test its properties. The Agency has thus modified this requirement in this final rule.

C. Economics

The Panel commented that total and annualized testing costs were incorrect. EPA based these costs on quotes by various testing laboratories. Cost ranges were given rather than specific costs because of uncertainty of the specific details of the testing protocols at the time of publication of the notice of proposed rulemaking (Ref. 18).

The Panel commented that EPA's belief that demand for ODA was sufficiently inelastic so that manufacturers could pass test costs to purchasers was incorrect. EPA based its belief on the following:

1. ODA is used as a component in many alkylamine products, thereby dispersing its demand over numerous end markets.

2. The alkylamine products which contain ODA tend to have relatively secure and specialized applications that are dictated by performance advantages/considerations in their markets.

3. Cationic surfactants, such as the alkylamines, normally are used in small amounts (e.g., between less than 1 and 10 percent) in relation to the weight of final products, thereby suggesting that they compose a minor share of actual end-product cost (Ref. 18).

The Agency believes this analysis is still correct, and therefore disagrees with the comment.

The Panel commented that EPA's estimated test costs are given in terms of 1983 dollars and are out of date. EPA considers this point to be well taken and has developed more recent figures which are found in Unit VI.

IV. Decision to Terminate Rulemaking Process for Subchronic Toxicity, Dermal Absorption, Neurobehavioral and Reproductive System Testing for ODA

In the proposed test rule for ODA (47 FR 45610; November 19, 1984), EPA included a 90-day dermal subchronic toxicity test. This test, in addition to the usual subchronic measurements, was to include dermal absorption, neurobehavioral observations, and emphasis on reproductive histopathology. Since this test was proposed, a 14-day dermal range-finding

rat study has been done with ODA by the Panel. The test showed erythema and sloughing at dosages of 12.5 to 61.5 mg/kg/day (Ref. 16). To produce systemic effects at levels below this, the material would have to be very potent. However, existing chronic data on mixtures containing ODA do not suggest such potency. Two-year studies on dogs and rats with oral administration of salts of ODA and an analog produced only minimal toxic effects and no specific organ effects (Refs. 27 and 28). Also, review of structural analog data by EPA does not suggest that oleylamine would be toxic at very low doses in repeated exposures for 90 days (Refs. 29 and 30). EPA believes that these data can be used to reasonably predict the systemic toxicity of ODA at levels to which humans are exposed. For these reasons, the Agency will no longer require the 90-day subchronic, dermal absorption, neurobehavioral, and reproductive tests and is hereby notifying the public of this decision. However, EPA remains concerned about the developmental, mutagenic, and oncogenic hazard potentials ODA may pose to human health and is requiring this testing as described below (see Unit V.).

V. Final Test Rule for ODA

A. Findings

EPA is basing the final testing requirements for ODA on the authority of section 4(a)(1) (A) and (B) of TSCA.

The section 4(a)(1)(A) findings for developmental toxicity are as follows:

EPA finds that the use of ODA may present an unreasonable risk of injury to human health from developmental toxicity because: (1) The available animal studies suggest that ODA has a developmental toxicity potential; and (2) approximately 2 million individuals in 1985 were potentially exposed to ODA as a result of its manufacture, processing, and use (Ref. 19).

EPA also finds that there are insufficient animal and human data to reasonably determine or predict the developmental toxicity of ODA and that testing is necessary to develop such data (49 FR 45610). The 4(a)(1)(A) finding of "may present an unreasonable risk" of developmental toxicity is based on available animal studies (Refs. 4 through 9) which suggest that oleylamine may cause such effects.

The section 4(a)(1)(B) findings, for developmental toxicity and a tiered mutagenicity testing scheme which may indicate the need for oncogenicity testing, are as follows:

ODA is produced in substantial quantities. The most recent production figure for oleylamine was reported by the USITC to be 6.643 million pounds in 1984 (Ref. 3). Production estimates by EPA for ODA, however, range from 18 to 29 million pounds for 1982 when the ODA portion of captive production as well as production of all commercial ODA-containing substances are taken into account. The estimated exposure of 2 million people in 1985 as a result of manufacture, processing, and use is clearly substantial (Ref. 19). EPA finds that there are insufficient animal and human data to reasonably determine or predict the developmental, mutagenic, or oncogenic effects of ODA and that testing is necessary to develop such data.

