

**ENVIRONMENTAL PROTECTION
AGENCY****40 CFR Part 799****(OPP 42012; TSH-FRL 2100-5)****Diethylenetriamine; Proposed Test
Rule****AGENCY:** Environmental Protection
Agency (EPA).**ACTION:** Proposed rule.

SUMMARY: Under section 4 of the Toxic Substances Control Act (TSCA), EPA is proposing that manufacturers and processors of diethylenetriamine (DETA) test this chemical for subchronic toxicity, mutagenicity, including gene mutation and cytogenetic tests, aerobic biodegradation, and anaerobic biodegradation. Testing would be performed according to protocols established in a subsequent rulemaking. This notice constitutes EPA's response to the Interagency Testing Committee's (ITC) designation of DETA as a priority candidate for testing.

DATES: Submit written comments on or before June 28, 1982. If persons request time for oral comment by June 14, 1982, EPA will hold a public meeting on July 13, 1982, on this rule in Washington, D.C. For further information on arranging to speak at the meeting see unit VI of this preamble.

ADDRESS: Address written comments to: Document Control Officer, Management Support Division (TS-793), Office of Pesticides and Toxic Substances, Environmental Protection Agency, Rm. E-401, 401 M St. SW., Washington, D.C. 20460. Include the document control number OPTS-42012 on all submissions.

FOR FURTHER INFORMATION CONTACT: Douglas G. Bannerman, Acting Director, Industry Assistance Office (TS-799), Rm. E-511, 401 M St. SW., Washington, D.C. 20460, Toll Free: (800-424-9065), in Washington, D.C.: (554-1404), outside the USA: (Operator-202-554-1404).

SUPPLEMENTARY INFORMATION: All specific chemical testing requirements are being consolidated in the new 40 CFR Part 799 being established in this document. Specific chemical testing rules which initially were published under 40 CFR Part 773 will be integrated into the organizational scheme for Part 799.

I. Introduction

Section 4(e) of TSCA (Pub. L. 94-469, 90 Stat. 2003; 15 U.S.C. 2601) established an Interagency Testing Committee (ITC) to recommend to EPA a list of chemicals to be considered for testing under section 4(a) or the Act. The ITC may

designate substances on the list for priority consideration by EPA. TSCA requires EPA to respond to such designations within 12 months of the date they are made either by initiating rulemaking under section 4(a) or by publishing in the Federal Register reasons for not initiating rulemaking.

The ITC designated DETA for priority consideration in its Eighth Report, published in the Federal Register of May 22, 1981 (46 FR 28138). The ITC recommended that DETA be tested for the following health effects: chronic effects, reproductive effects and teratogenicity. Today's notice constitutes EPA's response to the ITC's designation of DETA as a priority candidate for testing.

Under section 4(a)(1) of TSCA, EPA must require testing of a chemical substance to develop health and 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.

EPA's process for determining when these findings apply is described in EPA's first and second proposed test rules as published in the Federal Registers of July 18, 1980 (45 FR 48528) and June 5, 1981 (46 FR 30300).

Today under section 4(a), EPA is proposing health effects and chemical

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fate testing requirements for DETA based on EPA's findings for this chemical.

II. DETA

A. Profile

DETA, CAS no. 111-40-0, is an alkaline, hygroscopic, viscous liquid. The estimated annual production of DETA in 1979 ranged from 33-39 million pounds. The primary uses of DETA are for the production of paper wet-strength resins, epoxy-curing agents, chelating agents, lubricating oil and fuel additives, surfactants, and corrosion inhibitors. DETA also has a minor use as a decontaminant for military chemical agents.

B. Findings

The EPA is basing its proposed testing on the authority of section 4(a)(1)(A) of TSCA.

EPA finds that the manufacture, processing, use and disposal of DETA may present an unreasonable risk of injury to human health due to subchronic and mutagenic effects for the following reasons:

1. EPA has found that there are existing data which indicate a potential human health hazard from DETA with respect to these effects.

2. EPA believes that persons are exposed to DETA in the workplace, in using consumer products, and as a result of release of DETA into the environment.

