ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 799

[OPTS-42048B; FRL-2944-9]

Hydroquinone; Testing Requirements

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: On January 4, 1984, the EPA proposed, under section 4 (a) of the Toxic Substances Control Act (TSCA), that manufacturers and processors of hydroquinone (CAS No. 123-31-9) conduct health and environmental effects testing of that chemical (49 FR 438). EPA has reviewed the comments on the proposal as well as new testing results and additional data that have become available since the publication of the proposed rule. Based on these reviews the Agency is today promulgating a final test rule that requires manufacturers and processors of hydroquinone to evaluate hydroquinone's toxicokinetics and to determine its potential to produce nervous system, reproductive and teratogenic effects.

DATES: In accordance with 40 CFR 23.5 (50 FR 7271; February 21, 1985), this rule shall be promulgated for purposes of judicial review at 1 p.m. eastern ["daylight" or "standard" as appropriate] time on January 13, 1986. This rule shall become effective on February 12, 1986.

FOR FURTHER INFORMATION CONTACT: Edward A. Klein, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Rm. E-543, 401 M St., SW., Washington, DC 20460, Toll free (800-424-9065), In Washington D.C.: (554-1404), Outside the USA: (Operator-202-554-1404).

SUPPLEMENTARY INFORMATION: EPA is requiring health effects testing of hydroquinone as stated in this final rule.

I. Introduction

This notice is part of the overall implementation of section 4 of the Toxic Substances Control Act (TSCA, Pub. L 94-469; 90 Stat. 2006 *et seq.*; 15 U.S.C. 2603 *et seq.*) which contains authority for EPA to require development of data relevant to assessing the risks to health and the environment posed by exposure to particular chemical substances or mixtures.

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

environmental data if the Administrator finds that:

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

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

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

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

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

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

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

On January 4, 1984, EPA proposed, under section 4(a) of TSCA, that manufacturers and processors of hydroquinone conduct health and environmental effects testing of that chemical (49 FR 438). EPA, in response to requests by Goodyear Tire and Rubber Company and the Chemical Manufacturer's Association for additional time to comment, published a notice in the Federal Register of March 9, 1984 (49 FR 8969) extending the 60-day comment period an additional 30-days to April 3, 1984. On April 18, 1984, EPA also held a public meeting to allow interested persons to present oral comments on the proposed rule.

II. Background

A. Profile

Hydroquinone ($C_6H_4(OH)_2$, 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.

Hydroquinone is produced in a photographic grade for use as a developing agent and in a technical grade which is primarily used as a chemical intermediate in the production of rubber chemicals. Most of the technical grade hydroquinone is converted into chemical for use in polymers. Smaller amounts of the technical grade are used as polymerization inhibitors during the manufacture of vinyl monomers, as inhibitors for stabilizing unsaturated polyester resins and as a chemical intermediate to prepare other derivatives such as dyes and pigments. Hydroquinone is also used in dermatologic preparations designed to bleach hyperpigmented skin, and as such is regulated by the Food and Drug Administration.

The annual U.S. production volume of photograde, technical, and other grades of hydroquinone is estimated to be as high as 27 million pounds (Ref. 37). U.S imports of technical grade hydroquinone in 1981 totaled 50 thousand pounds (Ref. 32). The U.S. imports of photographic grade are negligible. The manufacturers of hydroquinone have commented that 26 million pounds of the chemical are manufactured and imported annually (Ref. 1).

B. ITC Recommendations

Section 4(e) of TSCA 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 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 teratogencity 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 11 million pounds. The carcinogenicity and teratogenicity recommendations were also based on suggestive evidence derived from animal studies.

C. Proposed Rule

EPA published a proposed rule in the Federal Register of January 4, 1984 (49 FR 438) which would require health effects, chemical fate and environmental effects testing for hydroquinone.

In evaluating the ITC's testing recommendations for hydroquinone, EPA considered all available relevant information including information presented in the ITC's report recommending testing consideration: production volume, use, exposure, and release information reported by manufacturers of hydroquinone under TSCA section 8(a) (40 CFR Part 712—Chemical Information Rule, Subpart B—Manufacturers Reporting—Preliminary Assessment Information); unpublished health and safety studies submitted by manufacturers, processors and distributors of hydroquinone 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. On the basis of the evaluation, as described in the proposed rule and the accompanying technical support document, EPA proposed metabolism (toxicokinetics), nervous system effects, reproductive effectives, teratogenicity (developmental toxicity), and mutagenicity testing requirements, as well as epidemiologic studies, for hydroquinone under both sections 4(a)(1)(A) and 4(a)(1)(B) of TSCA. EPA also proposed chemical fate and environmental effects testing requirements for hydryquinone under section 4(a)(1)(A) of TSCA. By these actions, EPA responded to the ITC's designation of hydroquinone.

