ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 799

[OPTS-42080D; FRL-3548-8]

Testing Consent Order; Triethylene Glycol Monomethyl, Monoethyl, and Monobutyl Ethers

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This rule announces that EPA has signed an enforceable Testing Consent Order with five manufacturers of triethylene glycol monomethyl ether (TGME; CAS No. 112-35-6), triethylene glycol monoethyl ether (TGEE; CAS No. 112-50-5), or triethylene glycol monobutyl ether (TGBE; CAS No. 143-22-6), who have agreed to perform certain toxicologic tests with TGME. This action is in response to the TSCA Interagency Testing Committee's (ITC) designation of these three chemicals for priority testing. Also, appearing elsewhere in this issue of the Federal Register, is a final rule requiring developmental neurotoxicity testing of TGME.

EFFECTIVE DATE: April 3, 1989.

FOR FURTHER INFORMATION CONTACT: Michael M. Stahl, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Room EB-44, 401 M Street, SW., Washington, DC 20460, (202) 554-1404, TDD (202) 554-0551.

SUPPLEMENTARY INFORMATION: Under procedures described in 40 CFR Part 790, five manufacturers of TGME, TGEE, or TGBE have entered into a Testing Consent Order with EPA in which they have agreed to perform certain toxicologic tests on TGME. This rule amends Subpart C of 40 CFR Part 799 to add TGME, TGEE and TGBE to the list of chemical substances and mixtures subject to Testing Consent Orders for which the export notification requirements of 40 CFR Part 707 apply.

Public reporting burden for this collection of information is estimated to average 506 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, PM-223, U.S. Environmental Protection Agency, 401 M Street SW., Washington, DC 20460; and to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB), Washington, DC 20503.

I. ITC Recommendations

The Interagency Testing Committee (ITC) designated TGME, TGEE, and TGBE for priority testing consideration in its Sixteenth Report published in the Federal Register of May 21, 1985 (50 FR 20930), and recommended pharmacokinetic and metabolic studies. The results of those studies would determine whether subchronic studies with emphasis on hematologic effects, as well as reproductive and developmental toxicity tests, should be performed.

II. Proposed Test Rule

EPA issued a proposed test rule, published in the Federal Register of May 15, 1986 (51 FR 17883), requiring that manufacturers and processors of the three triethylene glycol ethers conduct toxicologic testing on the glycol ethers they manufacture or process. This testing was based on EPA findings of the potential for unreasonable risk under TSCA section 4(a)(1)(A) and a finding of substantial production and exposure under TSCA section 4(a)(1)(B). These findings are more fully described in the proposed rule. A two-stage test rule was proposed. Subchronic toxicity, developmental toxicity, neurotoxicity, developmental neurotoxicity, and lower-tier mutagenicity comprised the first stage. Following review of data from these tests EPA would decide if the second-stage tests, oncogenicity, upper-tier mutagenicity, and reproductive toxicity, were needed.

III. Testing Consent Order Negotiation

Following the test rule proposal, the Chemical Manufacturers Association (CMA) informed EPA that members of CMA's Glycol Ether Panel were sponsoring a series of tests on TGME. They planned to conduct a 90-day dermal toxicity test and a dermal developmental toxicity study in the rabbit, an *in vivo* mouse micronucleus test, and an Ames assay. They had already initiated an oral Chernoff-Kavlock developmental toxicity screen in the rat and a 21-day dermal range-finding study in the rabbit, with the high dose at 1 gram/kilogram (g/kg) as a limit test, and an *in vitro* dermal absorption study using human skin. These tests were done on all three glycol ethers, with no obvious toxicity differences between the chemical substances.

By February 1987, EPA informed CMA that EPA was considering the option of a Testing Consent Order. On May 19, 1987, EPA issued a notice (52 FR 18738) to this effect, requesting public participation and announcing a meeting on May 28, 1987, to initiate testing negotiations.

After several scientific meetings, CMA's Glycol Ethers Panel submitted to EPA a draft Consent Order on September 30, 1987, which included all but one of the first-stage tests proposed by EPA for TGME, TGEE and TGBE, with TGME as the test substance representing all three. The only testing not agreed upon was for developmental neurotoxicity. After a period of intensive discussion on developmental neurotoxicity testing, a final Consent Order, excluding developmental neurotoxicity, was signed by March 8, 1989 by Cain Chemical Inc., The Dow Chemical Company, Eastman Kodak Company, Shell Chemical Company, and Union Carbide Corporation. In this Consent Order, the manufacturers agreed to perform certain toxicologic tests on TGME by specific dates according to the test standards in the Appendix of the Order. The final test rule for developmental neurotoxicity testing of TGME is published elsewhere in this Federal Register. EPA is deferring final decisions on further testing of TGEE and TGBE (51 FR 17883) until the results of the Consent Order testing are available (see Unit V).

IV. Use and Exposure

These glycol ethers are primarily co-produced during the manufacture of lower molecular weight glycol ethers. About 5 percent of production is purified further for use as chemical intermediates, but the majority is sold in a technical grade for use as a diluent in brake fluid.