3. EPA does not believe that the rule will result in a loss to society of the benefits of the substance because the Agency's economic evaluation has shown that (1) the relative magnitude of the test cost is minor, and (2) the demand for DETA is relatively inelastic due to limited potential for substitution in end-uses.

EPA also finds that there are insufficient data to predict the subchronic and mutagenic effects of DETA and that testing of DETA is necessary to develop such data.

In addition, EPA finds that the manufacture, processing, use, and disposal of DETA may present an unreasonable risk to human health due to oncogenic effects for the following reasons:

1. EPA has found that there are existing data which indicate a theoretical potential for the conversion of DETA to nitrosamines in the environment and that persons may be exposed to these nitrosamines as a result of release of DETA to the environment. Nitrosamines have been shown to be carcinogenic.

2. The data are insufficient to predict the existence of nitrosamines resulting from DETA release to the environment. Testing is needed to develop such data.

3. EPA does not believe that the rule will result in a loss to society of the benefits of DETA because the Agency's economic evaluation has shown that the impact of testing this substance will be low.

The Agency is proposing subchronic testing rather than a full chronic study because the Agency believes that a properly conducted 90-day study with full histopathology can be used as a surrogate for the lifetime study.

EPA is not proposing testing for reproductive and teratogenic effects, because, in the Agency's judgment, the limited data available do not suggest a potential for these effects.

The analysis and findings on which the above determinations are based are presented in the diethylenetriamine support document. The ITC recommendations and EPA's proposed testing requirements are summarized in the following table:

Effect	ITC recommendation	EPA proposed testing
Chronic.....	X.....	X. (Subchronic in lieu of full chronic test.)
Reproductive.....	X.....	
Teratogenicity.....	X.....	
Mutagenicity.....	X.....	X.
Chemical fate.....	X.....	X.

C. Test Substance

EPA is proposing that a relatively pure grade of DETA be used as the test substance. A purity of 99 percent is specified in this rule.

D. Persons Required to Test

Section 4(b) (3) (B) specifies that the activities for which the Administrator makes section 4 (a) findings (manufacture, 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, distribution, use or disposal. "Manufacture" is defined in section 3(7) of TSCA to include "import." Processors are required to test if the findings are based on processing, distribution, use, or disposal.

Because industrial workers, consumers and the general population may be exposed to DETA during manufacture, processing, use and disposal, EPA is proposing that persons who manufacture or process or who intend to manufacture or process this

chemical from the effective date of this test rule to the end of the reimbursement period be subject to the rule. The end of the reimbursement period ordinarily will be 5 years after the deadline for submitting the last final report under a test rule.

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 person required to test may apply to EPA for an exemption from that requirement.

EPA is not proposing to require the submission of equivalence data as a condition for exemption from the proposed testing. As noted above, EPA is interested in evaluating the effects attributable to DETA itself and has specified a relatively pure grade substance for testing.

E. Submission of study plans

In response to concerns about rigid generic test methodology requirements, EPA has changed its approach for providing test standards for TSCA section 4 test rules. EPA will issue generic test methodology guidelines rather than generic test methodology requirements. Good Laboratory Practice (GLP) standards will continue to be promulgated as generic requirements. (See the Federal Register of March 26, 1982: 47 FR 13012.)

Under the new approach, test rule development will be a two-phase process. In phase I, test rules will be promulgated for individual chemicals specifying the health and environmental characteristics for which test data are to be developed and the reporting requirements. In phase II, following promulgation of a test rule, those persons subject to the rule will be required to develop study plans for the development of data pertaining to the effects and characteristics specified in the rule. For guidance in preparing study plans, it is recommended that test sponsors consult the TSCA Test Guidelines; the OECD Guidelines, as adopted by the OECD Council on May 12, 1981; or the FIFRA Guidelines. For the potential biotransformation of DETA to a nitrosamine the test sponsor may wish to review the paper by Yordy and Alexander (J. Environ. Qual. 10:266-270; 1981). The Industry Assistance Office will provide assistance to sponsors in obtaining these documents.