B. Required Testing

The Agency believes that an oral developmental toxicity study, a tiered oral (where applicable) mutagenicity testing scheme, and possibly oncogenicity testing should be conducted for ODA. The Oleylamine Program Panel of the Chemical Manufacturers Associations has voluntarily conducted mutagenicity tests consisting of the following: Ames assay, chromosomal aberration assay in Chinese hamster ovary cells, and CHO/HGRPT mutation assay in the presence of exogenous metabolic activation (Refs. 24 through 26). The Ames and chromosomal aberration assays are negative and satisfy these portions of the Agency's current first-tier mutagenicity test battery. The CHO/HGPRT mutation assay results are equivocal and a retest will be required in a different cell line (see Oleylamine: Proposed Test Standards elsewhere in today's Federal Register.) The assay provides some indication of genotoxicity, both without and with metabolic activation. Apparently because of the high toxicity of the chemical in this test system, the activity demonstrated was variable over different doses and over repeat tests, and even within repeats for replicate (parallel) cultures of the same dose point. No dose response was observed. This may be due to difficulties in precise dose application in nanoliter per milliliter concentrations. The mammalian cell gene mutation retest in a different cell line and the *in vivo* mammalian bone-marrow cytogenetics test will complete the first tier of the mutagenicity battery. If indicated by first-tier results, second-tier mutagenicity, consisting of a rodent dominant lethal assay for chromosomal aberrations, and/or a sex-linked recessive lethal assay in *Drosophila melanogaster* for gene mutations, must be conducted. The third tier of mutagenicity testing is conditional upon positive second-tier mutagenicity test results. The oncogenicity bioassay is conditional upon positive results in one or more of the following mutagenicity tests: *in vivo* mammalian bone marrow cytogenetics, detection of gene mutation in somatic cells in culture, and sex linked recessive test in *Drosophila melanogaster*. However, EPA will not require initiation of the third-tier mutagenicity test(s) or oncogenicity test until all second-tier mutagenicity tests have been completed and a public review of the data is held by EPA. Test sponsors will be notified by Federal Register notice or certified letter of third-tier mutagenicity and oncogenicity testing decisions. The route of administration of ODA in the oncogenicity test, if required, shall be oral as explained in Unit III.A. EPA is proposing test standards for these tests elsewhere in today's Federal Register. The tests are to be conducted in accordance with EPA's TSCA Good Laboratory Practices standards under 40 CFR Part 792.

Although the anticipated route of human exposure to ODA is dermal, the route required for testing is oral, for the reasons stated in Unit III.A. In such cases, EPA uses pharmacokinetic data to extrapolate between routes of exposure for risk assessment purposes. As these data are not available for ODA, the Agency intends to propose a comparative oral/dermal pharmacokinetics study for ODA after publication of this final rule.

C. Test Substance

EPA is requiring that ODA of at least 90.0 percent purity be used as the test substance. The vehicle should be one such as mineral oil for which there are historical toxicological data and which will not interfere with test results.

D. Persons Required To Test

Section 4(b)(3)(B) specifies that the activities for which the Agency makes section 4(a) findings (manufacturing, processing, distribution, use and/or disposal) determine who bears the responsibility for testing. Manufacturers are required to test if the findings are based on manufacturing ("manufacture" is defined in section 3(7) of TSCA to include "import"). Processors are required to test if the findings are based on processing. (Section 3(10) of TSCA, defines "process" as the preparation of a chemical substance or mixture, after its manufacture, for distribution in commerce.) Both manufacturers and processors are required to test if the exposures giving rise to the potential

risk occur during use, distribution, or disposal.

Because EPA has found that existing data are inadequate to assess health risks from the manufacture, processing and use of ODA, EPA is requiring that persons who manufacture or process, or who intend to manufacture or process ODA at any time from the effective date of this test rule to the end of the reimbursement period are subject to the testing requirements of this rule. The end of the reimbursement period will be 5 years after the submission of the final report required under the test rule. As discussed in the Agency's Test Rule Development and Exemption Procedures (40 CFR Part 790), EPA expects that manufacturers will conduct testing and that processors will ordinarily be exempted from testing.