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

1. EPA found that hydroquinone is produced in substantial quantities, and that the manufacture, processing and use of hydroquinone may result in substantial human exposure to the chemical. Furthermore, EPA found 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. Finaly, EPA found 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.

The findings were 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 27 million pounds (Ref. 37).

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 was 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 using solutions containing hydroquinone. The Agency believed that both workers and hobbyists would receive inhalation and dermal exposure.

2. In addition, EPA found that the manufacture, processing and use of hydroquinone may present an unreasonable risk of injury to human health. There was 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. Exposure to hydroquinone may be sufficient to result in such effects. The existing data were inadequate to reasonably predict or determine the effects of these exposures to hydroquinone and testing was necessary for these effects. Therefore, EPA believed that requiring epidemiologic studies and testing of hydroquinone for nervous system effects, mutagenicity, teratogenicity, reproductive effects, and carcinogenicity could also be based upon section 4(a)(1)(A) of TSCA.

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

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

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

Although the ITC did not recommend environmental effects testing for hydroquinone, the Agency was concerned with effluents from photoprocessing facilities and proposed a series of environmental effects tests. Based on existing aquatic toxicity data and the limited data on photoprocessing effluents, the Agency believed 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 was needed to provide data to establish whether an unreasonable risk to freshwater and saltwater aquatic species existed.

The Agency also proposed chemical fate testing for hydroquinone. EPA believed that this testing was 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 needed information to establish biodegradation rates in order to assess the levels of hydroquinone exposure to aquatic organisms.

TABLE 1—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.

III. Response to Public Comments

The comments received by the Agency in response to the proposed rule for hydroquinone were from individual companies, the National Association of Photographic Manufacturers, and the Chemical Manufacturers' Association. The Agency did not receive any comments which, in the Agency's judgment, rebutted the substantial production and substantial human exposure findings for hydroquinone. However, new information concerning the environmental release of hydroquinone has become available since publication of the proposed rule and has led EPA to reconsider its chemical fate and environmental effects testing requirement. Major issues identified during the comment period are discussed below.

A. Human Exposure

EPA cited the NOHS (1980) survey that estimated that approximately 470,000 U.S. workers, in 137 occupations, are potentially exposed to hydroquinone annually. Also of concern were 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 and the process utilizes hydroquinone. Workers and hobbyists may receive inhalation and dermal exposures.

EPA also found that the manufacture, processing and use of hydroquinone may present an unreasonable risk of injury to human health.

The industry has commented that there are two major uses for hydroquinone, photographic uses and rubber chemical uses. Regarding the photographic uses, they report that only four percent of still pictures taken by amateurs are in black and white (Ref. 2) and that only 30,000 kg (66,000 lbs) (Ref. 2) of hydroquinone are used by home darkroom hobbyists each year and this use is in dilute solutions (0.2–0.3 percent) (Refs. 3, 5, and 27).

The industry estimates that about 800,000 people use black and white developers in home darkrooms (Ref. 1). Each person averages eight sessions per year, with the average exposure time of 5 to 10 minutes each of these developing and printing sessions (Refs. 1 and 5). As a result of these limited periods and label warnings on containers, commenters believe dermal absorption of hydroquinone is extremely minimal and that inhalation exposure is also unlikely because of hydroquinone's low vapor pressure (Ref. 5).

The Agency believes that in many instances the industry's conclusion, that consequential exposure of photohobbyists to hydroquinone is unlikely, may be accurate. It also appears that both the number of photohobbyists potentially exposed to hydroquinone and the levels of exposure are much lower than the Agency's earlier estimates. However, EPA still believes there are a substantial number of photohobbyists that are intensively involved in black and white photography much more frequently than the "average" photohobbyist profiled by the industry. This would result in longer and more frequent exposure periods for these individuals.

