

40 CFR Part 799**(OPTS-42048; FRL 2480-4)****Hydroquinone; Proposed Test Rule****AGENCY:** Environmental Protection Agency (EPA).**ACTION:** Proposed rule.

SUMMARY: Under section 4(a) of the Toxic Substances Control Act (TSCA), EPA is proposing that manufacturers and processors of hydroquinone perform tests to evaluate hydroquinone's toxicokinetics and tests to evaluate its potential nervous system, reproductive, teratogenic, and mutagenic effects. Epidemiologic studies that evaluate the explicit types and risks of adverse health effects resulting from human exposure to hydroquinone are also proposed. In addition, the Agency is proposing that chemical fate and environmental effects testing be performed. This notice constitutes EPA's response to the Interagency Testing Committee's designation of hydroquinone as a priority candidate for testing.

DATES: Submit written comments on or before March 5, 1984. If persons request an opportunity for oral comment by February 21, 1984, EPA will hold a public meeting on March 19, 1984 on this rule in Washington, D.C. For further information on arranging to speak at the meeting see unit V of this preamble.

ADDRESS: Submit written comments in triplicate to: TSCA Public Information Office (TS-799), Office of Pesticides and Toxic Substances, Environmental Protection Agency, Rm. E-108, 401 M St. SW., Washington, D.C. 20460. Include the document control number [OPTS-42048] on all submissions.

FOR FURTHER INFORMATION CONTACT: Jack P. McCarthy, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Rm. E-543, 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:**I. Introduction**

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

The ITC designated hydroquinone for priority consideration in its Fifth Report, published in the Federal Register on December 7, 1979 (44 FR 70684). The ITC recommended that hydroquinone be considered for testing for carcinogenicity and teratogenicity, and that epidemiology, human metabolism and environmental fate studies also be considered.

The ITC's recommendations were based on the widespread use of the chemical substance by people having little knowledge of its health and environmental effects. The ITC estimated that the U.S. production of hydroquinone in 1977 was about 21 million pounds.

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

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

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

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

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

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

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

EPA uses a weight of evidence approach in making a section 4(a)(1)(A)(i) finding in which both exposure and toxicity information are considered to make the finding that the chemical may present an unreasonable risk. For the finding under section 4(a)(1)(B)(i), EPA considers only production, exposure, and release information to determine if there is or may be substantial production and substantial or significant exposure or substantial release. For the second finding under both sections 4(a)(1)(A)(ii) and 4(a)(1)(B)(ii), EPA examines toxicity and fate studies to determine if existing information is adequate to reasonably determine or predict the effects of human exposure to, or environmental release of, the chemical. In making the third finding, that testing is necessary, EPA considers whether any ongoing testing will satisfy the information needs for the chemical and whether testing which the Agency might require would be capable of developing the necessary information.

EPA's process for determining when these findings apply is described in detail in EPA's first and second proposed test rules. The section 4(a)(1)(A) findings are discussed in the Federal Register of July 18, 1980 (45 FR 48528) and June 5, 1981 (46 FR 30300), and the section 4(a)(1)(B) findings are discussed in the Federal Register of June 5, 1981 (46 FR 30300).

In evaluating the ITC's testing recommendations for hydroquinone, EPA considered all available relevant information including the following: information presented in the ITC's report recommending testing consideration; production volume, use,

exposure, and release information reported by manufacturers of hydroquinone under the TSCA section 8(a) Preliminary Assessment Information Rule (40 CFR Part 712); unpublished health and safety studies submitted by the manufacturers of hydroquinone under the TSCA section 8(d) Health and Safety Data Reporting Rule (40 CFR Part 718); and other published and unpublished data available to the Agency. On the basis of its evaluation as described in this proposed rule and the accompanying technical support document, EPA is proposing limited metabolism (toxicokinetics), nervous system effects, reproductive effects, teratogenicity, and mutagenicity testing requirements, as well as epidemiologic studies, for hydroquinone under section 4(a)(1)(B). The Agency believes that its proposed health effects testing requirements also can be based on section 4(a)(1)(A) of TSCA. EPA is also proposing chemical fate and environmental effects testing requirements for hydroquinone under section 4(a)(1)(A) of TSCA. By these actions, EPA is responding to the ITC's designation of hydroquinone for testing consideration.

II. Proposed Rule

A. Profile

Hydroquinone [C₆H₄(OH)₂] CAS No. 123-31-9, is a white crystalline solid at room temperature and is very soluble in water, ethanol, and acetone. It acts chemically as a reducing agent, being oxidized to quinone. Although the EPA Toxic Substances Inventory records that approximately 11 million pounds of hydroquinone were produced in the United States in 1977, data obtained

through the Preliminary Assessment Information Rule, issued under section 8(a) of TSCA (47 FR 28992), indicates that the annual production is significantly higher. These 8(a) data have been claimed as confidential business information and are not cited directly in this document. The annual production of photograde, technical, and other grades of hydroquinone from 1978 to 1980 has been estimated to be as high as 25 to 26 million pounds.

Hydroquinone is used as a photographic developer and as an organic intermediate in the manufacture of dyes and other chemicals. It is used directly as an antioxidant or is processed into derivatives that are used as antioxidants to inhibit the breakdown of nonfood industrial fats, oils, paints, and motor fuels. Hydroquinone is used in dermatologic preparations designed to bleach hyperpigmented skin and as a storage and in-process polymerization inhibitor for vinyl monomers and unsaturated resins.

B. Findings

EPA is basing its proposed hydroquinone health effects testing on the authority of section 4(a)(1) (A) and (B) of TSCA.

1. EPA finds that hydroquinone is manufactured, processed, and used in substantial quantities, and these activities may result in substantial human exposure. Furthermore, EPA finds that there are insufficient data available to reasonably determine or predict either the result of this exposure in the areas of carcinogenic, mutagenic, teratogenic, nervous system, and reproductive health effects or the incidence of hydroquinone-related effects among humans. Finally, EPA finds that testing of hydroquinone for these health effects and epidemiologic parameters is necessary to develop data needed to evaluate the health risks posed by exposure to hydroquinone.

These findings are based on the following information:

a. There are substantial amounts of hydroquinone produced in the United States each year. The annual U.S. production volume of hydroquinone is estimated to be as high as 26 million pounds.

b. In 1980 the National Institute for Occupational Safety and Health estimated that approximately 470,000 U.S. workers, in 137 occupations, are potentially exposed to hydroquinone annually. Of major concern to the Agency are the estimated 2.2 million photohobbyists who develop their own film and prints, because much of this involves the development of black and

white film which incorporates solutions containing hydroquinone. The Agency believes that both workers and hobbyists will receive inhalation and dermal exposure.

2. In addition, EPA has found that the manufacture, processing and use of hydroquinone may present an unreasonable risk of injury to human health. There is evidence of potential human health risks from nervous system, mutagenic, teratogenic, reproductive, and carcinogenic effects resulting from the manufacture, processing, and use activities associated with hydroquinone; there are existing data to support this belief with respect to these effects. Exposures to hydroquinone are sufficient to result in such effects. The existing data are inadequate to reasonably predict or determine the effects of these exposures to hydroquinone. Testing is necessary for these effects. Therefore, EPA believes that requiring epidemiologic studies and testing of hydroquinone for nervous system effects, mutagenicity, teratogenicity, reproductive effects, and carcinogenicity can also be based upon section 4(a)(1)(A) of TSCA.