Preliminary data from the National Occupational Exposure Survey (NOES), conducted by the National Institute for Occupational Safety and Health (NIOSH) from 1980 to 1983, indicate that approximately 250,000 workers, including 8,000 females, were potentially exposed to brake fluids in the workplace in 1980 (Ref. 1). Although there are no data on actual levels of dermal exposure in the workplace, the nature of brake system maintenance and repair suggests that complete exposure of both hands occurs regularly, even daily, for many professional mechanics. EPA has recently prepared an updated exposure profile of mechanics (at least 175,000 estimated) exposed to brake fluids with at least one contact per day, resulting in estimated exposures ranging from 520 to 2,300 milligrams (mg)/day for 250 days per year (Ref. 2). Furthermore, there is a potential for consumer exposure, since some individuals can be expected to

perform brake maintenance, including addition of brake fluid, on their automobiles.

V. Testing Program

The proposed test rule would have required that most of the tests be performed dermally, since that is the route of human exposure, and the manufacturers agree that this would be most useful for risk assessment. This Consent Order however, requires that the route of administration for the developmental toxicity and subchronic neurotoxicity tests be oral to assure that a sufficient dose will be administered for hazard identification.

As TGME has relatively low acute toxicity by the oral or dermal route, the previously completed study by CMA prior to the issuance of the Order used the 1 g/kg limit test for the initial range-finding. This study found essentially no effect in the 21-day test in the rabbit. Because EPA found a possible maximum human dermal exposure of 3,900 mg/day (Ref. 3), or 56 mg/kg/day for a 70 kg person, the high dose of the test should be greater than the 1 g/kg limit test dose. Dow scientists were able to apply 4 g/kg percutaneously to the Sprague-Dawley rat (Ref. 3) in a second range-finding study. However, in order to approach a 100-fold margin of exposure for TGME, the high dose should be at least 5 g/kg for neurotoxicity tests, which would require oral dosing. Despite the requirement to conduct some of these tests via the oral route, the manufacturers subject to the Order have informed EPA that they plan to do both oral subchronic neurotoxicity and dermal subchronic regular toxicity studies in the Sprague-Dawley rat, since they believe the dermal route to be more informative.

In the Consent Order, the five manufacturers agree to conduct the following studies in accordance with the cited test guidelines. A dermal subchronic study will be conducted in the Sprague-Dawley rat according to 40 CFR 798.2250, using at least 4 g/kg as the high dose. Three combined oral subchronic neurotoxicity tests will be conducted in the Sprague-Dawley rat, using at least 5 g/kg as a high dose, according to 40 CFR 798.6050, 798.6200, and 798.6400. Developmental toxicity studies in the Sprague-Dawley rat and the rabbit will be conducted by the oral gavage route of exposure using at least 5 g/kg as a high dose, according to 40 CFR 798.4900. The high doses listed above will be required unless range-finding studies indicate that lower doses will produce adequate toxicity for an evaluation.

The remaining studies to be performed are three mutagenicity tests: the *Salmonella typhimurium* reverse mutation assay, 40 CFR 798.5265; detection of gene mutation in somatic cells in culture, 40 CFR 798.5300; and a mouse *in vivo* micronucleus assay, 40 CFR 798.5395. If any of these indicate a hazard for genetic toxicity, EPA will consider the need for further testing.

TESTING PLAN FOR TGME

Test	Test standards	Report [1] date
Mutagenicity:		
Salmonella typhimurium.	40 CFR 798.5265..	12
Somatic cells in culture.	40 CFR 798.5300..	12
Mouse micronucleus.	40 CFR 798.5395..	12
Developmental toxicity.	40 CFR 798.4900..	12
Subchronic toxicity.	40 CFR 798.2250..	18
Subchronic neurotoxicity:		
Neurobehavioral battery.	40 CFR 798.6050..	18
Motor activity	40 CFR 798.6200..	18
Neuropathology.	40 CFR 798.6400..	18

[1] Months after effective date of Consent Order.

The above Table delineates the tests, test standards, and final reporting dates for all the tests incorporated in the Testing Consent Order. The test standards with modifications are attached to the Order. EPA will use the data generated by these tests to determine the potential risk to human health from exposure to TGME and to determine whether any additional testing of TGME, TGEE, or TGBE is necessary.

EPA believes that testing may not be necessary for all three glycol ethers. In the lower congeners (the monoethylene glycol ethers) the methyl compound is the most toxic of the three in developmental (Ref. 5), reproductive (Refs. 6, 7, and 8), and neurotoxic effects (Refs. 9 and 10). Therefore, EPA will wait until the TGME testing is completed before determining whether testing on the other two is necessary. Although EPA does not intend to withdraw at this time its May 15, 1986 (51 FR 17863) proposal for testing triethylene glycol ethers, EPA will not issue any final test rules on the types of tests covered in this Testing Consent Order for any of the three triethylene glycol ethers in the proposed test rule during the period in which testing on TGME is conducted pursuant to the Consent Order to EPA's satisfaction.

VI. Export Notification

The issuance of the Consent Order subjects any person who exports or intends to export TGME, TGEE, or TGBE to the export notification requirements of section 12(b) of TSCA. The specific requirements are listed in 40 CFR Part 707. On June 23, 1987, EPA established 40 CFR 799.5000 as a listing of Consent Orders issued by EPA (52 FR 23548). This listing serves as notification to persons who export or who intend to export chemical substances or mixtures which are the subject of Testing Consent Orders that 40 CFR Part 707 applies.

VII. Rulemaking Record

EPA has established a record for this rule and the Consent Order (docket number OPTS-42080D). This record contains the information EPA considered in developing the Consent Order and includes the following:

A. Supporting Documentation

(1) Testing Consent Order for TGME, TGEE, and TGBE.