Regarding exposure of individuals employed at photoprocessing plants, the industry reports that at least 90 percent of the photofinishing dollar volume is color negative films and prints, where no hydroquinone is used (Refs. 1 and 5). The industry, estimating there are 2,000 photofinishing labs in the U.S. (Refs. 1 and 5) versus the Agency's estimate of 10,000, states that only some of these facilities process black and white negative film and paper using developers containing hydroquinone. Additionally, since most labs use automatic processing equipment, any exposure would be likely to involve only one-half hour for one worker mixing chemicals once a week (Refs. 1 and 5). The industry cites both a NIOSH report concerning a photofinishing lab and an

industry study of airborne hydroquinone in a darkroom that showed no hydroquinone detected at a 0.02 mg/m³ limit of detection (Refs. 4 and 6).

While automated labs may result in minimal worker exposure to hydroquinone, the Agency believes there are varying amounts of automation found in the photoprocessing labs in the U.S. that develop black and white films and papers. Older, less sophisticated operations will involve more direct worker involvement with hydroquinone and greater exposure, especially dermal, will result. Moreover, the monitoring data provided to the Agency are extremely limited; thus, the Agency cannot be assured that the data are truly representative of all photoprocessing labs.

The industry has defined the group of hydroquinone manufacturing workers as 80 individuals at two plants (Ref. 1). They claim minimal worker inhalation exposure due to the closed production processes, with one facility reporting "an arithmetical average concentration of 0.79 mg/m³ (±0.52 standard deviation)" and the other reporting the "highest average concentration as 0.2 mg/m³" (Ref. 1). One production facility reported the arithmetic average air concentration in the unloading area as 0.13 mg/m³ (standard deviation ±0.15 mg/m³) (Ref. 1). These summary data were supplied by the industry; EPA is unable to interpret these further since frequency, averaging time and other supporting documentation were not provided.

The Agency agrees that exposure of certain manufacturing workers to hydroquinone may be limited. However, while the industry has described its production workforce as essentially 80 workers, the NIOSH NOHS Survey has estimated that, overall, approximately 470,000 U.S. workers in 137 occupations are potentially exposed to hydroquinone. Workers involved in distributing and processing hydroquinone as it is incorporated into rubber chemicals and other uses and the actual potential for exposures through these activities have not been characterized by the industry. While the Agency believes the 470,000 figure may overestimate the number of workers actually exposed to hydroquinone, the Agency believes that the available information indicates that substantial numbers of persons in the workplace are or may be receiving dermal and inhalation exposure to hydroquinone.

B. Human Health Effects

1. *Metabolism* (Toxicokinetics). EPA stated in the support document to the proposed rule that although 92 to 97 percent of hydroquinone administered to rats is excreted in the urine, studies in man, dog and rabbit show considerably lower percentages of hydroquinone absorption/excretion. These studies were incomplete and deficient in several areas. The Agency believed that the currently available data were not sufficient for purposes of reasonably predicting the toxicokinetic of hydroquinone. Toxicokinetic studies via dermal and oral routes were proposed because: (1) The primary route of human exposure to hydroquinone is expected to be direct dermal contact, although the potential exists for some direct ocular contact and inhalation of dust or vapors; and (2) the NTP is currently performing a 2-year bioassay on hydroquinone via an oral exposure route (gavage).

The industry has supplied the Agency with numerous comments on the toxicokinetics of hydroquinone based on new data and ongoing test programs. Also, they have discussed (1) the dermal uptake of hydroquinone, based on a study by Marty *et al.* (Ref. 7), where the chemical was applied to rodent and human skin and (2) a dermal absorption study in dogs by Kodak (Ref. 8). Based on the Marty study and the preliminary results of the Kodak study, the industry concludes that hydroquinone is poorly absorbed through the skin.

With regard to the Marty study, the Agency believes the hydroquinone formulation used, and to a lesser extent the methodology, render the use of this study questionable as an accurate characterization of actual hydroquinone penetration of human skin in the workplace. A major concern with this study is the use of a preparation of hydroquinone which contained 75 percent water. Hydroquinone is water soluble and when administered to the skin in a predominately aqueous form, it may have a tendency to stay in the solvent rather than penetrate the lipid membrane of the skin. Because of the expected low diffusional driving force of an aqueous solution of hydroquinone as compared to the expected higher diffusional driving force of hydroquinone itself, the Marty study may underestimate actual hydroquinone penetration that persons would experience when exposed to non-aqueous (e.g. powdered) forms of the chemical.