EPA is not proposing oncogenicity testing of hydroquinone, since the National Toxicology Program (NTP) is currently conducting a 2-year bioassay on hydroquinone. However, the Agency is proposing limited metabolism (toxicokinetic) studies of hydroquinone via dermal and oral routes of exposure. These studies will provide a reliable means by which the internal dose administered in the NTP bioassay can be related to doses expected to be received by workers and hobbyists.

In addition, the Agency has concluded that the acute toxicity (lethality) and the subchronic toxicity of hydroquinone are adequately characterized, and therefore, no further testing should be required at this time.

The Agency is basing its chemical fate and environmental effects testing on the authority of section 4(a)(1)(A) of TSCA. (1) EPA finds that there is evidence of potential environmental risks to aquatic organisms resulting from the processing and use activities associated with hydroquinone. (2) While there are existing data to support this belief with respect to these effects, the data are inadequate to reasonably predict or determine the effects of these exposures to hydroquinone. (3) Testing is necessary to develop data with respect to these effects.

Although the ITC did not recommend environmental effects testing for hydroquinone, the Agency is concerned with effluents from photoprocessing facilities and is proposing a series of

environmental effects tests. Based on existing aquatic toxicity data and the limited data on photoprocessing effluents, the Agency believes that the levels of hydroquinone in these effluents, although not so substantial as to dictate a section 4(a)(1)(B) finding, may present an unreasonable risk (section 4(a)(1)(A)) to aquatic organisms. Testing is needed to provide data to establish whether an unreasonable risk to freshwater and saltwater aquatic species exists.

The Agency is also proposing chemical fate testing for hydroquinone. EPA believes that this testing is essential, because the existing chemical fate data are limited and more data are needed to assess the magnitude of the possible risks to aquatic organisms. EPA needs information to establish biodegradation rates in order to assess the levels of hydroquinone exposure to aquatic organisms.

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

The analyses on which these findings are based are presented in the Technical Support Document, "Assessment of Testing Needs: Hydroquinone/Quinone," which is available from the TSCA Assistance Office. The ITC recommendations and EPA's proposed testing requirements are summarized in the following Table.

TESTING RECOMMENDATIONS FOR
HYDROQUINONE

Effect or study	ITC recommendation	EPA proposal
Mutagenicity.....	—	X
Carcinogenicity.....	X	—
Teratogenicity.....	X	X
Nervous System Effects.....	—	X
Reproductive Effects.....	—	X
Epidemiology.....	X	X
Metabolism (Toxicokinetics).....	X	X
Environmental Fate.....	X	X
Environmental Effects.....	—	X

* Not proposed since NTP is conducting a 2-year bioassay.

C. Test Substance

EPA is proposing for the mutagenicity, teratogenicity, reproductive effects, nervous system effects, toxicokinetics, chemical fate, and environmental effects testing that hydroquinone of at least 99 percent purity, available commercially, be used as the test substance. EPA has specified a relatively pure substance for testing because the Agency is interested in evaluating the effects attributed to hydroquinone itself. This requirement would increase the likelihood that any

toxic effects observed are related to hydroquinone and not to any impurities.

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 ("manufacture" is defined in section 3(7) of TSCA to include "import"). Processors are required to test if the findings are based on processing. Both manufacturers and processors are required to test if the exposures giving rise to the potential risk occur during use, distribution, or disposal. Because EPA has found that the manufacturing, processing, and use of hydroquinone give rise to exposures that may lead to an unreasonable risk, EPA is proposing that persons who manufacture or process, or who intend to manufacture or process hydroquinone at any time 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 submission of the last final report required under the 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 (as discussed in Unit II.F. below).

E. Approach to Adoption of Test Rules

1. *General Process.* On March 28, 1982, EPA announced a new approach to adoption of test rules (47 FR 13102). EPA intends to promulgate a general procedural rule in 40 CFR Part 770 which will contain the procedural requirements of this new approach. However, since that procedural rule is not in effect, this proposed rule contains specific procedures for adoption of this test rule. If the general rule is promulgated before this proposal becomes final, the hydroquinone rule will be modified to comport with the general procedural provisions.

Under the approach being followed for hydroquinone, test rule development will be a two-phase process. In phase I, EPA will propose that specific testing be

required for hydroquinone. This phase of the rulemaking will allow the public to comment on the decision to require testing and the specific types of tests to be required. Phase II begins after promulgation of the phase I rule. In phase II, EPA will receive proposed study plans for the specific tests adopted in the phase I rule. EPA will propose those study plans for public comment. After comment, the Agency will adopt the study plans, as proposed or modified, as specific test standards for the tests required by the phase I rule. Persons who submit the study plans will be obligated to perform the tests in accordance with the test standards adopted.

2. Letter of Intent to Test or Exemption Application. The proposed rule would require manufacturers and processors of hydroquinone to perform certain test sets. (The term "test set" is used because certain mutagenicity tests in the proposal are tiered, and EPA is proposing that the person who tests must perform all the required tests in that tier.) Once the rule is in effect, 30 days after publication in the Federal Register, each current manufacturer would have 30 days to submit, for each required test set in paragraphs (j), (k), and (l) of the rule, either a letter of intent to perform the test set or an application for exemption. Each manufacturer who submitted a letter of intent to perform a specific test set would be obligated, first, to submit, within 90 days of the effective date, a proposed study plan for the test set and, ultimately, to perform the testing.

If manufacturers of hydroquinone performed all the required test sets, processors of hydroquinone would not be required to test or to submit exemption applications. EPA would automatically grant them exemptions from the requirements of the rule.

If no manufacturer of hydroquinone submitted a letter of intent to perform a particular test set within the 30-day period, EPA would publish a notice in the Federal Register to notify all processors of hydroquinone. The notice would state that EPA had not received letters of intent to perform certain test sets and that current processors would have 30 days to submit, for each test set remaining, either a letter of intent to perform the test or an exemption application for that test set. Each processor who submitted a letter of intent to perform a specific test set would be obligated, first, to submit, within 90 days of the publication of the Federal Register notice, a proposed study plan for the test set and, ultimately, to perform the testing.

If no manufacturer or processor submitted a letter of intent to perform a particular test set, EPA would notify all manufacturers and processors, by letter or through the Federal Register, that all exemption applications would be denied and that within 30 days all manufacturers and processors would be in violation of the rule until a proposed study plan is submitted for that test set.

Any person not manufacturing hydroquinone at the time the rule goes into effect, who later begins manufacturing before the end of the reimbursement period, would be required to submit a letter of intent to test or an exemption application for each required test set, by the day the person begins manufacture. If EPA has published a notice in the Federal Register telling processors to submit letters of intent or exemption applications for certain test sets, any person not processing hydroquinone at the time the rule goes into effect, who later begins processing before the end of the reimbursement period, would be required to submit a letter of intent to test or an exemption application for each test set specified in the Federal Register notice by the day the person begins processing.

3. Submission and Adoption of Study Plans. Any manufacturer of hydroquinone who submitted a letter of intent to perform a test set would have to submit, within 90 days after the effective date of the rule, a proposed study plan for that test set. In the event manufacturers do not submit letters of intent for all the required test sets, any processor who submits a letter of intent to perform a specific test set would have to submit, within 90 days of the publication of the Federal Register notice notifying processors, a proposed study plan for that test set. Paragraph (e) of the rule describes the contents of a proposed study plan.