Manufacturers must state their intention to sponsor testing or to be exempted because other persons will perform testing in a letter to EPA within 30 days from the effective date of the test rule. The effective date of the rule will be 30 days from the date of publication of the final rule in the Federal Register. The letter of intent to be exempted will suffice as the application for exemption which was proposed as a requirement in the Federal Register of July 18, 1980 (45 FR 48512). Sponsors must submit their study plans to EPA within 90 days from the effective date of the test rule. After an opportunity for public comment, EPA will issue a rule adopting the study plans as proposed or modified. The approved and adopted study plans will become a the enforceable test requirements and will serve as the chemical specific test standards for the test rule. Testing would also be subject to EPA's generic GLP standards. Modification to the adopted study plans can be made only with EPA approval.

Processors will not be required to submit study plans and conduct testing unless manufacturers fail to sponsor the required tests. The basis for this decision is that manufacturers are expected to indirectly pass the costs of testing on to processors through any price increase of DETA.

F. Reporting Requirements

EPA is proposing that all data be reported in accordance with the EPA Good Laboratory Practice (GLP) standards proposed in the Federal Register's of May 9, 1979 (44 FR 28369) and November 21, 1980 (45 FR 77332) under 40 CFR Part 772, and with the supplementary reporting requirements listed in the proposed test rule. EPA has reviewed public comment on the proposed GLP standards and is now developing final GLP standards. The final GLP standards will apply to this rule.

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. For this rule, EPA is proposing the following deadlines for the submission of the Final Report for each test:

Test	Deadline (months)
Subchronic oral toxicity	15
Mutagenicity (gene mutation and cytogenicity) ...	15
Aerobic biodegradation	15
Anaerobic biodegradation	15

These deadlines are calculated from the effective date of the final rule. The deadlines include the time necessary for submission, review and adoption of

protocols; study performance; analysis of test results; and preparation of final report.

G. Major Issues for Public Comment

Should toxicity data from other ethyleneamines be used as a surrogate for DETA toxicity? Industry has commented that ethylenediamine (EDA), DETA and triethylenetetramine (TETA) are all alkyl amines with the same primary functional groups with the principal differences in the length of alkyl chain. Citing structural and biological activity relationships, they state that because the three substances share a number of physical and chemical properties, it is reasonable to suppose that their toxicological properties also will be somewhat similar. Union Carbide has studied the disposition of DETA and EDA administered orally and endotracheally to rats. They state that while both are readily absorbed, DETA is excreted more readily, retained to a lesser degree in tissues and is more likely to be excreted in an unmetabolized form than EDA.

While the Agency agrees that certain similarities in physical and chemical characteristics exist, other concerns of chemical activity exist. Although both possess terminal primary amine groupings, DETA is a secondary amine, may form nitroso compounds or may possess other differences in metabolic activity because of its differing amino structure. There is a need for mechanisms to compare test results among the three chemicals and assess the comparative toxicology of those ethyleneamines possessing secondary amines, which may form nitroso compounds, and those ethyleneamines which do not have any secondary amines.

To more firmly establish that the compounds may possess similar toxicological qualities, more extensive metabolism data (including the identification of metabolites) are needed to show that these compounds are metabolized in the same manner. Comparisons of metabolism and toxicity in other related compounds (e.g., alkyleneamines) would be informative. Comments that provide information regarding structure-activity comparisons between DETA and other compounds and the adequacy of these comparisons in predicting the toxicological characteristics of DETA are encouraged.

Microbial formation of nitrosamines from secondary amines in water, sewage and soil has been reported by several investigators. The Agency invites comments on protocols that should be used to quantify nitrosamine

formation during DETA biotransformation.

As stated earlier, the Agency is proposing a well conducted subchronic effects test in lieu of chronic effects testing. This testing would involve the exposure of animals via the oral route. Although the Agency's major exposure concern is via the dermal route, EPA is proposing oral dosing. Preliminary pharmacokinetics data (Union Carbide) suggest that DETA is absorbed by the oral route. Fewer potential complications involving absorption of the compound are anticipated by oral dosing as opposed to dermal exposure. One of the major shortcomings of dermal administration is uncertainty with regard to what quantity of chemical actually is absorbed, which in turn, complicates the assessment of dosage. The oral route is expected to provide a more adequate measure of the actual dose being received by the animals. The Agency requests comments on the appropriateness of this exposure route for testing purposes.