Because TSCA contains provisions to avoid duplicative testing, not every person subject to this rule must individually conduct testing. Section 4(b)(3)(A) of TSCA provides that EPA may permit two or more manufacturers or processors who are subject to the rule to designate one such person or a qualified third person to conduct the tests and submit data on their behalf. Section 4(c) provides that any persons required to test may apply to EPA for an exemption from that requirement. The Agency expects that the current manufacturers of ODA will form the reimbursement pool and sponsor the testing required. Manufacturers and processors who are subject to the testing requirements of this rule must comply with the test rules and exemption procedures in 40 CFR Part 790.

Manufacturers (including importers) subject to this rule are required to submit either a letter or intent to perform testing or an exemption application within 30 days after the effective date of the final test rule. The required procedures for submitting such letters and applications are described in 40 CFR Part 790.

Processors subject to this rule, unless they are also manufacturers, will not be required to submit letters of intent or exemption applications, or to conduct testing, unless manufacturers fail to submit notices of intent to test or later fail to sponsor the required tests. The Agency expects that the manufacturers will pass an appropriate portion of the costs of testing on to processors through the pricing of their products or reimbursement mechanisms. If manufacturers perform all the required tests, processors will be granted exemptions automatically. If manufacturers fail to submit notices of intent to test or fail to sponsor all the required tests, the Agency will publish a separate notice in the Federal Register to notify processors to respond; this procedure is described in 40 CFR Part 790.

E. Test Rule Development and Exemptions

Elsewhere in this issue of the Federal Register, the Agency is proposing in a related document [OPTS-42061B] that TSCA test guidelines be utilized as the test standards for the development of data under this rule for ODA. As discussed in that document and in the Federal Register of May 17, 1985 (50 FR 20652), EPA has reviewed the method for the development of test rules and has decided that for most section 4 rulemakings, the Agency will utilize single-phase rulemaking. In light of this decision, EPA has reevaluated the process for developing test standards for section 4 rulemakings initiated under a two-phase process and has determined that for certain of these two-phase rules, TSCA test guidelines are available for promulgation as relevant test standards. EPA has decided that where TSCA or other appropriate test guidelines are available, the Agency in most cases will propose the relevant guidelines as the test standards for those rules.

EPA believes that, in line with its commitment to expedite the section 4 rulemaking process, it is appropriate to propose the applicable TSCA test guidelines as test standards at the same time as a Phase I final test rule is issued. With regard to the rulemaking for ODA, TSCA test guidelines are available for the testing requirements included in this Phase I final rule. Thus, in the accompanying document the Agency is proposing these TSCA test guidelines as test standards.

The public, including the manufacturers and processors subject to the Phase I rule, will have an opportunity to comment on the use of the TSCA test guidelines. The Agency will review the submitted comments and will modify the TSCA guidelines, where appropriate, when the test standards are promulgated.

During the development of the test rule under the two-phase process, persons subject to the Phase I final rule are normally required to submit proposed study plans (see 40 CFR 790.50(a)(2)). However, because EPA is proposing applicable TSCA test guidelines as the test standards for the studies required by this Phase I final rule, persons subject to the rule, i.e., manufacturers and processors of ODA, are not required to submit proposed study plans for the required testing. Persons subject to this rule, however, are still required to submit notices of intent to test or exemption applications in accordance with 40 CFR 790.45. Moreover, once the test standards are promulgated, persons who have notified EPA of their intent to test must submit study plans (which adhere to the promulgated test standards) no later than 45 days before the initiation of each required test. (See 40 CFR 790.50 (a)(1)).

Processors of ODA subject to this rule, unless they are also manufacturers, will not be required to submit letters of intent, exemption applications, or study plans (before testing is initiated) unless manufacturers fail to sponsor the required tests. The basis for this decision is that manufacturers are expected to pass an appropriate portion of the test costs on to processors through the pricing of products containing ODA.

EPA's final regulations for the issuance of exemptions from testing requirements are in 40 CFR Part 790. In accordance with those regulations, any manufacturer or processor subject to this Phase I test rule may submit an application to EPA for an exemption from conducting any or all of the tests required under this rule. If manufacturers perform all the required testing, processors will be granted exemptions automatically without having to file applications.

In the related Federal Register document, cited in the first paragraph of Unit V.E. and appearing elsewhere in this issue of the Federal Register, EPA is proposing deadlines for the submission of test data.

F. Reporting Requirements

EPA is requiring that all data developed under this rule be reported in accordance with the EPA Good Laboratory Practice (GLP) standards pursuant to 40 CFR Part 792.