EPA proposed generic test methodology requirements (generic test standards) in the Federal Register of May 9, 1979 (44 FR 27334), July 26, 1979 (44 FR 44054), and November 21, 1980 (45 FR 77332). In response to concerns about the rigidity of generic methodology requirements, EPA has changed its approach for providing test standards for TSCA section 4 test rules. It has issued generic test methodology guidelines to replace the previously proposed generic test methodology requirements. The TSCA Guidelines have been published by the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650), for health effects (PB 82-232984), chemical fate (PB 82-

233006), and environmental effects (PB-82-232992), respectively. Good Laboratory Practice (GLP) standards for development of data on health effects of chemical substances under TSCA were proposed in the Federal Register of May 9, 1979 (44 FR 27334) and July 26, 1979 (44 FR 44054), and for chemical fate and environmental effects testing in the Federal Register of November 21, 1980 (44 FR 77357). GLP standards for development of data on physical and chemical properties, persistence, and ecological effects of chemical substances under TSCA were proposed in the Federal Register of November 21, 1980 (44 FR 77357). These GLP standards will be promulgated as generic requirements. The final TSCA GLP regulations will apply to the hydroquinone test rule.

For guidance in preparing study plans, EPA recommends that test sponsors consult the TSCA Test Guidelines and the TSCA GLP standards as referenced above, the Organization for Economic Cooperation and Development's (OECD) Guidelines, as adopted by the OECD Council on May 12, 1981, or the FIFRA Pesticide Registration Guidelines: Proposed Data Requirements, published by the National Technical Information Service (see the Federal Register of November 24, 1982 (47 FR 53192), for a list of these guidelines).

Failure to submit a study plan would be a violation of the rule.

EPA would review the proposed study plans. If they were incomplete, the manufacturer or processor would be notified of the deficiency and would have 15 days to provide appropriate information to make the plan complete. If the information were not provided in 15 days, the manufacturer or processor would be in violation of the rule. In addition, EPA would return to the appropriate stage of the process and require manufacturers or processors, as appropriate, to submit letters of intent, exemption applications, and study plans.

If the proposed study plan were complete, EPA would propose the study plan for public comment. In particular, the request for comments would focus on whether the study plan would ensure that data from the test set would be reliable and adequate. There would be a 45-day comment period and the opportunity to present views orally upon request. After considering the public comment, EPA would adopt the study plan as proposed, or as modified in response to comment, as the test standard for the required test set.

The person who submitted the proposed study plan would be required

to perform the testing according to that standard. Failure to perform the testing would be a violation of the rule.

F. Exemptions

EPA's proposed policy on application for exemptions from section 4 testing requirements was published in the Federal Register of July 18, 1980 (45 FR 48512). EPA intends to promulgate its final procedures for exemptions in 40 CFR Part 770. The exemption procedures described below and included in the proposed rule language are consistent with EPA's current thinking on exemption procedures. If the general rule is promulgated before this proposal becomes final, the hydroquinone rule will be modified to comport with the general procedural provisions.

Any manufacturer or processor of hydroquinone would be able to apply for an exemption. Any person who has applied for an exemption would not be in violation of the rule until such time as EPA denies the application.

If manufacturers perform all the required testing, processors would be granted exemptions automatically without having to file applications.

When EPA has received a proposed study plan for a test set and has adopted the plan as the test standard, EPA would conditionally grant all exemption applications for that test set. If the test sponsor later fails to perform the testing, EPA would notify all persons who had submitted exemption applications for that test set that the exemptions would be denied, unless within 30 days a manufacturer or processor notified EPA of its intent to perform the testing in accordance with the adopted test standards.

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

G. Reporting Requirements

EPA is proposing that all data developed under this rule be reported in accordance with its final GLP Standards, which will appear in 40 CFR Part 792.

EPA is required by TSCA section 4(b)(1)(C) to specify the time period during which persons subject to a test rule must submit test data. These deadlines will be established in the phase II rulemaking in which study plans are approved.

TSCA section 14(b) governs Agency disclosure of all test data submitted pursuant to section 4 of TSCA. Upon

receipt of data required by this rule, the Agency will publish a notice of receipt in the Federal Register as required by section 4(d).

H. Enforcement Provisions

The Agency considers failure to comply with any aspect of a section 4 rule to be a violation of section 15 of TSCA. Section 15(1) of TSCA makes it unlawful for any person to fail or refuse to comply with any rule or order issued under section 4. Section 15(3) of TSCA makes it unlawful for any person to fail or refuse to (1) establish or maintain records, (2) submit reports, notices, or other information, or (3) permit access to or copying of records required by the Act or any 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 section 11. Section 11 applies to any "establishment, facility, or other premises in which chemical substances or mixtures are manufactured, processed, stored, or held before or after their distribution in commerce. . . ." The Agency considers a testing facility to be a place where the chemical is held or stored and, therefore, subject to inspection. Laboratory audits/inspections 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 any final rule for hydroquinone. These inspections may be conducted for purposes which include verification that testing has begun, that schedules are being met, that reports accurately reflect the underlying raw data and interpretations and evaluations thereof, and that the studies are being conducted according to EPA GLP standards and the protocols established in the phase II 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 such other requirements as are necessary to provide such assurance. The Agency maintains that laboratory inspections are necessary to provide this assurance.

Violators of TSCA are subject to criminal and civil liability. Persons who submit materially misleading or false information in connection with the requirement of any provision of this rule may be subject to penalties calculated

as if they never submitted their data. Under the penalty provision of section 16 of TSCA, any person who violates section 15 could be subject to a civil penalty of up to \$25,000 per day for each violation. Each day of operation in violation may constitute a separate violation. This would be applicable primarily to manufacturers or processors that fail to submit a letter of intent to perform testing or an exemption request, and that continue manufacturing or processing after the deadlines for such submissions. Knowing or willful violations could lead to the imposition of criminal penalties of up to \$25,000 for each day of violation and imprisonment for up to one year. Other remedies are available to EPA under sections 7 and 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 18 of TSCA apply to "any person" who violates various provisions of TSCA. EPA may, at its discretion, proceed against individuals as well as companies themselves. In particular, this includes individuals who report false information or who cause it to be reported. In addition, the submission of false, fictitious, or fraudulent statements is a violation under 18 U.S.1001.

I. Issues for Public Comment

1. EPA has proposed only limited metabolism (toxicokinetic) studies via oral and dermal routes of exposure in lieu of full metabolism investigations. Of concern, however, is the presence of unconjugated hydroquinone and unconjugated metabolites in the systemic circulation after penetration through the skin. This is of concern because hydroquinone is a suspected carcinogen, and, at this time, it is assumed that unconjugated rather than conjugated hydroquinone is the carcinogenic agent. The Agency is requesting comments on possible additional study requirements for the skin penetration investigation of hydroquinone. Specifically, it may be useful to ascertain the time-course and distribution of unconjugated hydroquinone after topical application, since hydroquinone reaching the blood via this route may be metabolized differently than that via the oral route.

2. Some xenobiotics are known to penetrate skin more readily after repeated applications. The skin penetrating potential of hydroquinone, unknown, and thus, the possible differences between single and repeated exposures remain obscured. The

Agency, therefore, is requesting comments on whether or not repeated topical exposures during the required toxicokinetic testing may be more definitive as regards the true penetrating potential of hydroquinone.

3. The Agency is concerned with the effect of chronic exposures to hydroquinone on aquatic organisms. Therefore, EPA has proposed a series of acute and chronic tests on aquatic organisms with hydroquinone. The data derived from these tests will be used to determine whether an unreasonable risk exists to aquatic species. Further, if it is determined from these data that hydroquinone poses an unreasonable risk, this universe of data could be used to establish water quality criteria under the Clean Water Act.