(2) **Federal Register** notices pertaining to this rule and the Consent Order consisting of:

(a) Notice containing the ITC designation of TGME, TGEE, and TGBE.

(b) Rules requiring TSCA sections 8 (a) and (d) reporting on TGME, TGEE, and TGBE.

(c) Proposed TSCA section 4(a) test rule on TGME, TGEE, and TGBE.

(d) Notice soliciting interested parties for Testing Consent Order negotiation on TGME, TGEE, and TGBE.

(3) Communications consisting of:

(a) Letters.

(b) Contact reports of telephone conversations.

(c) Meeting summaries.

B. References

(1) NIOSH. National Occupational Exposure Survey (1980–1983). Cincinnati, OH: Department of Health and Human Services. National Institute for Occupational Safety and Health (1985).

(2) OTS. Memorandum from R. Craig Matthiessen to Carol Glasgow on Response to Comment on Exposure to the Triethylene Glycol Ethers. Office of Toxic Substances (July 10, 1980).

(3) OTS. Report by Roger Swarup on test rules exposure analysis of triethylene glycol monomethyl ether, triethylene glycol monoethyl ether, triethylene glycol monobutyl ether. Office of Toxic Substances (July 24, 1985).

(4) Yano, B.L., Phillips, J.E. and Battjes, J.E. "Triethylene glycol monomethyl ether: 2-week dermal

toxicity study in male and female Sprague-Dawley rats." Dow Chemical Company ID: K-005610-001 (1987).

(5) European Chemical Industry Ecology & Toxicology Centre. (ECETOC). Technical Report No. 17. "The toxicology of glycol ethers and its relevance to man: an up-dating of ECETOC Technical Report No. 4." Brussels, Belgium: ECETOC (1985).

(6) NTP. "Ethylene glycol monomethyl ether: Reproduction and fertility assessment in CD-1 mice when administered in drinking water." NTIS Publication #86-163136/XAB Washington, DC (1985).

(7) NTP. "2-Ethoxyethanol: Reproduction and fertility assessment in CD-1 mice when administered in water." NTIS Publication #85-118651/XAB Washington, DC (1984).

(8) NTP. "Ethylene glycol monobutyl ether: Reproduction and fertility assessment in CD-1 mice when administered in drinking water." NTIS Publication #85-226827/XAB Washington, DC (1985).

(9) Goldberg, M.E., Haun, C. and Smyth, H.F., Jr. "Toxicologic implication of altered behavior induced by an industrial vapor." *Toxicology and Applied Pharmacology* 4:148-162 (1962).

(10) Goldberg, M.E., Johnson, H.E., Pozzani, U.C. and Smyth, H.F., Jr. "Effect of repeated inhalation of vapors of industrial solvents on animal behavior. I. Evaluation of nine solvent vapors on pole-climb performance in rats." *American Industrial Hygiene Association Journal* 25:369-375 (1964).

VIII. Other Regulatory Requirements

Paperwork Reduction Act

The information collection requirements contained in this rule have been approved by OMB under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3502 *et seq.* and have been assigned OMB control number 2070-0033.

Public reporting burden for this collection of information is estimated to average 506 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, PM-223, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460; and to the Office of Information and Regulatory Affairs, Office of Management and Budget, Washington, DC 20503, marked "Attention: Desk Officer for EPA."

List of Subjects in 40 CFR Part 799

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

Dated: March 24, 1989.

Susan F. Vogt,

Acting Assistant Administrator for Pesticides and Toxic Substances.

Therefore, 40 CFR 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. Section 799.5000 is amended by adding triethylene glycol monomethyl, monoethyl, and monobutyl ethers in the table in CAS Number order, to read as follows:

§ 799.5000 Testing consent orders.

* * * * *

CAS number	Substance or mixture name	Testing	Federal Register citation
*	*	*	*
112-35-6	Triethylene glycol monomethyl ether.	Health effects.	53 FR....., April 3, 1989.
112-50-5	Triethylene glycol monoethyl ether.	Health effects.	.....do.
143-22-6	Triethylene glycol monobutyl ether.	Health effects.	.....do.
*	*	*	*

[FR Doc. 89-7789 Filed 3-31-89; 8:45 am]

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40 CFR Part 799

[OPTS-42080E; FRL-3549-2]

Triethylene Glycol Monomethyl Ether; Final Test Rule

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: EPA is issuing a final test rule under section 4 of the Toxic Substances Control Act (TSCA) requiring manufacturers and processors of triethylene glycol monomethyl ether (TGME, CAS No. 112-35-6) to perform developmental neurotoxicity testing. This action is in response to the TSCA Interagency Testing Committee's (ITC) designation of TGME for priority testing. Also, appearing elsewhere in this issue of the Federal Register, is a Testing Consent Order rule for triethylene glycol monomethyl ether, triethylene glycol monoethyl ether, and triethylene glycol monobutyl ether.

DATES: For purposes of judicial review in accordance with 40 CFR 23.5, this rule shall be promulgated at 1 p.m. eastern (standard or daylight as appropriate) time on April 17, 1989. This rule shall become effective on May 17, 1989.

FOR FURTHER INFORMATION CONTACT: Michael M. Stahl, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Room EB-44, 401 M Street SW., Washington, DC 20460, (202) 554-1404, TDD (202) 554-0551.

SUPPLEMENTARY INFORMATION: EPA is promulgating a final test rule requiring developmental neurotoxicity testing of TGME.