Limitations to the study are also imposed by the use of rats for the parenteral dosing while mice were used for *in vivo* topical administration. While both species are equally sensitive to the toxic effects of orally administered hydroquinone, usually the excretion kinetics of parenteral dosing are developed utilizing the same species; there may be significant species differences with respect to biotransformation and excretion of hydroquinone.

The industry has informed the Agency of an ongoing testing program that will explore the area of metabolic fate of hydroquinone, percutaneous absorption and blood elimination kinetics. Although the data from these studies may provide adequate information to relate dose levels of hydroquinone from expected human exposures to doses administered in a bioassay being conducted by the National Toxicology Program, the Agency does not currently have the complete industry studies in hand for evaluation. Therefore, the Agency is requiring the metabolism testing delineated in the proposed rule.

2. *Developmental toxicity and reproductive effects.* At oral doses of 30 mg/kg/day and higher, Racz reported that hydroquinone prolonged the diestrus period of the sexual cycle in female albino rats (Ref. 9). Skalka (Ref. 10), subcutaneously injecting male rats at a dose of 100 mg/kg/day for 51 days, reported decreased weights in testes, epididymides, seminal vesicles and adrenal glands; histological changes in testes indicating disrupted spermiogenesis; and diminished DNA content of sperm heads. Telford *et al.* reported that at a dose level of 0.5g of hydroquinone in the diet administered to female rats during pregnancy, fetal resorptions resulted (Ref. 11). Because of the aforementioned reproductive system effects, the Agency proposed reproductive effects testing for hydroquinone.

There were no reports in the literature of hydroquinone studies explicitly dealing with teratogenic or developmentally toxic effects; however because of the evidence of fetal resorptions, the Agency determined that testing of hydroquinone for developmental toxicity is warranted.

The industry, commenting on EPA's basing hydroquinone's teratogenic activity on the Telford *et al.* study (Ref. 11), stated that the increased fetal resorptions are not necessarily indicative of terata formation and moreover, the study is incompletely described. The industry commented that the poor quality of the study and the low human exposure do not justify teratology testing.

Concerning reproductive effects, the industry stated that in a study by Ames *et al.* (Ref. 12), feeding hydroquinone at a level of 0.3 percent in the diet of female rats for 10 days prior to insemination caused no impairment. They also commented that the results of

the Racz study do not suggest a female reproductive problem. They expressed no surprise at reproductive effects in male rats in the Skalka study (Ref. 10) because 51 subcutaneous injections of 100 mg/kg were used while the subcutaneous LD_{50} in rats has been reported to be between 300 and 350 mg/kg.

The industry has pointed out that the Agency's questions raised by these papers are being addressd by a dominant lethal assay and a teratology study, both being conducted by Kodak. Industry argues that preliminary evidence indicates the absence of adverse effects in these studies and refutes any suggestion of reproductive toxicity by the data of Skalka and Telford.

While the industry's comments relative to teratogenicity and reproductive effects are valid in some respects, they do not alleviate the Agency's concerns. The Agency considers the Telford *et al.* study (Ref. 11) showing resorptions very meaningful. Although the industry's comment that resorptions do not necessarily indicate terata is valid, resorptions do indicate some type of developmental toxicity of which terata are but one aspect. The Agency's concern, therefore, is over the potential of hydroquinone to be a developmental toxicant. The four manifestations of developmental toxicity are death (which includes resorptions), malformations (terata), growth retardation, and functional deficits.

It is true that the Ames *et al.* reproductive study (Ref. 12) was negative; however, dose levels may not have been high enough; no toxic effects of any kind were reported. This study may be a false negative.

EPA and CMA disagree on the dosing regimen and levels in the Racz *et al.* study (Ref. 9). If the industry's contention that the animals first received a high dose, which was lowered later, is correct, then this study is of questionable value.

The Skalka study (Ref. 10) showed clear testicular toxicity via the subcutaneous route. Although subcutaneous dosing is not representative of expected routes of human exposure to hydroquinone, the results of this study suggest that if hydroquinone is absorbed as a result of dermal or inhalation exposures it could produce testicular toxicity. The industry is correct in pointing out that the testicular effects were noted at about 0.3 LD_{50}, a high dose. However, EPA cannot ignore the positive effects noted and cannct predict the effects of other dose levels and other routes of exposure. The Agency needs further data before this effect can be assessed.