However, it is anticipated that chronic testing of hydroquinone on aquatic species may present some technical problems in that it appears difficult to maintain the compound in test systems (see Hydroquinone/Quinone Technical Support Document). The Agency is requesting comments, from a technological standpoint, on the feasibility of conducting these chronic aquatic toxicity studies. If the methods for the chronic studies prove to be unsatisfactory, EPA may require supplemental acute testing of embryo-juvenile life stages of fish and larvae of invertebrates.

4. EPA is proposing two epidemiologic studies to evaluate the magnitude of the potential health risks, identified by the Agency, in individuals exposed to hydroquinone. The Agency is requesting comments on:

a. The suitability of the Agency's selection of endpoints (i.e., ocular lesions, total cancers for one study; total birth defect incidence, spontaneous abortions, and testicular effects for the other study).

b. The Agency's suggestion that the study design specified, which uses cancer as a guide, will also assist in detecting unreasonable risks from other morbid endpoints.

Further, is there enough information regarding human responses to hydroquinone exposure for the Agency to be more explicit in its design requests and still (1) gain information on a variety of endpoints and (2) not restrict the investigations?

5. As indicated in the Technical Support Document for Hydroquinone/Quinone, the Agency believes that the presence of quinone in the environment is primarily a result of the release of hydroquinone which is converted to quinone in the environment. The Agency is proposing environmental effects and chemical fate testing for quinone as well

as environmental effects and chemical fate testing for hydroquinone. As proposed, manufacturers and processors of quinone would be responsible for testing quinone for environmental effects, regardless of the fact that most quinone in the environment might result from release of hydroquinone.

Requiring manufacturers and processors of quinone to conduct environmental effects and chemical fate testing of quinone may be inequitable if the quinone in the environment results primarily from hydroquinone manufacture and processing. However, section 4(b)(3)(B) of TSCA specifies that testing must be conducted by "[e]ach person who manufactures or intends to manufacture *such substance*" and "[e]ach person who processes or intends to process *such substance*." EPA believes that this language requires the approach contained in the proposal for quinone testing. However, the Agency is considering requiring the manufacturers and processors of hydroquinone to either conduct or share in the cost of conducting environmental effects and chemical fate testing for quinone. This could be accomplished either by transferring the quinone environmental effects and chemical fate testing requirements to the hydroquinone test rule or by adding manufacturers and processors of hydroquinone to those required to test under the quinone test rule. EPA solicits comments on these alternative approaches to testing quinone for chemical fate and environmental effects.

III. Economic Analysis of Proposed Rule

To assess the potential economic impact of this proposed rule, EPA has prepared a Level I economic analysis that examines the costs of the required testing and analyzes four market characteristics of the chemical substance: (1) Demand sensitivity, (2) cost characteristics, (3) industry structure, and (4) market expectations.

The Level I analysis of hydroquinone, which estimates the total testing costs to range from \$682,600 to \$1,577,700, 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. Stable or moderate market growth is expected for hydroquinone.
2. The relative magnitude of the test cost is minor, i.e., on an annualized unit cost basis, the hydroquinone test costs are estimated to average 0.7 to 1.6 cents per pound. The unit costs represent 0.31 to 0.71 percent of the price of hydroquinone.
3. Because the market for hydroquinone is stable or growing

somewhat and demand in its primary uses is inelastic, it appears that the direct cost of testing hydroquinone can be passed on to consumers with little or no economic impact.

Because the Level I analysis indicates very little potential for an adverse economic impact, EPA has determined that a more comprehensive and detailed Level II economic evaluation is not needed for hydroquinone.

IV. 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 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 test programs negotiated with industry in place of rulemaking. Copies of the study, "Chemical Testing Industry: Profile of Toxicological Testing, October, 1981," can be obtained from NTIS, under publication number PB 82-140773.

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

V. Public Meetings

If persons indicate to EPA that they wish to present comments on this proposed rule to EPA officials who are directly responsible for developing the rule and supporting analyses, EPA will hold a public meeting on March 19, 1984 in Washington, D.C. Persons who wish to present comments at the meeting should call the TSCA Assistance Office (TAO), Toll Free: (800-424-9065). In Washington, D.C.: (554-1404). Outside the U.S.A. (Operator-202-554-1404) by February 21, 1984. The meeting will not be held if members of the public do not indicate they wish to make oral presentations. 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.

While the meeting will be open to the public, active participation will be limited to those persons who arranged to present comments and to designated EPA participants. Attendees should call the TAO before making travel plans to check whether the meeting will be held.

Should a meeting be held, the Agency will transcribe the meeting and include the written transcript in the public record. Participants are requested, 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.

VI. Rulemaking Record

EPA has established a record for this rulemaking, docket number [OPTS-42048]. This record includes the 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. Confidential business information (CBI), while part of the record, is not available for public review. A public version of the record, from which CBI has been deleted, is available for inspection in the OPTS Reading Room from 8:00 a.m. to 4:00 p.m., Monday through Friday, except legal holidays, in Rm. E-107, 401 M St. SW., Washington, D.C.

The record includes the following information:

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

(a) Notice of proposed rulemaking on hydroquinone.

(b) Notice containing the ITC designation of hydroquinone to the Priority List [44 FR 70664, December 7, 1979].

(c) Notices relating to EPA's health effects, chemical fate, and environmental effects test guidelines (44 FR 27334, May 9, 1979; 44 FR 44054, July 26, 1979) and EPA Good Laboratory Practice standards (44 FR 27334 May 9, 1979; 44 FR 44054, July 26, 1979).

(d) Notice of proposed rulemaking on exemption policy and procedures.

(e) Final reimbursement policy and procedures.

(2) Support Documents consisting of:

(a) Hydroquinone/Quinone technical support document.

(b) Economic analysis support document.

(3) Communications before proposal consisting of:

(a) Written public comments.

(b) Summaries of telephone conversations.

(c) Meeting summaries.

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

(4) Report—Chemical Testing Industry: Profile of Toxicological Testing. October, 1981.

VII. 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. This test rule 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 proposed for hydroquinone is less than \$408,800 over the testing and reimbursement period. Second, because the cost of the testing will be distributed over a large production volume, the rule will have only very minor effects (annualized unit costs are less than 1.6 cents per pound) on producers' costs or users' prices for this chemical substance. 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 impact 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. Any comments from OMB to EPA, and any EPA response to those comments, will be included in the public record.

VIII. Regulatory Flexibility Act

Under the Regulatory Flexibility Act, (15 U.S.C. 601, *et seq.*, 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 because:

(1) Small processors will not perform testing themselves and will not participate in the organization of the testing effort.

(2) They will experience only minor costs in securing exemption from testing requirements.

(3) They are unlikely to be affected by reimbursement requirements.

(4) There are no small manufacturers of hydroquinone which will be affected by this rule.

IX. Paperwork Reduction Act

The information collection requirements in this proposed rule have been submitted for approval to the OMB under the Paperwork Reduction Act of 1980, 44 U.S.C. 3501 *et seq.* Comments on these requirements should be submitted to the Office of Information and Regulatory Affairs of OMB marked Attention: Desk Officer for EPA. The final rule package will respond to any OMB or public comments on the information collection requirements.

X. Guidelines and Study Plans

The following guidelines and/or study plans cited in this proposed test rulemaking are available from: National

Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, (703) 487-4650.