In addition, because the Agency is concerned primarily about dermal exposures, it may be necessary to require performance of a dermal absorption study to provide data needed to evaluate the risk posed by dermal exposure. EPA requests comments on the necessity of such dermal absorption testing and, based on comments received, may include such a requirement in the final test rule.

In addition to the issue of appropriate route of exposure, the Agency is also interested in comments about the duration of testing. In general, the Agency has felt that a subchronic test would generally be sufficient to study chronic endpoints. Nevertheless, according to a chronic study by Fujino, discussed in the support document, life-time exposures to DETA resulted in the shortening of lifespans. The Agency requests comments on the appropriateness of a 90-day subchronic study to adequately characterize the life-shortening potential of DETA. Should a full-life chronic study be performed? Does the Fujino study provide a sufficient basis for concern about life-shortening effects to justify the extra expense of a full chronic study?

III. Economic Analysis of Proposed Rule

To assess the potential economic impact of this proposed rule, EPA has prepared a Level I economic evaluation that examines the costs of the required testing and analyzes four market characteristics of the chemical: (1) Demand sensitivity, (2) cost

characteristics, (3) industry structure, and (4) market expectations.

Based on a total testing cost of \$89,300-\$264,900 and an annualized cost of \$23,100-\$68,600, the Level I analysis of DETA indicates that the potential for adverse economic effects due to the estimated testing costs is low. This conclusion is based on the following observations: (1) The demand for DETA is relatively inelastic due to limited potential for substitution in end uses; (2) the market expectations for DETA are generally favorable; and (3) the relative magnitude of the test cost is minor, i.e., an estimated .06 to .20 cents per pound.

Because the Level I analysis indicates no potential for an adverse economic impact, EPA has determined that a more comprehensive and detailed Level II economic evaluation is not needed for DETA.

IV. Available of Test Facilities and Personnel

Section 4(b)(1) requires EPA to consider "the reasonably foreseeable 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 and voluntary test programs negotiated with industry in place of rulemaking. Copies of the study can be obtained through the Industry Assistance Office (IAO).

The tentative conclusions reached in the Laboratory Availability study were: (1) The chemical testing industry's anticipation of increased testing requirements has prompted the rapid expansion of testing facilities in recent years. (2) Currently, excess capacity exists in all major testing areas, and surveyed laboratories indicated they could perform about 20 percent more testing. (3) Measurable industry concentration exists, but it is not enough to restrict market entry or control key resources. (4) Currently, capital and professional manpower are the most constraining resources on industry expansion. Capital is understandably a cyclical constraint. However, the constraint imposed by a shortage of professional personnel can be long term because of the lengthy period required for professional preparation. (5) Current personnel numbers appear adequate relative to present testing levels.

On the basis of this study, the Agency believes that there will be available resources to perform the testing in this proposed rule.

V. Environmental Impact Statement

EPA is not required to prepare environmental impact statements (EIS), under the National Environmental Policy Act (NEPA), 41 U.S.C. 4321, for test rules. EPA has determined that voluntary preparation of an EIS is not appropriate for regulations issued under section 4 of TSCA. See the preamble to the Agency's rules for compliance with NEPA published in the Federal Register of November 6, 1979 (44 FR 84174).

VI. Public Meetings

If persons wish to present comments on these proposed rules to EPA officials who are directly responsible for developing the rule and supporting analyses, EPA will hold a public meeting on July 13, 1982 in Washington, D.C. This meeting is scheduled after the deadline for submission of written comments, so that issues raised in the written comments can be discussed by EPA and the public commenters. Information on the exact time and place of the meeting is available from the Industry Assistance Office.

Persons who wish to attend or present comments at the meeting should call the OTS Industry Assistance Office by June 14, 1982. While the meeting will be open to the public, active participation will be limited to those persons who arranged to present comments and designated EPA participants. Attendees should call the Industry Assistance Office before making travel plans since the meeting will not be held if members of the public do not wish to make oral comments.

The Agency will transcribe the meeting and include the written transcript in the public record. Participants are invited, but not required, to submit copies of their statements prior to or on the day of the meeting. All such written materials will become part of EPA's record for this rulemaking.