Public reporting burden for this collection of information is estimated at 1375 hours including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, PM-223, U.S. Environmental Protection Agency, 401 M Street, SW., Washington, DC 20460; and to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB), Washington, DC 20503.

I. Introduction

A. Test Rule Development Under TSCA

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

Under section 4(a) of TSCA, EPA must require testing of a chemical to develop data if the Administrator makes certain findings as described in TSCA under section 4(a)(1) (A) or (B). Detailed discussions of the statutory section 4 findings are provided in the Agency's first and second proposed test rules

published in the Federal Registers of July 18, 1980 (45 FR 48510) and June 5, 1981 (46 FR 30300).

B. Regulatory History

The Interagency Testing Committee (ITC) designated TGME for priority testing consideration in its sixteenth report published in the Federal Register of May 21, 1985 (50 FR 20930). In response to this designation, EPA issued a proposed test rule in the Federal Register of May 15, 1986 (51 FR 17883) requiring that manufacturers and processors of TGME test the chemical for developmental neurotoxicity among other health effects, under sections 4(a)(1) (A) and (B) of TSCA. EPA recently entered a Consent Order with five manufacturers of triethylene glycol ethers to conduct certain toxicologic tests of TGME (notice published elsewhere in this Federal Register). Regarding developmental neurotoxicity testing, EPA has chosen to proceed by issuing a final test rule.

II. Response to Comments

The proposed rule (51 FR 17883) also proposed the developmental neurotoxicity guideline (40 CFR 795.250), and comments were received on both the proposed rule and guideline. Responses to comments on the guideline were published when the guideline was promulgated with the diethylene glycol butyl ether and diethylene glycol butyl ether acetate final test rule (53 FR 5932; February 26, 1988).

Only the Chemical Manufacturers Association (CMA) Glycol Ethers Program Panel and the American Industrial Health Council (AIHC) commented on the proposed test rule. Responses to those comments are given below.

A. Findings

EPA based the proposed test rule on both TSCA sections 4(a)(1) (A) and (B).

CMA and AIHC commented that the Agency did not provide justification for the section 4(a)(1)(A) finding. Comments 1 through 4 address this finding.

1. *Comment:* CMA commented that "the toxicity data on which EPA relies do not demonstrate any likelihood of unreasonable risks". They further went on to state "EPA argues that adverse effects would be expected from human exposures to the triethylene glycol ethers (51 FR 17885)."

Response: EPA has not reached any conclusion as to effects of exposure, but has merely found "that the use of the triethylene glycol ethers * * * *may* present an unreasonable risk * * * *". EPA has based its finding of potential unreasonable risk on (1) a toxicity prediction by use of a structure-activity relationship, discussed below in EPA's response to comments 2 and 3a, and (2) human exposure potential as discussed in the response to comment 5. Findings are detailed in Unit III.A. Testing is required because available data are insufficient to show whether "adverse effects would be expected". If EPA knew with certainty the extent of the risk, EPA would not require testing.

2. *Comment:* AIHC commented on EPA's structure-activity relationship (SAR) analysis, which was conducted only with ethylene glycol monomethyl ether (EGME). AIHC believes that a more refined SAR analysis should be used. The AIHC comments refer to the fact that "Data on series of glycol ethers and experience using similar materials has never resulted in neurologic effects similar to those observed with EGME for any other glycol ether".

Response: EPA is not aware of specific neurotoxicity testing on the higher congeners, the diethylene or triethylene glycol ethers, but Goldberg *et al.* (Refs. 1 and 2) have done adult neurotoxicity testing with the monoethylene compounds, just as Nelson *et al.* (Refs. 3, 6, and 7) have done with developmental neurotoxicity. Furthermore, the results of Goldberg *et al.*'s 1962 study with EGME (Ref. 1) on active avoidance paralleled the effects seen in the offspring exposed *in utero* to EGME (Ref. 3). In addition, effects of EGME seen in adult humans (Ref. 4) are comparable to the symptoms, ataxia and lethargy, seen in rat acute toxicity studies with TGME (Ref. 5). Without data on the higher congeners, EPA believes it cannot reasonably predict the neurotoxicity potential of TGME, and that testing is necessary.

3a. *Comment:* AIHC also commented that EPA's use of a single study (Ref. 3) to support the requirement for developmental neurobehavioral toxicity testing may be inadequate.

Response: In addition to the reference used in the proposed rule to support the requirement for developmental neurotoxicity (Ref. 3), Nelson's group tested another ethylene glycol ether, ethylene glycol monoethyl ether (EGEE), following prenatal exposure in rats (Refs. 6 and 7). At 100 ppm (Ref. 6) statistically significant changes occurred with the rotorod test, the activity wheel test, and avoidance conditioning. At 200 ppm, a maternally toxic dose, even greater alterations were observed in these tests (Ref. 7). All these results (Refs. 3, 6, and 7), constitute an adequate basis for concern about the potential for developmentally neurotoxic effects.

3b. *Comment:* AIHC and CMA questioned the use of a 1984 paper by Nelson *et al.* (Ref. 3) to support the finding. The comments quoted all or part of the following sentence in this paper: "The absence of more robust differences here raises doubt regarding the biological significance of the difference in this group, as compared with those seen in the 2ME 7–13 group."

Other AIHC and CMA comments discuss the following problems with the protocol of the same paper: (1) No appropriate controls of the exposed males; and (2) no randomization in assigning females in the various exposure groups, which they felt might account for the "consistency of the neurochemical findings".