EPA is required by TSCA section 4(b)(1)(C) to specify the time period during which persons subject to a test rule must submit test data. The Agency is proposing these deadlines in the related document appearing elsewhere in this issue of the Federal Register.

TSCA section 12(b) requires that persons who export or intend to export to a foreign country any substance subject to testing requirements under TSCA section 4 notify EPA of such exportation or intent to export. While the results of required testing may not be available for some time, a notice to the foreign government about the export of such substances subject to test rules serves to alert them to the Agency's concern about the substances. It gives these governments the opportunity to

request such data that the Agency may currently possess plus whatever data may become available as a result of testing activities. Thus, upon the effective date of this rule, persons who export or intend to export ODA must submit notices to the Agency pursuant to TSCA section 12(b)(1) and 40 CFR Part 707 (see 45 FR 82844; December 16, 1980).

TSCA section 14(b) governs Agency disclosure of all test data submitted pursuant to section 4 of TSCA. Upon receipt of data required by this rule, the Agency will announce the receipt within 15 days in the Federal Register as required by section 4(d). Test data received pursuant to this rule will be made available for public inspection by any person except in those cases where the Agency determines that confidential treatment must be accorded pursuant to section 14(b) of TSCA.

G. Enforcement Provisions

The Agency considers failure to comply with any aspect of a section 4 rule to be a violation of section 15 of TSCA. Section 15(1) of TSCA makes it unlawful for any person to fail or refuse to comply with any rule or order issued under section 4. Section 15(3) of TSCA makes it unlawful for any person to fail or refuse to: (1) Establish or maintain records; or (2) submit reports, notices, or other records required by the Act or any regulations issued under TSCA.

Additionally, TSCA section 15(4) makes it unlawful for any person to fail or refuse to permit entry or inspection as required by section 11. Section 11 applies to any "establishment, facility, or other premises in which chemical substances or mixtures are manufactured, processed, stored, or held before or after their distribution in commerce . . ." The Agency considers a testing facility to be a place where the chemical is held or stored and, therefore, subject to inspection. Laboratory audits and/or inspections will be conducted periodically in accordance wiht the procedures outlined in TSCA section 11 by designated representatives of the EPA for the purpose of determining compliance with the final rule for ODA. These inspections may be conducted for purposes which include verification that testing has begun, that schedules are being met, that reports accurately reflect the underlying raw data and interpretations and evaluations thereof, and that the studies are being conducted according to EPA GLP standards and the test standards established in the second phase of this rulemaking.

EPA's authority to inspect a testing facility also derives from section 4(b)(1) of TSCA, which directs EPA to promulgate standards for the development of test data. These standards are defined in section 3(2)(B) of TSCA to include those requirements necessary to assure that data developed under testing rules are reliable and adequate, and such other requirements as are necessary to provide such assurance. The Agency maintains that laboratory inspections are necessary to provide this assurance.

Violators of TSCA are subject to criminal and civil liability. Persons who submit materially misleading or false information in connection with the requirement of any provision of this rule may be subject to penalties calculated as if they had never submitted their data. Under the penalty provisions of section 16 of TSCA, any person who violates section 15 could be subject to a civil penalty of up to $25,000 per day for each violation. This provision would be applicable primarily to manufacturers or processors who will fail to submit a letter of intent or an exemption request and who continue manufacturing or processing after the deadlines for such submissions. This provision would also apply to processors that fail to submit a letter of intent or an exemption application and continue processing after the Agency has notified them of their obligation to submit such documents (see 40 CFR 790.48(b)). Intentional violations could lead to the imposition of criminal penalties up to $25,000 for each day of violation and imprisonment for up to 1 year. Other remedies are available to EPA under sections 7 to 17 of TSCA, such as seeking an injunction to restrain violations of TSCA section 4.

Individuals as well as corporations could be subject to enforcement actions. Sections 15 and 16 of TSCA apply to "any person" who violates various provisions of TSCA. EPA may, at its discretion, proceed against individuals as well as companies themselves. In particular, this includes individuals who report false information or who cause it to be reported. In addition, the submission of false, fictitious, or fraudulent statements is a violation under 18 U.S.C. 1001.