VII. Public Record

EPA has established a public record for this rulemaking (docket number OPTS-42012) which is available for inspection in the OPTS Reading Room, Rm. E-107, 401 M St. SW., Washington, D.C., from 8:00 a.m. to 4:00 p.m., Monday through Friday, except legal holidays. This record includes basic information the Agency considered in developing this proposal, and appropriate Federal Register notices. The Agency will supplement the record with additional information as it is received.

VIII. 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. The regulation for this chemical substance is not major because it does not meet any of the criteria set forth in section 1(b) of the Order. First, the actual annual cost of the testing prescribed for DETA is less than \$68,600 over the testing and reimbursement period. Second, because the cost of the required testing will be distributed over a large production volume the rule will have only very minor effects (less than 0.7 percent a year) on producers' costs or users' prices for this chemical. Finally, taking into account the nature of the market for this substance, the low level of costs involved, and the expected nature of the mechanisms for sharing the costs of the required testing, EPA concludes that there will be no significant adverse economic effects of any type as a result of this rule.

This proposed regulation was submitted to the Office of Management and Budget (OMB) for review as required by Executive Order 12291.

IX. Regulatory Flexibility Act

Under the Regulatory Flexibility Act (RFA), (15 U.S.C. 601, Pub. L. 96-354, September 19, 1980), EPA is certifying that this test rule, if promulgated, will not have a significant impact on a substantial number of small businesses.

The basis for this decision is the same as that discussed in detail in the Federal Register of June 5, 1981 (46 FR 30315).

X. Paperwork Reduction Act

The Paperwork Reduction Act of 1980 (PRA) (44 U.S.C. 3501 *et seq.*) authorizes the Director of OMB to review certain information collection requests by Federal agencies. The test rule proposed in this notice, if promulgated, could result in the submission of several types of information related to the required testing, including study plans and final reports for each test required by persons sponsoring the tests. For the reasons set out in the Federal Register of June 5, 1981 (46 FR 30315), EPA believes that the test rule contained in this notice does not constitute an information collection request as defined in the Paperwork Reduction Act.

List of Subjects in 40 CFR Part 799

Testing, Environmental protection, Hazardous material, Chemicals.

Dated: April 22, 1982.

Anne M. Gorsuch,
Administrator.

Therefore, it is proposed that a new Part 799 be added to Chapter I of 40

CFR, consisting at this time of Subpart B § 799.1575, to read as follows:

PART 799—IDENTIFICATION OF SPECIFIC CHEMICAL SUBSTANCE TESTING REQUIREMENTS

Subpart A—[Reserved]

Subpart B—Specific Chemical Testing

§ 799.1575 Diethylenetriamine (DETA).

(a) *Identification of test substance.* (1) Diethylenetriamine (CAS No. 111-40-0) shall be tested in accordance with this Part.

(2) Diethylenetriamine of at least 99 percent purity shall be used as the test substance.

(b) *Persons required to test.* (1) All persons who manufacture, process or intend to manufacture or process DETA from the effective date of this rule to the end of the reimbursement period shall submit study plans, conduct tests and submit data as specified by this Part.

(2) Any person subject to the requirements of this section may apply to EPA for an exemption from study plan and data submission and testing in accordance with Subpart E of Part 770.

(c) *Study plans.* (1) *Testing.* Testing shall be performed using an EPA-approved study plan. All data must be developed and reported in accordance with the EPA Good Laboratory Practice (GLP) standards in 40 CFR Part 772.

(2) *Submission.* (i) No later than 30 days after the effective date of this rule, each person who manufactures DETA must notify EPA by letter of his intent either to submit a proposed study plan or to be exempted from testing for each effect for which testing is required in this rule.

(ii) Manufacturers of DETA who indicate they will perform testing must submit proposed study plans on or before 90 days after the effective date of this rule. Only one set of study plans should be prepared and submitted by persons who are jointly sponsoring testing.

(iii) If no letter of intent to submit a proposed study plan is submitted by any manufacturer for all effects in this rule, EPA will so notify the manufacturers of DETA. EPA will also publish a notice of this fact and then (A) no later than 30 days after publication of such a notice, each processor must notify EPA by letter of his intent either to submit a proposed study plan for each effect that will not be covered by manufacturer study plans or to be exempted from testing and (B) processors who indicate they will perform testing must submit proposed study plans on or before 90 days after publication of such a notice.