NTIS Publication No.	Title	Price
PB-82-140773	Chemical Testing Industry: Toxicological Testing.	\$16.00
PB-82-232984	TSCA Health Effects Guidelines.	40.00
PB-82-232992	Environmental Effects Guidelines.	60.00
PB-83-153908	OECD Test Guidelines for Hazard Evaluation: Wildlife and Aquatic Organisms.	11.50
PB-82-233006	TSCA Chemical Fate.	40.00
PB-83-153916	FIFRA Pesticides Registration Guidelines: Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals.	11.50

List of Subjects in 40 CFR Part 799

Testing, Environmental protection, Hazardous material, Chemicals.

(Sec. 4, Pub. L. 94-469, 90 Stat. 2003; (15 U.S.C. 2061))

Dated: December 23, 1983.

Alvin L. Alm,
Acting Administrator.

PART 799—[AMENDED]

Therefore, it is proposed that a new § 799.2200 be added to Subpart B of proposed Part 799 to read as follows:

§ 799.2200 Hydroquinone.

(a) *Identification of test substance.* (1) Hydroquinone (CAS No. 123-31-9) shall be tested in accordance with this section.

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

(b) *Persons required to submit study plans, conduct tests and submit data.* (1)

All persons who manufacture or process hydroquinone from the effective date of this section (30 days from the publication date of the final rule in the Federal Register) to the end of the reimbursement period shall submit letters of intent to test, exemption applications, and study plans and shall conduct tests and submit data as specified in paragraphs (c), (d), (e), (h), (j), (k) and (l) of this section.

(2) Any person subject to the requirements of this section may apply to EPA for an exemption from study plan submission and testing requirements. Any such application shall be in accordance with paragraph (h) of this section.

(c) *Submission of notice of intent to test or exemption application.* (1) No later than 30 days after the effective date of this section, each person manufacturing hydroquinone as of the effective date of this section must, for

each test set required by paragraphs (j), (k), and (l) of this section, either notify EPA by letter of his/her intent to perform the test set or submit an application for an exemption from the study plan submission and testing requirements for the test set.

(2) If, by the date specified in paragraph (c)(1) of this section, no manufacturer of hydroquinone has notified EPA of its intent to perform testing for a test set required by paragraphs (j), (k), or (l) of this section, EPA will publish a notice in the Federal Register of this fact specifying the test sets for which no notice of intent has been submitted. No later than 30 days after publication of such a notice, each person processing hydroquinone as of the effective date of this section must, for each test set specified in the Federal Register notice, either notify EPA by letter of his/her intent to perform the test set or submit an application for an exemption from the study plan submission and testing requirements for the test set.

(3) Any person not manufacturing hydroquinone as of the effective date of this section who, before the end of the reimbursement period, manufactures hydroquinone must comply with the requirements of paragraphs (c)(1) and (d)(1) of this section. For purposes of this paragraph (c)(3), the manufacturer must submit the notice of intent to test or exemption application required by paragraph (c)(1) of this section by the date manufacture begins and must submit any proposed study plan required by paragraph (d)(1) of this section within 60 days of the date manufacture begins.

(4) If a Federal Register notice has been published under paragraphs (c)(2) or (d)(4) of this section, any person not processing hydroquinone as of the effective date of this section who, before the end of the reimbursement period, processes hydroquinone must comply with the requirements of paragraphs (c)(2) and (d)(2) of this section. For purposes of this paragraph (c)(4), the processor must submit the notice of intent to test or exemption application required by paragraph (c)(2) of this section by the date processing begins and must submit any proposed study plan required by paragraph (d)(2) of this section within 60 days of the date processing begins.

(5) Any manufacturer or processor of hydroquinone which has notified EPA under paragraphs (c) (1), (2), (3), or (4) of this section of its intent to perform testing for a test set required by paragraph (j), (k), or (l) of this section, must submit a proposed study plan for the test set as required in paragraph (d)

of this section and must perform that test set in accordance with the test standards in paragraph (m) of this section.

(d) *Submission of proposed study plans.* (1) Manufacturers of hydroquinone which notify EPA under paragraph (c)(1) of this section that they intend to perform a test set must submit a proposed study plan for the test set in accordance with paragraph (e) of this section no later than 90 days after the effective date of this section. Manufacturers may jointly submit a single proposed study plan if they plan to sponsor or perform the test set jointly. Any manufacturer which, having notified EPA of its intent to perform a test set, fails to submit a proposed study plan for that test set will have been in violation of this section as if no letter of intent to perform the test set had been submitted.

(2) Processors of hydroquinone which notify EPA under paragraphs (c)(2) of this section that they intend to perform a test set must submit a proposed study plan for the test set in accordance with paragraph (e) of this section no later than 90 days after the publication of the notice specified in paragraph (c)(2) of this section. Processors may jointly submit a single proposed study plan if they plan to sponsor or perform the test set jointly. Any processor which, having notified EPA of its intent to perform a test set, fails to submit a proposed study plan for that test set will have been in violation of this section as if no letter of intent to perform the test set had been submitted.

(3) If EPA determines in accordance with paragraph (f)(1)(i) of this section that a proposed study plan is incomplete and the manufacturer or processor has not, after notice from EPA, submitted appropriate information to make the study plan complete within 15 days, the manufacturer or processor will have been in violation of this section as if no letter of intent to perform the test set had been submitted.

(4) If either:

(i) By the date specified in paragraph (d)(1) of this section a manufacturer of hydroquinone, which notified EPA of its intent to perform a test set, has failed to submit a proposed study plan for that test set, or

(ii) A proposed study plan submitted under paragraph (d)(1) of this section has been found to be incomplete under paragraph (f)(1)(i) of this section and the manufacturer has not submitted appropriate information to make the study plan complete within 15 days, EPA will publish a notice in the Federal Register of this fact specifying the test set. The requirements of paragraphs

(c)(2) and (d)(2) of this section for processors to submit letters of intent to perform testing, applications for exemption, and proposed study plans will apply.

(5) If either:

(i) By the date specified in paragraph (c)(2) of this section no processor of hydroquinone has notified EPA of its intent to perform testing for any test set identified in a Federal Register notice published under paragraphs (c)(2) or (d)(4) of this section,

(ii) By the date specified in paragraph (d)(2) of this section any processor of hydroquinone, which notified EPA of its intent to perform a test set, has failed to submit a proposed study plan for that test set, or

(iii) A proposed study plan submitted under paragraph (d)(2) of this section has been found to be incomplete under paragraph (f)(1)(i) of this section and the processor has not submitted appropriate information to make the study plan complete within 15 days, all applications for exemption from the requirements to submit study plans and to perform tests for the specific test set involved will automatically be denied. EPA will notify each manufacturer and processor of hydroquinone, which applied for an exemption for the specific test set involved, of this automatic denial either by letter or by notice in the Federal Register. Each manufacturer or processor of hydroquinone for which an exemption application has been automatically denied will be in violation of this section 30 days from the time that it receives the notice letter or 30 days from the time that the notice is published in the Federal Register, whichever comes first. The violation will continue until a manufacturer or processor of hydroquinone submits a proposed study plan for each test set involved.

(6) Any manufacturer or processor of hydroquinone may submit a proposed study plan for any test set required by this section at any time, regardless of whether the manufacturer or processor previously submitted an application for exemption from testing for that test set.

(e) *Content of study plans.* (1) All study plans are required to contain the following information:

(i) A citation to this section.

(ii) The specific test set covered by the study plan.

(iii)(A) The names and addresses of the test set sponsors.

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

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

(D)(1) The name and address of the testing facility and the names, addresses, and telephone numbers of the testing facility's administrative officials and project manager(s) responsible for this testing.

(2) Brief summaries of the training and experience of each professional involved in the study including study director, veterinarian(s), toxicologist(s), pathologist(s) and laboratory assistants.