Response: These comments (3a, 3b) refer to toxicity testing in the Nelson paper (Ref. 3) (paternal exposure, neurochemical alterations) which EPA is not requiring in this rule, and which do not bear on the proposed finding that TGME exposure may present an unreasonable risk of developmental neurotoxicity.

4. *Comment:* CMA also commented on the rationale for developmental neurotoxicity testing for risk assessment purposes, and concluded that "although such testing may be of academic interest, it is of no proven value to the risk assessment needs that must exist to justify section 4 testing requirements".

Response: At the time of the proposal, EPA had not previously required developmental neurotoxicity testing and had never used such testing for risk assessment purposes. However, EPA has long recognized that there is a need for this testing, as is discussed below. To fulfill this need, EPA has developed a guideline for this test (40 CFR 795.250).

In the early 1970's, the scientific community became concerned that exposure of the mother to drugs or toxic chemicals may result in neurologic effects in the offspring, as reports proliferated indicating that children born to chronic alcoholic mothers not only had physical malformations, but an increased incidence of mental retardation or performance deficits (Refs. 8 and 9). The fetal alcohol syndrome, as it is now termed (Ref. 10), is no longer considered an unproven theory, and there have been numerous studies investigating neurobehavioral problems in offspring exposed to other substances *in utero* (Ref. 11).

Scientists from various governmental agencies (National Institute for Environmental Health Sciences, NIEHS; National Center for Toxicological Research, NCTR; Food and Drug Administration, FDA; National

Toxicology Program, NTP; National Institute for Occupational Safety and Health, NIOSH; and EPA) instituted a Collaborative Behavioral Teratology Study (CBTS) in 1978 to evaluate the intra- and interlaboratory reliability and sensitivity of several behavioral test methods as a preliminary for developing tests useful for "safety evaluation in the area of postnatal function" (Ref. 12). CBTS was initiated, in part, because of a belief that available tests had not been validated sufficiently for regulatory agencies' risk assessment needs.

In addition, EPA's Scientific Advisory Panel (SAP) recently reviewed the rationale for developmental neurotoxicity testing and concluded that EPA should require that such testing be conducted in a number of instances including "strong structure-activity relationships to known neurotoxicants" (Ref. 13).

5. *Comment:* CMA submitted the only comment on the section 4(a)(1)(B) finding, stating that the NIOSH figures are not specific enough about the number of persons exposed to the chemical or the duration or extent of any such exposure to serve as the basis for requiring testing under TSCA sections 4(a)(1)(B). CMA also asserted that EPA failed to take into account instructions to the worker about handling the fluid carefully.

Response: EPA believes that the record supports the TSCA section 4(a)(1)(B) finding of "significant or substantial human exposure" for TGME. EPA has routinely used and intends to continue to use NIOSH survey statistics to make section 4(a)(1)(B) findings where appropriate unless better estimates of occupational exposure are developed. Furthermore, EPA has recently prepared an updated exposure profile of the estimated 175,000 mechanics exposed to brake fluids with at least one contact per day resulting in exposures ranging from 250 to 2,300 mg/day for 250 days per year (Ref. 14). In addition, the NIOSH figures are not the total basis for the section 4(a)(1)(B) finding, and as stated in the proposed rule, EPA believes that consumer exposure also occurs through the use of products containing TGME, since some individuals can be expected to add brake fluid or perform brake maintenance on their own automobiles. Thus EPA has properly concluded that substantial numbers of people may be exposed to TGME and that many of these people may be exposed to significant levels of TGME.

B. Route of Exposure

Comment: Several comments suggested that the oral route of exposure would be more appropriate than the dermal route in treating females caged with offspring.

Response: EPA agrees and has changed the route of administration to oral by gavage.

C. Economic Impact

Comment: CMA commented that the proposed testing would be too expensive and would have a substantial economic impact on manufacturers.

Response: EPA has greatly reduced the impact of this final test rule by requiring testing only of TGME, which will represent all three of the glycol ethers in the proposed test rule. If EPA concludes that testing of the other two is necessary after evaluating the data from this test, it will require this by a separate final rule.

III. Final Test Rule

A. Findings

This test rule is based on the authority of TSCA section 4(a)(1) (A) and (B). Under section 4(a)(1)(A) EPA finds that the use of TGME may present an unreasonable risk of developmental neurotoxicity on the basis of SAR with EGME and EGEE (Refs. 3, 6, and 7), both of which demonstrate developmental neurotoxicity, and the exposure to brake fluid which may contain TGME during use at levels up to 250 to 2,300 mg/day for up to 250 days per year by mechanics (Ref. 14). Other workplace personnel may be exposed to even higher levels (Ref. 20). Under section 4(a)(1)(B) EPA finds that TGME is produced in substantial quantities (30 million lbs. in 1986) (Ref. 15). EPA also finds that there is or may be substantial human exposure to brake fluids (which may contain TGME) in the workplace, where approximately 250,000 workers including 8,000 females (Ref. 16) are exposed. An updated exposure report (Ref. 14) confirms exposure in that an estimated 175,000 of these 250,000 workers are mechanics exposed to brake fluids at least once a day. There also may be substantial consumer exposure to TGME during maintenance of consumers' own vehicles. EPA also finds that there is or may be significant human exposure to TGME in the workplace.

EPA also finds that there are no available data to reasonably predict or determine the developmental neurotoxicity of TGME and that testing is necessary to develop this data.