(iv) If no study plan is proposed for each effect included in this rule, every manufacturer of DETA will be considered in violation of the rule beginning on the 91st day after the rule takes effect, and every processor of DETA in violation beginning 90 days after the publication of the notice described in paragraph (c)(2)(iii) of this section until such a study plan is submitted by an appropriate sponsor.

(3) *Content.* (i) All study plans are required to contain the following information:

(A) Identity of the test rule.

(B)(1) The names and addresses of the test sponsors.

(2) The names and addresses of the responsible administrative officials and project manager(s) in the principal sponsor's organization.

(3) The name, address, and telephone number of the appropriate individual for oral and written communications with EPA.

(4)(i) The name and address of the testing facility and the names and addresses of the testing facility's administrative officials and project manager(s) responsible for this testing.

(ii) Brief summaries of the training and experience of each professional involved in the study including Study Director, Veterinarian(s), Toxicologist(s), Pathologist(s) and Pathology Assistants.

(C) Identity and data on the substances or mixtures being tested including appropriate physical constants, spectral data, chemical analysis and stability under test and storage conditions.

(D) Study protocol including rationale for: species/strain selection; dose selection (and supporting data); route(s) or method(s) of exposure; a description of diet to be used and its source, including nutrients and contaminants and their concentrations; for *in vitro* test systems, a description of culture medium and its source; and a summary of expected spontaneous chronic diseases (including tumors), genealogy, and life span.

(E) Schedule for initiation and completion of major phases of long term tests; schedule for submission of interim progress and final reports to EPA.

(ii) Information given under paragraph (c)(3)(i)(B)(4) of this section is not required in proposed study plans if the information is not available at the time of submission; however, the information must be submitted before the initiation of testing.

(4) *Adoption.* Upon receipt of proposed study plans, EPA will publish a notice requesting comments on the ability of the study plans to ensure that

data from the tests are reliable and adequate. EPA will provide a 45-day comment period, and will provide an opportunity for an oral presentation on the request of any person. EPA may extend the comment period if it appears from the nature of the issues raised by EPA's review or public comment that further comment is warranted. Following the close of the comment period, EPA will publish a final rule adopting the study plans as proposed or modified.

(5) *Modification of study plans during conduct of study.* (i) *Application.* Any test sponsor who wishes to modify the adopted study plan for any test required under this rule must submit an application in accordance with this section. Application for modification shall be made in writing or by phone to the Chief, Test Rules Development Branch, Office of Toxic Substances, with written confirmation to follow as soon as feasible. Written confirmation of a request for a modification should be submitted to the Document Control Officer. Applications must include appropriate explanation of why the modification is necessary.

(ii) *Adoption.* To the extent feasible, EPA will seek comment on all substantive changes in study plans. EPA will issue a notice in the *Federal Register* requesting comments on requested modifications in accordance with section 4(b)(5) of TSCA. However, EPA will act on the requested modification without seeking public comment (A) if EPA believes that an immediate modification to a study plan is necessary in order to preserve the accuracy of an ongoing study or (B) if EPA determines that a modification clearly does not pose any substantive issues. EPA will notify the sponsor of the Agency's approval or disapproval. When the Agency approves a modification, it will publish a notice in the *Federal Register* indicating that the study plan has been modified.

(d) *Health effects testing—(1) Mutagenicity testing—(i) Required testing.* Gene mutation and cytogenetics testing shall be conducted with DETA.

(ii) *Reporting requirements.* (A) In addition to the reporting requirements as specified in the EPA GLP standards in 40 CFR Part 772, the following specific information shall be reported:

(1) Sufficient procedural detail to permit a reconstruction of the study and an adequate assessment of both study design and results obtained.

(2) Details of the protocol used for metabolic activation.

(3) Test chemical vehicle.

(4) Methods used for maintenance of cell cultures.

(5) Animal husbandry techniques.

(6) Cell density at time of treatment.

(7) Treatment conditions, including duration of treatment.

(8) Time of cell harvest.