(iv) Identity and data on the chemical substance being tested, including appropriate physical constants, spectral data, chemical analysis, and stability under test and storage conditions.

(v) 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.

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

(2) Information specified under paragraph (e)(1)(iii)(D) 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.

(f) *Review and adoption of study plans.* (1) Upon receipt of a proposed study plan, EPA will review the study plan to determine whether it complies with paragraph (e) of this section.

(i) If EPA determines that the proposed study plan does not comply with paragraph (e) of this section, EPA will notify the submitter that the submission is incomplete and will identify the deficiencies and the steps necessary to complete the submission. The submitter will have 15 days from the day it receives this notice to submit appropriate information to make the study plan complete. If the submitter fails to provide appropriate information to complete the study plan within this time, the submitter will have been in violation of this section as if no study plan had been submitted.

(ii) If EPA determines the proposed study plan complies with paragraph (e) of this section, EPA will publish a notice in the Federal Register requesting comments on the ability of the study

plan to ensure that data from the test set will be reliable and adequate. EPA will provide a 45-day comment period and will provide an opportunity for an oral presentation upon 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 from public comments that further comment is warranted.

(2) After receiving and considering public comment, EPA will adopt the study plan, including time deadlines and reporting schedules, as proposed or as modified in response to EPA review and public comments, as test standards for the testing of hydroquinone in paragraph (m) of this section.

(g) *Modification of study plans during conduct of study—(1) Application.* Any test set sponsor who wishes to modify the adopted study plan for any test set required under this section must submit an application in accordance with this paragraph. Application for modification shall be made in writing to the Chief, Test Rules Development Branch, Office of Toxic Substances, or by phone with written confirmation to follow as soon as feasible. Applications must include appropriate explanation of why the modification is necessary.

(2) *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. However, EPA will act on the requested modification without seeking public comment if either:

(i) EPA believes that an immediate modification to a study plan is necessary in order to preserve the accuracy or validity of an ongoing study, or

(ii) EPA determines that a modification clearly does not pose any significant substantive issues. EPA will notify the sponsor of EPA'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.

(h) *Exemption applications.* (1) Any manufacturer or processor of hydroquinone may submit an application to EPA for an exemption from submitting proposed study plans for, and from performing, any or all of the test sets specified in paragraphs (j), (k), and (l) of this section. The application must include the name and address of the manufacturer or processor and must identify the specific requirements of the section from which the exemption is sought.

(2) No manufacturer or processor of hydroquinone will be in violation of the

requirement to perform a specific test set under paragraph (j), (k), or (l) of this section if it has submitted a timely application for an exemption for that test set and the application has not been denied by EPA.

(3) EPA will conditionally grant any requested exemption for a specific test set required by paragraph (j), (k), or (l) of this section if EPA has received a complete proposed study plan for that test set in accordance with paragraph (e) of this section and has adopted the study plan in accordance with paragraph (f)(2) of this section.

(4) EPA will deny any exemption for a specific test set in paragraph (j), (k), or (l) of this section if the test set sponsor fails to perform the test or to submit data as required in the test set standards adopted under paragraph (m) of this section.

(5) If manufacturers of hydroquinone perform all the test sets required by paragraphs (j), (k), and (l) of this section, processors of hydroquinone will automatically be granted an exemption from the study plan submission and testing requirements without the need to file an application for exemption.

(i) *Test results.* A positive or negative test result in any of the health effects tests enumerated in paragraph (j) of this section is defined as specified in the TSCA Health Effects Test Guidelines published by the National Technical Information Service (NTIS) under publication number PB 82-232984.

(j) *Health effects testing—(1) Toxicokinetic Studies—(i) Required testing.* Skin and oral dosing studies, which provide data regarding both rate and extent of absorption, shall be conducted with hydroquinone.

(ii) *Study plans.* At present, EPA has no approved guidelines or protocols for determining the penetrating potential of xenobiotics through skin. The best available guidance may be the method of Feldman and Maibach (1969). In addition, Chapter 5 of the *Dermatotoxicology (in vivo percutaneous absorption, Webster R., Maibach H. In: Dermatotoxicology, Second edition, 1983, edited by F. Marzulli and H. Maibach. Hemisphere Publishing Corporation, New York)* contains a thorough discussion of *in vitro* percutaneous absorption testing. The purpose of this test is to determine the rate and extent of hydroquinone penetration through skin. Concurrent intravenous dosing of a separate group of animals is mandatory and collection of urine and feces from all test animals should be sensitive enough to characterize the penetration of the applied dose during the first 24 hours of

observation. In addition, urine and fecal collection should continue until at least 90 percent of the administered dose is recovered, but no longer than 14 days. To determine the rate and extent of gastrointestinal absorption of hydroquinone, an acute methodology, such as that described in the TSCA Health Effects Testing Guidelines, using at least two doses would be appropriate. One dose should be of the same magnitude as that used in the National Toxicology Program cancer bioassay, preferably the medium dose. The low dose should reflect actual human exposure levels. As with the skin penetration study, urine and fecal collection should be sensitive enough to characterize the penetration of the applied dose during the first 24 hours of observation; and collection should continue until at least 90 percent of the administered dose is recovered, but not longer than 14 days.

(2) *Mutagenic effects—Chromosomal aberrations*—(i) *Required testing.* A dominant lethal assay shall be conducted in rodents with hydroquinone.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Health Effects Test Guidelines for Chromosomal Effects, published by NTIS (PB 82-232984), should be consulted. Additional guidance may be obtained from the OECD Test Guidelines for Genetic Toxicology, and the FIFRA Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83-153916).

(3) *Mutagenic effects—Gene Mutation*—(i) *Required testing.* (A) A gene mutation assay, in mammalian cells in culture, shall be conducted with hydroquinone.

(B) Hydroquinone shall be tested in a *Drosophila* sexlinked recessive lethal (SLRL) assay if the results of the gene mutation assay are positive.

(C) A mouse-specific locus assay shall be conducted with hydroquinone if a positive result is produced in the *Drosophila* SLRL assay.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Health Effects Test Guidelines for Gene Mutations, published by NTIS (PB 82-232984), should be consulted. Additional guidance may be obtained from the OECD Test Guidelines for Genetic Toxicology and the FIFRA Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83-153916).

(4) *Teratogenicity*—(i) *Required testing.* Teratogenicity studies in both a

rodent and a non-rodent species shall be conducted with hydroquinone. These tests must be conducted using the oral route of exposure.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Health Effects Test Guidelines for Specific Organ/Tissue Toxicity-Teratogenicity, published by NTIS (PB 82-232984), should be consulted. Additional guidance may be obtained from the OECD Test Guidelines for Health Effects, and the FIFRA Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83-153916).

(5) *Reproductive Effects*—(i) *Required testing.* A two-generation reproductive effects study in the rodent shall be conducted with hydroquinone. Oral dosing shall be the route of administration of the test substance in this study.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Health Effects Test Guidelines for Specific Organ/Tissue Toxicity—Reproduction/Fertility Effects, published by NTIS (PB 82-232984), should be consulted. Additional guidance may be obtained from the FIFRA Pesticide Registration Guidelines—Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83-153916).