Because EPA's concerns in the areas of developmental toxicity and reproductive effects have not been allayed, the Agency is requiring testing in these areas as described in the proposed rule.

3. *Oncogenicity.* EPA reported that several long-term animal bioassays (mice) were negative although they did not meet current testing standards. In one study (Ref. 13) bladder carcinomas were produced in mice implanted with cholesterol pellets containing hydroquinone. This test is not recognized as a valid measure of carcinogenic potential. However, because of this positive result and the positive result in a *in vitro* cell transformation assay (Ref. 14), further oncogenicity testing is warranted. Because the NTP is conducting a 2-year bioassay with hydroquinone, no additional oncogenicity studies were proposed in the rule.

Industry has commented that although the Agency has asserted that hydroquinone is a suspected carcinogen, EPA has provided no support and industry is unaware of any studies in any animal species that demonstrate this assertion.

While the two studies cited are viewed by EPA as suggestive that the compound may be carcinogenic, the NTP bioassay is needed to confirm or refute the suspicions. This study is planned to be completed by mid-1986.

4. *Mutagenicity and Cytotoxicity.* The Agency concluded in the proposed rule published in the **Federal Register** of January 4, 1984 (49 FR 438), that the mutagenicity studies involving hydroquinone showed equivocal results. Hydroquinone had been reported: (a) to be mutagenic in one *Salmonella* test (Ref. 33), (b) to be mutagenic in a bacterial DNA repair assay (Ref. 34), and (c) by the National Toxicology Program, to induce sister chromatid exchanges and chromosomal aberrations in Chinese hampster ovary cells (Ref. 35). Prior to issuance of the proposed rule, Goodyear (Ref. 36) submitted data including: (i) DNA damage in *E. coli*, (ii) sex-linked recessive lethal (SLRL) assay in *Drosophila m.*, (by Serva and Murphy) (iii) *Salmonella* microbial assay (Ames), and (iv) *in vitro* cell transformation assay. The DNA damage assay and the cell transformation assay were reported as postive, while the *Salmonella* microbial assay was negative. The SLRL assay was reported negative but there were inadequacies in the protocol and reporting. With postive results in cytogenetics and sister chromatid exchange in tests by the NTP, EPA considered a dominant lethal test in mice to be the appropriate next step in testing for chromosomal effects.

Hydroquinone had not been adequately tested for its ability to induce gene mutations. Because of equivocal result in the *Salmonilla typhimurium*/mammalian microsomal assay, EPA proposed that hydroquinone be tested for its ability to induce gene mutations in mammalian cells in culture. Positive results in this test would dictate a SLRL assay in *Drosophila*, and, if the latter test was positive, a mouse specific locus assay.

With regard to the proposed gene mutation test requirement, Goodyear Tire and Rubber Company has now submitted a complete report of the *Drosophila* SLRL test by Serva and Murphy (Ref. 15). The Agency has reviewed the data and agrees that this test adequately demonstrates that hydroquinone does not increase recessive lethal mutations under the test conditions. A second *Drosophila* test was part of a battery of three assays reported by Gocke *et al.* (Ref. 16) which included the *Salmonella*/mammalian liver microsome test (Ames test), the Basc test on *Drosophila* detecting sex-linked recessive lethal mutations, and the micronucleus test detecting chromosome aberrations in mouse bone-marrow cells. This second *Drosophila* test also provides sufficient information to indicate no increase in recessive lethal mutations under the test conditions. Therefore, EPA finds no further gene mutation testing of hydroquinone to be necessary at this time.

With regard to the proposed chromosomal aberration tests, positive results were reported in the mouse bone marrow micronucleus test by Gocke (Ref. 16). Because hydroquinone caused a dose-dependent increase in the number of micronclei found in mouse bone marrow, a dominant lethal test in rodents was indicated.

Kodak has submitted a dominant lethal assay of hydroquinone in rats (Ref. 17) and the Agency has reviewed this study. This assay showed no lethality up to a dose causing signs of clinical toxicity and some spontaneous death.

Since negative results have been reported in two SLRL tests and the dominant lethal assay in rats submitted by Kodak is also negative, EPA concludes that no further testing for gene mutations or chromosomal aberrations is necessary at this time.

5. *Nervous System Effects.* The Agency concluded that the test data

identified did not adequately characterize the possible neurotoxic effects of hydroquinone. Proposed testing included a functional observational battery, neuropathology and motor activity or operant behavior.