(9) Methods used for preparation of slides for examination.

(10) Photographs of representative aberrations, e.g., breaks or gaps, must be prepared but need not be submitted.

(11) The data shall be arranged so as to show whether the study goals were achieved with the designated biologic end point(s). Data shall include the number of events per unit in each experimental and control unit replicate.

(B) No interim reports are required.

(C) The Final Report shall be submitted to EPA no later than 15 months after the effective date of this rule.

(2) *Subchronic effects*—(i) *Required testing.* Ninety day subchronic oral toxicity testing shall be conducted with DETA. Testing must be performed in at least two mammalian species. A variety of rodent species may be used, although the rat is the preferred species. Commonly used laboratory strains should be employed. The commonly used non-rodent species is the dog, preferably of a defined breed; the beagle is frequently used. If other mammalian species are used, the tester should provide justification/reasoning for their selection.

(ii) *Reporting requirements.* (A) In addition to the reporting requirements as specified in the EPA GLP standards in 40 CFR Part 772, the following specific information shall be reported:

(1) Toxic response and other effects data by sex and concentration in tabular form.

(2) Individual animal data, arranged by test group (dose level and sex) for the following:

(i) Dosages given and rationale for selection including basis for establishment of maximum tolerated dose (MTD).

(ii) Time of death during study (scheduled and nonscheduled) or whether animals survived to termination.

(iii) Date of observation of toxic signs, pharmacological effect or behavioral abnormality and its subsequent course.

(iv) Measured food consumption at weekly intervals.

(v) Body weight data.

(vi) Results of ophthalmological examination, when performed.

(vii) Hematological test employed and all results.

(viii) Clinical biochemistry tests employed and all results.

(ix) Necropsy findings.

(x) Detailed description and classification of all histopathological findings.

(xi) Statistical evaluation of test results where appropriate.

(B) No interim reports are required.

(C) The Final Report shall be submitted to EPA no later than 15 months after the effective date of this rule.

(e) *Chemical fate testing*—(1) *Aerobic transformation.*—(i) *Required testing.* Testing to assess nitrosamine formation resulting from aerobic biodegradation shall be conducted for DETA.

(ii) *Reporting requirements.* (A) In addition to the reporting requirements specified in the EPA GLP standards in 40 CFR Part 772, the following specific information shall be reported: (1) Information on the inoculum, including source, collection date, handling, storage and adaptation possibilities (i.e., whether the inoculum has been exposed to the test substance either before or after collection and prior to use in the test).

(2) Results from each test, reference, and control system at each sampling time, including an average result for the triplicate test substance systems and the standard deviation for that average.

(3) The average percent apparent biodegradation or organic substance loss for test, and reference systems at each sampling time.

(4) A graph of percent biodegradation versus time for each test and reference substance for each method employed.

(5) Identification, quantification and average percent of nitrosamine(s) formed in test systems at each sampling time.

(B) No interim reports are required.

(C) The Final Report shall be submitted to EPA no later than 15 months after the effective date of this rule.

(2) *Anaerobic biotransformation*—(i) *Required testing.* Testing to assess nitrosamine formation resulting from anaerobic biodegradation shall be conducted for DETA.

(ii) *Reporting requirements.* (A) In addition to the reporting requirements specified in the EPA GLP standards in 40 CFR Part 772, the following specific information shall be reported: (1) Information on the inoculum, including source, collection date, handling, storage and adaptation possibilities (i.e., whether the inoculum has been exposed to the test substance either before or after collection and prior to use in the test).

(2) Results from each test, reference, and control system at each sampling time, including an average result for the

triplicate test substance systems and the standard deviation for that average.

(3) The average percent apparent biodegradation or organic substance loss for test and reference systems at each sampling time.

(4) A graph of percent biodegradation versus time for each test and reference substance for each method employed.

(5) Identification, quantification and average percent of nitrosamine(s) formed in test systems at each sampling time.

(B) No interim reports are required.

(C) The Final Report shall be submitted to EPA no later than 15 months after the effective date of this rule.

(Sec. 4, Toxic Substances Control Act (Pub. L. 94-469, 90 Stat. 2003, 15 U.S.C. 2601))

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