(6) *Epidemiology*—(i) *Required testing.* Two epidemiologic studies shall be conducted for hydroquinone. One study shall be a cohort study designed to detect a 50 percent increase in total cancer incidence with at least 80 percent probability when both random and nonrandom sources of error have been taken into account. Incidence of and mortality from the following additional specific endpoints shall be included: specific cancers and a variety of ocular effects including loss of visual acuity and conjunctival or corneal changes. The other study shall be a study of teratogenic and adverse reproductive effects. This study shall conform to category 5 or category 4 of the levels of inferential knowledge specified by the 1979 Draft Interagency Regulatory Liaison Group's Guideline for Documentation of Epidemiological Studies. It shall be designed to detect a relative risk of 2 in the rate of total defects among live-borns, if of category 5, or an odds ratio of 2, if of category 4, with at least 90 percent probability at 5 percent significance. Both spouses shall be included, and spontaneous abortions (with recorded gestational age), testicular effects, and effects on sperm formation shall be studied.

(ii) *Study plans.* For guidance in preparing study plans, the following paper should be consulted: Epidemiology Workgroup, Interagency Regulatory Liaison Group, Nov. 1979. Draft IRLG Guideline for Documentation of Epidemiology Studies.

(7) *Neurotoxicity*—(i) *Required testing.* The following neurotoxicity testing shall be conducted for hydroquinone using an animal with oral exposure:

- (A) A functional observation battery,
- (B) A neuropathology test, and
- (C) A motor activity test or an operant behavior test.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Health Effects Test Guidelines for Neurotoxicity, published by NTIS (PB 82-232984), should be consulted. Additional guidance may be obtained by consulting the FIFRA Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals (PB 83-153916).

(k) *Chemical fate testing*—(1) *Aerobic biodegradation*—(i) *Required testing.* An aerobic biodegradation test shall be conducted with hydroquinone using natural waters representative of aquatic environments that may be exposed to hydroquinone. Transformation of hydroquinone may be determined using either compound-specific analytical techniques or radiolabeled test compound. Regardless of the analytical method chosen, it shall be adequate to determine both disappearance of parent compound and the extent of interconversion of hydroquinone and quinone.

(ii) *Study plans.* The Agency has not published guidelines for the type of biodegradation test suggested for hydroquinone. However, any natural waters die-away or similar test method should be suitable, provided that it meets the requirements set forth above. Examples of methods that may be used to develop an acceptable study plan are described in Saeger, V.W. and Tucker, E.S., "Biodegradation of phthalic Acid Esters in River Water and Activated Sludge," Applied Environmental Microbiology 37, 29-34 (1976), and Spain, J.C., Pritchard, P.H., and Bourquin A.W., Effects of Adaptation on Biodegradation Rates in Sediment/Water Cores from Estuarine and Freshwater Environments, Applied Environmental Microbiology 40, 726-734 (1980).

(2) [Reserved]

(l) *Environmental effects testing*—(1) *Aquatic freshwater acute toxicity*—(i) *Required testing.* Acute toxicity tests

shall be conducted with hydroquinone with freshwater animals in eight different species provided that, of the eight species:

(A) At least one is a salmonid fish.

(B) At least one is a non-salmonid fish.

(C) At least one is a Planktonic crustacean.

(D) At least one is a benthic crustacean.

(E) At least one is a benthic insect.

(F) At least one of the benthic species is a detritivore.

(ii) *Study plans.* For guidance in preparing study plans, the STCA Environmental Effects Test Guidelines for acute toxicity testing, published by NTIS (PB 82-232992), should be consulted. Additional guidance may be obtained by consulting the OECD Test Guidelines for Effects on Biotic Systems, the FIFRA Guidelines for Hazard Evaluation: Wildlife and Aquatic Organisms (PB 83-153908), and the Water Quality Criteria Guidelines, published in the Federal Register on November 28, 1980 (45 FR 79341).

(2) *Aquatic freshwater chronic toxicity—(i) Required testing.* Chronic toxicity testing shall be conducted with hydroquinone for three species of aquatic animals provided that of the three species:

(A) At least one is fish.

(B) At least one is an invertebrate.

(C) At least one is a freshwater species (the other two may be saltwater species).

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Environmental Effects Test Guidelines for chronic toxicity testing, published by NTIS (PB 82-232992), should be consulted. Additional guidance may be obtained by consulting the FIFRA Guidelines for Hazard Evaluation: Wildlife and Aquatic Organisms (PB 83-153908) and the Water Quality Criteria Guidelines (45 FR 79341).

(3) *Aquatic freshwater plants—(i) Required testing.* Testing shall be conducted with hydroquinone with a freshwater alga, or a chronic test shall be conducted with hydroquinone with a freshwater vascular plant.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Environmental Effects Test Guidelines for algal and macrophytic toxicity testing, published by NTIS (PB 82-232992), should be consulted. Additional guidance may be obtained by consulting the FIFRA Guidelines for Hazard Evaluation: Wildlife and Aquatic Organisms (PB 83-153908), the OECD Test Guidelines for Effects on Biotic Systems, and the Water Quality Criteria Guidelines.

(4) *Freshwater bioconcentration testing—(i) Required testing.* A bioconcentration factor test shall be conducted with hydroquinone with a freshwater aquatic animal species.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Environmental Effects Test Guidelines, published by NTIS (PB 82-232992), should be consulted. Additional guidance may be obtained by consulting the FIFRA Guidelines for Hazard Evaluation: Wildlife and Aquatic Organisms (PB 83-153908), the OECD Test Guidelines for Degradation and Accumulation, and the Water Quality Criteria Guidelines.

(5) *Aquatic saltwater acute toxicity—(i) Required testing.* Acute toxicity tests shall be conducted with hydroquinone with saltwater animals in eight different species provided that of the eight species:

(A) At least two different fish families are included.

(B) At least five different invertebrate families are included.

(C) Either the Mysidae or Penaeidae family or both are included.

(D) At least one of the invertebrate families is in a phylum other than Arthropoda.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Environmental Effects Test Guidelines for acute toxicity testing, published by NTIS (PB 82-232992), should be consulted. Additional guidance may be obtained by consulting the OECD Test Guidelines for Effects on Biotic Systems, and the FIFRA Guidelines for Hazard Evaluation: Wildlife and Aquatic Organisms (PB 83-153908), and the Water Quality Criteria Guidelines.

(6) *Aquatic saltwater chronic toxicity—(i) Required testing.* Chronic toxicity tests shall be conducted for three species of aquatic animals provided that of the three species:

(A) At least one is a fish.

(B) At least one is an invertebrate.

(C) At least one is a saltwater species (the other two may be freshwater species).

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Environmental Effects Test Guidelines for chronic toxicity testing, published by NTIS (PB 82-232992), should be consulted. Additional guidance may be obtained by consulting the FIFRA Guidelines for Hazard Evaluation: Wildlife and Aquatic Organisms (PB 83-153908) and the Water Quality Criteria Guidelines.

(7) *Aquatic saltwater plants—(i) Required testing.* Testing shall be conducted with hydroquinone with saltwater alga, or a chronic test shall be

conducted with hydroquinone with a saltwater vascular plant.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Environmental Effects Test Guidelines for algal and macrophytic toxicity testing, published by NTIS (PB 82-232992 and PB 83-257709), should be consulted. Additional guidance may be obtained by consulting the FIFRA Guidelines for Hazard Evaluation: Wildlife and Aquatic Organisms (PB 83-153908), the OECD Test Guidelines for Effects on Biotic Systems, and the Water Quality Criteria Guidelines.

(8) *Saltwater bioconcentration testing—(i) Required testing.* A

bioconcentration factor test shall be conducted with a saltwater aquatic animal species.

(ii) *Study plans.* For guidance in preparing study plans, the TSCA Environmental Effects Test Guidelines, published by NTIS (PB 82-232992), should be consulted. Additional guidance may be obtained by consulting the FIFRA Guidelines for Hazard Evaluation: Wildlife and Aquatic Organisms (PB 83-153908), the OECD Test Guidelines for Degradation and Accumulation, and the Water Quality Criteria Guidelines.