Data resulting from the developmental neurotoxicity screen will help EPA determine whether TGME is developmentally neurotoxic and whether further testing is necessary, and are relevant to determining whether exposure to TGME during use does or does not present an unreasonable risk to human health.

B. Required Testing and Test Standard

EPA is requiring that developmental neurotoxicity be conducted on TGME in accordance with the specific guideline in 40 CFR 795.250, as published in the Federal Register of February 26, 1988 (53 FR 5947).

C. Test Substance

EPA is requiring that TGME of at least 90 percent purity shall be used as the test substance. TGME of such purity is available at reasonable cost.

D. Persons Required To Test

Section 4(b)(3)(B) specifies that the activities for which EPA makes section 4(a) findings (manufacture, processing, distribution in commerce, use, and/or disposal) determine who bears the responsibility for testing a chemical. Manufacturers and persons who intend to manufacture the chemical are required to test if the findings are based on manufacturing ("manufacture" is defined in section 3(7) of TSCA to include "import"). Processors and persons who intend to process the chemical are required to test if the findings are based on processing. Manufacturers and processors and persons who intend to manufacture and process the chemical are required to test if the exposures giving rise to the potential risk occur during distribution in commerce, use, or disposal of the chemical.

Because EPA has found that the use of TGME gives rise to exposure that may lead to an unreasonable risk, EPA is requiring that persons who manufacture or process, or who intend to manufacture or process, TGME, other than as an impurity, at any time from the effective date of this final test rule to the end of the reimbursement period are subject to the testing requirements contained in this final rule. The end of the reimbursement period will be 5 years after the last final report is submitted or an amount of time equal to that which was required to develop data, whichever is later.

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 the requirement. EPA promulgated procedures for applying for TSCA section 4(c) exemptions in 40 CFR Part 790.

Manufacturers (including importers) subject to this rule are required to submit either a letter of intent to perform testing or an exemption application within 30 days after the effective date of this final test rule. The required procedures for submitting such letters and applications are described in 40 CFR Part 790. Although EPA has not identified any individuals who manufacture TGME as a byproduct, such persons will be subject to the requirements of this test rule.

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. EPA expects that the manufacturers will pass an appropriate portion of the costs of testing on to processors through the pricing of their products or other 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, EPA will publish a separate notice in the **Federal Register** to notify processors to respond; this procedure is described in 40 CFR Part 790.

EPA is not requiring the submission of equivalence data as a condition for exemption from the required testing for TGME. As noted in Unit III.C., EPA is interested in evaluating the effects attributable to TGME and has specified a relatively pure substance for testing.

Manufacturers and processors subject to this test rule must comply with the test rule development and exemption procedures in 40 CFR Part 790 for single-phase rulemaking.

E. Reporting Requirements

EPA requires that all data developed under this rule be reported in accordance with its TSCA Good Laboratory Practice (GLP) standards, which appear in 40 CFR Part 792.

In accordance with 40 CFR Part 790, under single-phase rulemaking procedures, test sponsors are required to submit individual study plans at least 45 days before initiation of each test.

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 proposed rule would have required that for range finding for this developmental neurotoxicity test, developmental toxicity testing in the rat be completed before initiating the developmental neurotoxicity study. However, developmental toxicity testing in the rat is being performed by the manufacturers under a negotiated Testing Consent Order using the TSCA guideline in 40 CFR 798.4900, as modified (Ref. 17), and developmental neurotoxicity testing under this rule shall be initiated when the results of the developmental toxicity study are submitted to EPA. If neither developmental or maternal toxicity is seen in the developmental toxicity study, the high dose in the developmental neurotoxicity study shall be 5 grams/kilogram (g/kg). The developmental neurotoxicity test results shall be submitted within 21 months of EPA's publication in the **Federal Register** of a notice announcing the receipt of the developmental toxicity test results. Interim progress reports for the developmental neurotoxicity study shall be provided to EPA at 6-month intervals after the initiation of this test, until the final report is submitted to EPA.

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, EPA will publish a notice of receipt in the **Federal Register** as required by section 4(d).

Persons who export a chemical which is subject to a section 4 test rule are subject to the export reporting requirements of section 12(b) of TSCA. Final regulations interpreting the requirements of section 12(b) are in 40 CFR Part 707. In brief, as of the effective data of this test rule, an exporter of TGME must report to EPA the first annual export or intended export of TGME to each country. EPA will notify the foreign country concerning the test rule for TGME.

F. Enforcement Provisions

EPA 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, (2) submit reports, notices, or other information, or (3) permit access to or copying of records required by TSCA or any regulation or rule 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 TSCA 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 * * *." EPA considers a testing facility to be a place where the chemical is held or stored and, therefore, subject to inspection. Laboratory inspections and data audits will be conducted periodically in accordance with the authority and procedures outlined in TSCA section 11 by duly designated representatives of EPA for the purpose of determining compliance with this final rule for TGME. These inspections may be conducted for purposes which include verification that testing has begun, schedules are being met, and reports accurately reflect the underlying raw data, interpretations, and evaluations, and to determine compliance with TSCA GLP standards and the test standards established in this rule.