The industry has commented that the information requested by the Agency is either already available or may be readily available from ongoing testing programs. They state that only acute tests conducted in intact animals provide any meaningful data because they account for the blood-brain barrier; research type neuropharmacologic and neurophysiologic studies are inapplicable.

The commenters state that the NTP hydroquinone oncogenicity and chronic toxicity studies will generate data similar to those developed in a functional observational battery. The neuropathology data can similarly be obtained from modified NTP studies. Finally, they believe that motor activity data have already been reported by Christian *et al.* (Ref. 18). EPA agrees that the motor activity data derived from this study satisfy the motor-activity or operant behavior testing endpoint. EPA, however, disagrees that ongoing and planned NTP testing could generate data similar to a functional observational battery because the NTP protocols, developed for the purposes of oncogenicity testing, severely limit the quality and extent of clinical observation. Therefore, a functional observational battery is required as proposed.

The industry has also stated that the NTP studies could be readily modified to adequately screen for neuropathology. While this may be true, the two-year bioassay for hydroquinone has already progressed to the stage of sacrificing of test animals and this option is no longer available. Therefore, neuropathology testing for hydroquinone is required.

6. *Epidemiology.* The ITC recommended epidemiologic studies for hydroquinone if an appropriate cohort could be identified.

Limited epidemologic studies involving exposure to hydroquinone have been identified by the Agency. The existing literature includes occupational cross-sectional studies and case reports of exposure of populations through dermal application and accidental ingestion, as well as experimental exposure to hydroquinone by either ingestion or topical application. To date, the most reliable reported human effects attributed to hydroquinone exposure have been restricted to the eye and skin. A positive correlation between the degree of eye injury and duration of occupational exposure to hydroquinone has been reported (Refs. 19 through 22).

Additional concern for potential human risk comes from two studies of Kodak employees. First, a case-control study of brain cancers by Greenwald *et al.* (Ref. 24) observed elevated odds ratio with black and white developer exposure. Hydroquinone is known to be a component of black and white developer mixes. Secondly, a cohort study of photographic processors in nine Eastman Kodak Color Print and processing laboratories also reports an excess of brain cancer mortality. Individual exposures were not examined in this study, but hydroquinone and quinone were identified among the many possible exposures (Ref. 23).

EPA proposed that a cohort study be conducted, 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 considered. Incidence and mortality from a full spectrum of endpoints were to be examined (e.g., specific forms of cancer, and a variety of ocular effects including loss of visual acuity and conjunctival or corneal changes). Additionally, to address the Agency's concerns regarding the possibility of teratogenic effects and adverse reproductive effects, the Agency believed a study of these areas would be appropriate. Such a study, preferably prospective and including both spouses, would complement the Agency's request for animal teratology and reproductive studies.

The industry commenters believe a suitable study population does not exist. Commenters identified two populations for possible study, manufacturing workers and photohobbyists, and stated that a study of either population is not feasible (Ref. 5). A small number of employees work in the manufacturing of hydroquinone, totaling 100 workers between two different plants. Industry stated that epidemiologic study of this population would have low power to detect small relative risks for cancer or reproductive endpoints. The Agency agrees with this comment. EPA also agrees with the comment that photohobbyists may not be a feasible population for study due to potentially lower exposure levels and multiple chemical exposures (Ref. 1).

The Agency has been unable to identify another group, aside from the aforementioned, that may prove to be a suitable population for epidemiologic study. Therefore, the Agency is not requiring epidemiologic studies at this time.

C. Chemical Fate and Environmental Effects

The ITC, in its Fifth Report, stated that there is substantial opportunity for human and environmental exposure to hydroquinone and possibly to its oxidation products, semiquinone and quinone, and recommended environmental fate testing.

The Agency based its chemical fate and environmental effects testing for hydroquinone on the authority of section 4(a)(1)(A) of TSCA.

Although the ITC did not recommend environmental effects testing for hydroquinone, the Agency was concerned with effluents from photoprocessing facilities and proposed a series of environmental effects tests. Based on existing aquatic toxicity data and the limited data on photoprocessing effluents, the Agency believed that the levels of hydroquinone in those effluents, although not so substantial as to indicate a section 4(a)(1)(B) finding, could present an unreasonable risk to aquatic organisms.