(m) *Test Standards.* (1) Sponsors and testing facilities must adhere to the EPA Good Laboratory Practice Regulations in Part 792 of this chapter.

(n) *Enforcement.* (1) If a manufacturer or processor, which notified EPA under paragraph (c) (1), (2), (3), or (4) of this section of its intent to perform testing for a test set required by paragraphs (j), (k), or (l) of this section, fails to perform the test set in accordance with the test standards in paragraph (m) of this section, that failure will be a violation of this section.

(2) EPA will publish a notice in the Federal Register to inform all manufacturers and processors that all exemptions for performance of that test set will be denied unless, within 30 days of the publication of the notice, a manufacturer or processor of hydroquinone notifies EPA by letter that it intends to perform that test set in accordance with the test standards in paragraph (m) of this section.

(3) Any person who fails or refuses to comply with any aspect of this section is in violation of section 15 of the Act.

(o) *Availability of study plans.* The TSCA and FIFRA guidelines for the various study plans are available from the National Technical Information Service (NTIS). Address and telephone number: National Technical Information

Service, 5285 Port Royal Road, Springfield, VA 22161, (703-487-4650).

[FR Doc. 84-71 Filed 1-3-84; 8:55 am]
BILLING CODE 4910-01-01

40 CFR Part 799

[OPTS-42053; FRL 2482-8]

Toxic Substances; Alkyl Epoxides; Response to the Interagency Testing Committee

AGENCY: Environmental Protection Agency (EPA).

ACTION: Advance notice of proposed rulemaking.

SUMMARY: This Advance Notice of Proposed Rulemaking (ANPR) is the Agency's response to the Interagency Testing Committee's (ITC) designation of the chemical category "alkyl epoxides" and its recommendation that the alkyl epoxides be considered for health effects and chemical fate testing. This notice addresses those alkyl epoxides on the Toxic Substances Control Act (TSCA) Chemical Substances Inventory other than ethylene oxide, propylene oxide, and 1,2-butylene oxide, which are addressed in other Federal Register notices. EPA is publishing this notice to inform the public of the rationale to be used in selecting the chemicals for testing, to define the regulatory approaches that are being considered, and to seek public comments on EPA's approach in proposing a test rule.

DATE: Interested persons are invited to comment on this ANPR. All comments should be submitted on or before March 5, 1984.

ADDRESS: Submit written comments identified by the document control number (OPTS 42053) in triplicate to: TSCA Public Information Office (TS-793), Office of Pesticides and Toxic Substances, Environmental Protection Agency, Rm. E-108, 401 M St. SW., Washington, D.C. 20460.

FOR FURTHER INFORMATION CONTACT: Jack P. McCarthy, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Environmental Protection Agency, Room E-543, 401 M St. SW., Washington, D.C. 20460, Toll Free: (800-424-9085), In Washington, D.C. (554-1404), Outside the USA: (Operator-202-554-1404).

SUPPLEMENTARY INFORMATION:

I. Background

A. ITC Report

Section 4(a) of TSCA (Pub. L. 94-469, 90 Stat. 2008 et seq.; 15 U.S.C. 2601 et seq.) authorizes the Administrator of

EPA to promulgate regulations requiring testing of chemical substances and mixtures in order to develop data relevant to determining the risks that such chemicals may present to health and the environment.

Section 4(e) of TSCA established the ITC to recommend to the Administrator of EPA those chemicals that should receive priority consideration for the development of test rules under section 4(a).

The ITC transmitted its First Report to the Administrator of EPA, as published in the Federal Register of October 12, 1977 (42 FR 55026), and designated the category "alkyl epoxides" for priority testing consideration for mutagenicity, carcinogenicity, teratogenicity, other chronic effects (with emphasis on organ effects and behavioral changes), and environmental fate. Epidemiological studies were also recommended for priority consideration for two or three of the highest exposure compounds, if suitable cohorts could be identified.

In order to make a section 4(a)(1)(A) finding, EPA must determine that the manufacture, distribution in commerce, processing, use or disposal of a chemical substance or mixture, or any combination of such activities, may present an unreasonable risk of injury to health or the environment, that insufficient data exist to characterize the potential effects of that chemical to human health and the environment, and that testing is necessary to develop such data. In order to make a section 4(a)(1)(B) finding, EPA must determine that a substance is produced in substantial quantities and that there is or may be significant or substantial human exposure or substantial environmental release of that substance, that there are insufficient data to characterize the potential effects of that chemical to human health and the environment, and that testing is necessary to develop such data.

B. Category Members

The ICC defined the alkyl epoxides category as noncyclic aliphatic hydrocarbons bearing one or more epoxide functional groups.

EPA has identified from the non-confidential (public) TSCA Chemical Substances Inventory six short-chain up to four carbon atoms) alkyl epoxides and eight longer chains (greater than nine carbon atoms) alkyl epoxides and eight longer-chains (greater than nine carbon atoms) alkyl epoxides that fit the alkyl epoxides chemical category definition. No additional alkyl epoxides are listed in the confidential portion of the Inventory. Of the short-chain compounds, three are addressed in

separate Federal Register documents: ethylene oxide (Ref. 1), propylene oxide (Ref. 2), and 1,2-butylene oxide (Ref. 3). This notice addresses the remaining three short-chain compounds and eight long-chain substances:

Chemical	CAS No.
Short-Chain	
2,3-Epoxybutane	CAS No. 2089-89-7
Isobutylene oxide	CAS No. 989-89-8
1,2,4-Dioxepinane	CAS No. 1484-89-8
Long-Chain	
1,2-Epoxydecane	CAS No. 2089-89-8
1,2-Epoxyundecane	CAS No. 2089-89-8
1,2-Epoxydodecane	CAS No. 2089-89-8
1,2-Epoxytridecane	CAS No. 2089-89-8
1,2-Epoxytetradecane	CAS No. 2089-89-8
1,2-Epoxytridecane	CAS No. 2089-89-8
1,2-Epoxyundecane	CAS No. 2089-89-8
1,2-Epoxydodecane	CAS No. 2089-89-8
1,2-Epoxytridecane	CAS No. 2089-89-8

II. Response to ITC Report

EPA has reviewed the ITC report, the data on which their recommendations were based, the information obtained on alkyl epoxides under the TSCA section 8(a) Preliminary Assessment Information Rule (40 CFR Part 712), unpublished health and safety studies submitted by manufacturers of alkyl epoxides under the TSCA section 8(d) Health and Safety Data Reporting Rule (40 CFR part 716), and other published and unpublished data available to the Agency. EPA is publishing in this Federal Register notice its tentative conclusions as to appropriate action the Agency may take on the alkyl epoxides not addressed in other Federal Register notices.

EPA previously indicated that, although it would generally initiate testing action through publication of a proposed rule, it would initiate action on some chemical categories and certain complex chemicals through publication of an ANPR, as it is doing in this case. There are several reasons, both general to categories and specific to the long-chain alkyl epoxides, why the Agency has chosen to apply this approach in this situation. EPA believes that there are definite advantages to using an ANPR to initiate the process of section 4 rulemaking for certain categories of chemicals.

The Agency has found that in attempting to develop testing rules for a category of chemical substances, the issues that require attention are more complex and numerous than in rulemaking for a single chemical. For example, the Agency is attempting to determine whether it is scientifically valid to obtain data for one or more representative chemicals within the category rather than to test each chemical, in order to avoid unnecessary