VI. Economic Analysis of Final Test Rule

To assess the economic impact of this rule, EPA has prepared an economic analysis that evaluates the potential for significant economic impacts on the industry as a result of the required testing. The economic analysis estimates the costs of conducting the required testing and evaluates the potential for significant adverse economic impact as a result of these test costs by examining four market characteristics of ODA: (1) Price sensitivity of demand, (2) industry cost characteristics, (3) industry structure, and (4) market expectations.

Total testing costs for the final rule for ODA are estimated to range from $775,290 to $1,020,200. This estimate includes the costs for both the required minimum series of tests and the conditional ones. The annualized test costs (using a cost of capital of 25 percent over a period of 15 years) range from $200,908 to $264,375.

Because of the extensive occurrence of ODA in numerous mixed alkylamine products, total production of this chemical is not represented by the data published for oleylamine by the USITC (Ref. 3). EPA estimated total ODA production in 1984, contained in alkylamine products, to be 17 to 28 million pounds. Using the lower-bound production figure of 17 million pounds, the average unit test costs for all products would then range from 1.2 to 1.6 cents per pound of the ODA contained in the amine products. EPA estimates that under worst-case assumptions this cost is one percent of total 1984 product value of the major alkylamines which contain ODA.

Based on these costs and the market characteristics of ODA, the economic analysis indicates that the potential for significant adverse economic impact as a result of this test rule is low. This conclusion is based on the following observations: (1) The estimated unit test costs are small, and (2) the demand for ODA manufacture is inelastic (Ref. 23).

VII. Availability of Test Facilities and Personnel

Section 4(b)(1) of TSCA requires EPA to consider "the reasonably forseeable availability of the facilities and personnel needed to perform the testing required under the rule." Therefore, EPA conducted a study to assess the availability of test facilities and personnel to handle the additional demand for testing services created by section 4 test rules. Copies of the study, "Chemical Testing Industry: Profile of Toxicological Testing", October 1981, can be obtained through the NTIS Under publication number PB 82-140773.

On the basis of this study, the Agency believes that there will be available test facilities and personnel to perform the testing required in this test rule.

VIII. Rulemaking Record

EPA has established a public record for this rulemaking (docket number OPTS-42061A). This record includes the basic information the Agency

considered in developing this rule, and appropriate Federal Register notices.

This record includes the following information:

A. Supporting Documentation

(1) Federal Register notices pertaining to this action consisting of:

(a) Notice containing the Thirteenth ITC Report designating oleylamine to the Priority List (48 FR 55674, Dec. 14, 1983), and comments received in response thereto.

(b) Notice of the proposed test rule on oleylamine and comments received in response (49 FR 45610, Nov. 19, 1984).

(c) Notice announcing the final decision to require testing of oleylamine.

(d) Notice adding oleylamine to the list of chemicals subject to the preliminary assessment information rule (48 FR 55685, Dec. 14, 1983).

(e) Notice of final rule on EPA's TSCA Good Laboratory Practice Standards (48 FR 53922, Nov. 29, 1983).

(f) Notice of final rule on test rule development and exemption procedures (49 FR 39774, Oct. 10, 1984).

(g) Notice of final rule concerning data reimbursement (48 FR 41786, Sept. 19, 1983).

(h) Notice of interim final rule on test rule development and exemption procedures (50 FR 20652, May 17, 1985).

(i) Notice of extension of comment period of proposed test rule for oleylamine (50 FR 3808, Jan. 28, 1965).

(j) Toxic Substance Control Act Guidelines: Final Rule (50 FR 39252, Sept. 27, 1985).

(2) Support documents consisting of:

(a) Oleylamine technical support document for proposed rule.

(b) Economic impact analysis of notice of proposed rulemaking for oleylamine.

(c) Economic impact analysis of final test rule for oleylamine.

(3) Communications consisting of:

(a) Written public and intraagency or interagency memoranda and comments.

(b) Summaries of telephone conversations.

(c) Summaries of meetings.

(4) Reports—published and unpublished factual materials, including contractors' reports.