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(12)(B) of TSCA to include those requirements necessary to assure that data developed under testing rules are reliable and adequate, and to include such other requirements as are necessary to provide such assurance. EPA 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 which may be calculated as if they never submitted their data. Under the penalty provisions of section 16 of TSCA, any person who violates section 15 of TSCA could be subject to a civil penalty of up to $25,000 for each violation with each day of operation in violation constituting a separate violation. This provision would be applicable primarily to manufacturers that fail to submit a letter of intent or an exemption request and that continue manufacturing 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 EPA has notified them of their obligation to submit such documents (see 40 CFR 790.28(b)). Knowing or willful violations could lead to the imposition of criminal

penalties of up to $25,000 for each day of violation or imprisonment for up to 1 year, or both. In determining the amount of penalty, EPA will take into account the seriousness of the violation and the degree of culpability of the violator as well as all the other factors listed in TSCA section 16. Other remedies are available to EPA under section 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 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.

IV. Economic Analysis of Final Rule

To assess the potential economic impact of this rule, EPA has prepared an economic analysis (Ref. 18) that evaluates the potential for significant economic impact on the industry as a result of the required testing. The economic analysis estimates the cost 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 TGME: (1) Price sensitivity of demand, (2) industry cost characteristics, (3) industry structure, and (4) market expectations. If there is no indication of adverse effect, no further economic analysis is performed; however, if the first level of analysis indicates a potential for significant economic impact, a more comprehensive and detailed analysis is conducted which more precisely predicts the magnitude and distribution of the expected impact.

Total testing costs for the final rule for TGME are estimated to range from $113,800 to $151,900. To predict the financial decision-making practices of manufacturing firms, these costs have been annualized. Annualized costs are compared with annual revenue as an indication of potential impact. The annualized costs represent equivalent constant costs which would have to be recouped each year of the payback period to finance the testing expenditure in the first year.

The annualized test costs (using a cost of capital of 7 percent over a period of 15 years) range from $13,494 to $16,677. Based on the 1986 estimated production volume for TGME of 29.6 million pounds, the unit test costs will be about 0.06 cents per pound. In relation to the selling price of $5.00 per gallon for TGME, these costs are equivalent to 0.17 percent of price.

Based on these costs and the uses of TGME, the economic analysis indicates that the potential for significant adverse economic impact as a result of this testing rule is low. This conclusion is based on the following observations:

1. The estimated unit test costs are very low, 0.17 percent of current price in the upper-bound case.

2. The overall demand for TGME appears relatively inelastic.

Refer to the economic analysis for a complete discussion of test cost estimation and the potential for economic impact resulting from these costs.

V. Availability of Test Facilities and personnel

Section 4(b)(1) of TSCA 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 survey to assess the availability of test facilities and personnel to handle the additional demand for testing services created by this section 4 test rule (Ref. 19). On the basis of this study, EPA believes that there will be available test facilities and personnel to perform the testing specified in this rule.

VI. Rulemaking Record

EPA has established a record for this rulemaking proceeding (docket number OPTS 42080E). This record includes:

A. Supporting Documentation

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

(a) Notice containing the ITC designation of TGME to the Priority List (50 FR 20930; May 21, 1985).

(b) Rules requiring TSCA section 8(a) and 8(d) reporting on TGME (50 FR 20909; May 21, 1985).

(c) Notice of EPA's proposed test rule on TGME (51 FR 17883; May 15, 1986).

(d) TSCA developmental neurotoxicity test guideline final rule (53 FR 5947; February 26, 1988).

(e) Notice of final rulemaking on data reimbursement (48 FR 31786; July 11, 1983).

(f) Notice of interim final rule on single-phase test rule development and exemption procedures (50 FR 20652; May 17, 1985).

(g) TSCA GLP standards (48 FR 53992; November 29, 1983).

(2) Communications consisting of:

(a) Written public comments.

(b) Transcript of public meeting.

(c) Summaries of phone conversations.

(d) Summaries of public meetings.

(e) Letters.

B. References

(1) Goldberg, M.E., Haun, C. and Smyth, H.F., Jr. "Toxicologic implication of altered behavior induced by an industrial vapor." *Toxicology and Applied Pharmacology* 4:148–162 (1962).

(2) Goldberg, M.E., Johnson, H.E., Pozzani, U.C. and Smyth, H.F., Jr. "Effect of repeated inhalation of vapors of industrial solvents on animal behavior. I. Evaluation of nine solvent vapors on pole-climb performance in rats." *American Industrial Hygiene Association Journal* 25:369–375 (1964).

(3) Nelson, B.K., Brightwell, W.S., Burg, J.R., and Massari, V.J. "Behavioral and neurochemical alterations in the offspring of rats after maternal or paternal inhalation exposure to the industrial solvent 2-methoxyethanol." *Pharmacology, Biochemistry & Behavior* 20:269–279 (1984).

(4) Zavon, M.R., "Methyl cellosolve intoxication." *American Industrial Hygiene Association Journal* 24:36–41 (1963).

(5) MB Research Laboratories, Inc. Report on oral LD50 in rats for Olin (1977) and cover letter from Nicholas Barone of Olin Corporation on TSCA 8(d) submission 878216036. Received by the Office of Toxic Substances, USEPA, June 12, 1985.

(6) Nelson, B.K., Brightwell, S., Setzer, J.V., Taylor, B.J., and Hornung, R.W. "Ethoxyethanol behavioral teratology in rats." *Neurotoxicology* 2:231–249 (1981).

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(8) Jones, K.L., Smith, D.W., Streissguth, A.P. and Myrianthopoulos, N.C. "Outcome in offspring of chronic alcoholic women." *Lancet* I:1076–1078 (1974).