B. References

(1) USEPA. U.S. Environmental Protection Agency. Assessment of Testing Needs: Oleylamine (9-octadecenylamine) support document. Washington, DC Office of Toxic Substances. (1984)

(2) USITC. U.S. International Trade Commission. Synthetic Organic Chemicals. U.S. Production and Sales, 1982. Washington, DC: U.S. Government Printing Office, USITC pub. 1422. (1983)

(3) USITC. U.S. International Trade Commission. Synthetic Organic Chemicals. U.S. Production and Sales, 1984. Washington, DC: U.S. Government Printing Office, USITC pub. 1745. (1985)

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(5) Bio/dynamics Inc. A Segment III Perinatal and Postnatal Study of Amine Fluoride 335/242 in Rats. Project No. 72R–819. Philadelphia, PA: Menley & James Laboratories. (1973)

(6) Bio/dynamics Inc. A Segment I Rat Fertility Study of Amine Fluoride 335/242. Project No. 72R–817. Philadelphia, PA: Menley & James Laboratories. (1973)

(7) Bio/dynamics Inc. Amine Fluoride 335/242 Segment II Rabbit Teratology Study. Project No. 72R–818. Philadelphia, PA: Menley & James Laboratories. (1973)

(8) Bio/dynamics Inc. A Segment II Rat Teratology Study of Amine Fluoride 335/242. Project No. 72R–820. Philadelphia, PA: Menley & James Laboratories. (1973)

(9) Bio/dynamics Inc. Segment II Rat Teratology Study of Amine Fluoride 335/242 (repeat of previous study). Project No. 73R–880. Philadelphia, PA: Menley & James Laboratories. (1973)

(10) BLS. Bureau of Labor Statistics. U.S. Department of Labor. U.S. DOL 1983 Annual Survey. Washington, DC (1984)

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(16) CMA. Chemical Manufacturers Association, 2501 M Street, NW., Washington, DC 20037. 14-Day Dermal Toxicity Range-Finding Study of Oleylamine in Rats. Protocol No. CMA–SC. (1985)

(17) Rice. D.P. "The absorption, tissue distribution, and excretion of dodecyldimenthylamine oxide (DDAO) in selected animal species and the absorption and excretion of DDAO in man". *Toxicology and Applied Pharmacology* 39:377–389. (1977)

(18) USEPA. U.S. Environmental Protection Agency. Memorandum from Hollis Call to Bob Sanford. Response to Industry Comments Regarding the Economic Analysis of ODA. Washington, DC. (1985)

(19) BLS. Bureau of Labor Statistics. U.S. Department of Labor. U.S. DOL 1985 Annual Survey. Washington, DC. (1986)

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(23) USEPA. U.S. Environmental Protection Agency. Economic Impact Analyses of Final Test Rule for 9-Octadecenylamine (Oleylamine). Washington, DC, Office of Toxic Substances. (1986)

(24) CMA. Chemical Manufacturers Association, 2510 M Street, NW., Washington, DC 20037. *Salmonella*/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test). (1985).

(25) CMA. Chemical Manufacturers Association, 2510 M Street, NW., Washington, DC 20037. Chromosome Aberration Assay in Chinese Hamster Ovary (CHO) Cells. (1985)

(26) CMA. Chemical Manufacturers Association, 2510 M Street, NW., Washington, DC 20037. CHO/HGPRT Mutation Assay in the Presence and Absence of Exogenous Metabolic Activation. (1985)

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(28) Bio/dynamics Inc. A Chronic Oral Toxicity Study of Amine Fluorides 335/242 in Dogs. Project No. 72R–815. Philadelphia, PA: Menley & James Laboratory. (1975)

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Confidential Business Information (CBI), while part of the record, is not available for public review. A public version of the record, from which CBI has been deleted, is available for inspection from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays, in Rm. NE–G004, 401 M St., SW., Washington, DC.

IX. Other Regulatory Requirements

A. Classification of Rule

Under Executive Order 12291, EPA must judge whether a regulation is "major" and therefore subject to the requirement of a Regulatory Impact Analysis. EPA has determined that this test rule is not major because it does not meet any of the criteria set forth in section 1(b) of the Order; i.e., it will not have an annual effect on the economy of at least $100 million, will not cause a major increase in prices, and will not

have a significant adverse effect on competition or the ability of U.S. enterprises to compete with foreign enterprises.

This regulation 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 (15 U.S.C. 601 *et seq.*, Pub. L. 96–354, September 19, 1980), EPA certifies that this test rule will not have a significant impact on a substantial number of small businesses for the following reasons:

1. There are no small manufacturers of oleylamine known to EPA.

2. Small processors are not likely to perform testing themselves, or to participate in the organization of the testing effort.