(9) Hanson, J.W., Jones, K.L. and Smith, D.W. "Fetal alcohol syndrome. Experience with 41 patients." *Journal of the American Medical Association* 235:1458–1460 (1976).

(10) Jones, K.L. and Smith, D.W. "Recognition of the fetal alcohol syndrome in early infancy." *Lancet* II:999–1001 (1973).

(11) Riley, E.P. and Vorhees, C.V. (Eds.). "*Handbook of Behavioral Teratology*". NY: Plenum (1986).

(12) Kimmel, C.A. and Buelke-Sam, J. "Collaborative behavioral teratology

study: Background and overview." *Neurobehavioral Toxicology and Teratology* 7:541–545 (1985).

(13) Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel Subpanel. A set of scientific issues being considered by the Agency concerning neurotoxicity testing under FIFRA. Report of SAP subpanel recommendations. October 16, 1987.

(14) OTS. Memorandum from R. Craig Matthiessen to Carol Glasgow on Response to Comment on Exposure to the Triethylene Glycol Ethers. Office of Toxic Substances (July 7, 1988).

(15) USITC. "Synthetic organic chemicals. United States production and sales, 1986." Washington, DC: U.S. International Trade Commission, U.S. Government Printing Office (1986).

(16) NIOSH. National Occupational Exposure Survey (1980–1983). Cincinnati, OH: Department of Health and Human Services. National Institute for Occupational Safety and Health (1985).

(17) USEPA. "Testing Consent Order for triethylene glycol monomethyl, monoethyl, and monobutyl ethers." U.S. Environmental Protection Agency (1989).

(18) OTS. "Economic impact analysis of final test rule for triethylene glycol monomethyl ether." Office of Toxic Substances (1988).

(19) Mathtech, Inc. Memorandum from J.K. Orrell to Edmund Coe, OTS, on Developmental Neurotoxicity Laboratory Capability. (September 19, 1988).

(20) OTS. Report by Roger Swarup on test rules exposure analysis of triethylene glycol monomethyl ether, triethylene glycol monoethyl ether, triethylene glycol monobutyl ether. Office of Toxic Substances (July 24, 1985).

VII. Other Regulatory Requirements

A. Executivce Order 12291

Under Executive Order 12291, EPA must judge whether a rule is "major" and therefore subject to the requirement of a Regulatory Impact Analysis. EPA has determined that this 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 costs or prices, and will not have a significant adverse effect on competition or the ability of U.S. enterprise to compete with foreign enterprises.

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

B. Regulatory Flexibility Act

Under the Regulatory Flexibility Act (5 U.S.C. 601 et seq., Pub. L. 96 354, September 19, 1980), EPA is certifying that this test rule will not have a significant impact on a substantial number of small businesses because: (1) they are not likely to perform testing themselves, or to participate in the organization of the testing effort; (2) they will experience only very minor costs, if any, in securing exemption from testing requirements; and (3) they are unlikely to be affected by reimbursement requirements.

C. Paperwork Reduction Act

The information collection requirements contained in this rule have been approved by OMB under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3502 *et seq.* and have been assigned OMB control number 2070–0033.

Public reporting burden for this collection of information is estimated at 1375 hours, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Chief, Information Policy Branch, PM–223, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460; and to the Office of Information and Regulatory Affairs, Office of Management and Budget, Washington, DC 20503, marked "Attention: Desk Officer for EPA."

List of Subjects in 40 CFR Part 799

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

Dated: March 24, 1989.

Susan F. Vogt,

Acting Assistant Administrator for Pesticides and Toxic Substances.

Therefore, 40 CFR 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. By adding § 799.4440 to read as follows:

§ 799.4440 Triethylene glycol monomethyl ether.

(a) *Identification of test substance.* (1) Triethylene glycol monomethyl ether (TGME, CAS No. 112–35–6) shall be tested in accordance with this section.

(2) TGME of at least 90 percent purity shall be used as the test substance.

(b) *Persons required to submit study plans, conduct tests, and submit data.* All persons who manufacture or process TGME, other than as an impurity, after May 17, 1989, to the end of the reimbursement period shall submit letters of intent to conduct testing, submit study plans, conduct tests and submit data, or submit exemption applications as specified in this section, Subpart A of this part, and Parts 790 and 792 of this chapter for single-phase rulemaking.

(c) *Developmental neurotoxicity*—(1) *Required testing.* Developmental neurotoxicity testing shall be performed in the Sprague-Dawley rat by gavage in accordance with § 795.250 of this chapter except for the provision in paragraph (c)(3)(iii) of § 795.250.

(2) For the purpose of this section, the following provision also applies:

(i) *Dose levels and dose selection.* In the absence of developmental toxicity or maternal toxicity the maximum dose shall be 5 grams/kilogram.

(ii) [*Reserved*]

(3) *Reporting requirements*—(i) The developmental neurotoxicity test shall be completed and the final report submitted to EPA within 21 months of the initiation of the test. The test shall be initiated within 44 days of the publication in the Federal Register of notice of EPA's receipt of TGME developmental toxicity data.

(ii) Progress reports shall be submitted to EPA at 6- month intervals, beginning six months after the initiation of the test.

(d) *Effective date.* (1) The effective date of the final rule is May 17, 1989.

(2) The guideline cited in this section is referenced here as it exists on May 17, 1989.

(Information collection requirements have been approved by the Office of Management and Budget under control number 2070–0033.)

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