3. Small processors will experience only minor costs in securing exemption from testing requirements.

4. Small processors are unlikely to be affected by reimbursement requirements.

C. Paperwork Reduction Act

The Office of Management and Budget (OMB) has approved the information collection requirements contained in this final 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.

List of Subjects in 40 CFR Part 799

Testing, Environmental protection, Hazardous substances, Chemicals, Recordkeeping and reporting requirements.

Dated: August 7, 1987.

J.A. Moore,

Assistant Administrator for Pesticides and Toxic Substances.

Therefore, Part 799 is amended as follows:

PART 799—[AMENDED]

1. The authority citation for Part 799 continues to read as follows:

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

2. New § 799.3175 is added to read as follows:

§ 799.3175 Oleylamine.

(a) *Identification of test substance.* (1) 9-Octadecenylamine (hereafter ODA) (CAS Number 112–90–3) shall be tested in accordance with this section.

(2) The ODA test substance shall be at least 90 percent ODA. The vehicle shall be one such as mineral oil for which there are adequate historical toxicological data and which will not interfere in the test results.

(b) *Persons required to submit study plans, conduct tests, and submit data.* (1) All persons who manufacture or process ODA (other than as an impurity) from October 7, 1987 to the end of the reimbursement period shall submit letters of intent to conduct testing or exemption applications, study plans, and/or shall conduct tests in accordance with Part 792 of this chapter, and submit data as specified in this section, Subpart A and Part 790 of this chapter.

(2) Persons subject to this section are not subject to the requirements § 790.50(a)(2), (5), and (6) and (b) and § 790.87(a)(1)(ii) of this chapter.

(3) Persons who notify EPA of their intent to conduct tests in compliance with the requirements of this section must submit plans for those tests no later than 45 days before the initiation of each of those tests.

(4) In addition to the requirements of § 790.87 (a)(2) and (3) of this chapter, EPA will conditionally approve exemption applications for this rule if EPA has received a letter of intent to conduct the testing from which exemption is sought and EPA has adopted test standards and schedules in a final Phase II test rule.

(c) *Health effects testing*—(1) *Developmental toxicity—(i) Required testing.* An oral developmental toxicity study shall be conducted with ODA in two mammalian species, rat and rabbit.

(ii) [Reserved]

(2) *Mutagenic effects—chromosomal aberrations*—(i) *Required testing.* (A) An oral *in vivo* mammalian bone marrow cytogenetics test: Chromosomal analysis shall be conducted for ODA.

(B) An oral rodent dominant lethal assay shall be conducted for ODA if it produces a positive result in the *in vivo* mammalian bone marrow cytogenetics test conducted pursuant to paragraph (c)(2)(i)(A) of this section.

(C) An oral rodent heritable translocation assay shall be conducted for ODA if it produces a positive result in the rodent dominant lethal assay conducted pursuant to paragraph (c)(2)(i)(B) of this section and if so required in a **Federal Register** notice or certified letter sent to test sponsors.

(ii) [Reserved]

(3) *Mutagenic effects—gene mutations*—(i) *Required testing.* (A) A detection of gene mutation in somatic cells in culture assay shall be conducted with ODA.

(B) An oral sex linked recessive lethal test in *Drosophila melanogaster* shall be conducted for ODA if it produces a positive result in the detection of gene mutation assay in somatic cells in culture conducted pursuant to paragraph (c)(3)(i)(A) of this section.

(C) An oral mouse visible specific locus test shall be conducted for ODA if it produces a positive result in the sex linked recessive lethal test in *Drosophila melanogaster* conducted pursuant to paragraph (c)(3)(i)(B) of this section and if so required in a **Federal Register** notice or certified letter sent to test sponsors.

(ii) [Reserved]

(4) *Oncogenicity*—(i) *Required testing.* An oncogenicity bioassay shall be conducted orally for ODA if positive results occur in any of the following tests and if so required in a **Federal Register** notice or certified letter sent to test sponsors.

(A) *In vivo* mammalian bone marrow cytogenetics tests conducted pursuant to paragraph (c)(2)(i)(A) of this section.

(B) Detection of gene mutation in somatic cells in culture assay conducted pursuant to paragraph (c)(3)(i)(A) of this section.

(C) Sex linked recessive lethal test in *Drosophila melanogaster*, conducted pursuant to paragraph (c)(3)(i)(B) of this section.

(ii) [Reserved]

[Information collection requirements approved by the Office of Management and Budget under control number 2070–0033.]

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