The Agency proposed chemical fate testing for hydroquinone because the existing chemical fate data were limited and more data were needed to assess the magnitude of the possible risks to aquatic organisms. EPA needed information to establish biodegradation rates in order to assess the levels of hydroquinone exposure to aquatic organisms.

In the "Environmental Release" section of its technical support document for the proposed rule, EPA reported that concentrations of hydroquinone in photographic processing effluents range from 10 to 390 ppm and noted that there was no information regarding the total volume of release. A pilot plant study of photographic effluents by Eastman Kodak reported hydroquinone concentrations to be less than 0.04 mg/L (0.04 ppm) after biodegradation by treatment with an activated sludge (Ref. 25). However, although natural aquatic ecosystems may contain acclimated organisms, the ability of these ecosystems to degrade various concentrations of hydroquinone and quinone is unknown.

The Agency proposed chemical fate testing of hydroquinone that would establish the rate of biodegradation in order to assess possible risks to aquatic organisms.

EPA was concerned with the levels of hydroquinone remaining in effluents from photoprocessing activities (after treatment) because at levels approaching 0.04mg/L, hydroquinone

could present an unreasonable risk of injury to aquatic organisms. The Agency proposed aquatic testing to provide data regarding no-effect levels, LC_{50}'s and dose-response relationships. These tests would involve both freshwater and saltwater organisms and included acute tests, acute-chronic ratios in aquatic animals, tests with algae or chronic testing with vascular plants, and bioconcentration tests in aquatic animal species. This variety of tests would provide sufficient data to support regulatory action under the Clean Water Act.

The comments the Agency has received from the industry adequately support their contention that manufacturing processes and darkroom hobbyists do not provide consequential environmental releases of hydroquinone.

With regard to possible releases of hydroquinone from photoprocessors, the results of a Kodak survey by Ambrose *et al.* (Ref. 26) suggest that the majority of 34 plants sampled discharged effluents containing 30 μg/L to mg/L of hydroquinone. Irrespective of dilution, the concentration of hydroquinone will be reduced to 50 μg/L from mg/L if 95 percent removal occurs as in typical POTW (Ref. 28). Further, the combined effects of dilution with domestic and other wastes entering the POTW and dilution after discharge to the river will normally lead to at least an additional 10 to 100 fold reduction in hydroquinone concentration (0.5–5μg/L) (Ref. 28). Therefore, since it appears that the sample is representative of the industry, EPA considers it is reasonable to estimate that maximum in-stream hydroquinone concentrations should not exceed 5μg/L.

Additionally, the industry has provided information that indicates hydroquinone and quinone will be released from photoprocessing plants as hydroquinone monosulfonate which is less toxic to aquatic life (Ref. 1).

The Agency also was concerned with the possible direct discharge of hydroquinone and hydroquinone monosulfonate from photoprocessing plants to receiving waters. The study by Ambrose *et al.* (Ref. 26) suggests that motion picture photofinishers represent a category that may deserve more attention. Only five labs were sampled, but two of those discharged effluents containing 3–6.9 mg/L of hydroquinone and 16.4–41.2 mg/L of hydroquinone monosulfonate. All four samples from these two labs contain hydroquinone and hydroquinone monosulfonate.

The industry, however, has provided information on the use of hydroquinone for motion picture processing. According to Kodak (Refs. 29 and 30), this use has substantially decreased in the last 5 years from 14,000 kg/yr to less than 4,000 kg/yr. Furthermore, Kodak states that "all" large photoprocessors are located in urban areas and are, therefore, likely to discharge to POTW's and that any direct dischargers would be subject to the NPDES permit program and effluent limitations and guidelines of 40 CFR Part 459. Kodak also has provided statistics to show that currently there are 500 motion picture processors in the U.S. (Ref. 30).

The industry's comments do not completely support their statement that "no consequential environmental release occurs from photoprocessing operations" (Ref. 1). The commenters state that 99 percent of the plants discharge into POTW's; the remaining 1 percent must be assumed to be discharging directly to receiving waters (Ref. 1). The Agency has only been able to identify limited information regarding the actual number of plants that would comprise this 1 percent, and has no information regarding the volume of discharges or the flow of the receiving waters. However, in conducting a search through EPA's Water Permit Compliance Systems records (Ref. 31), the indication was that this segment (approximately 40 dischargers) is a very minor segment of the entire hydroquinone/hydroquinone monosulfonate discharge in terms of total releases. Additionally, the decline in use of hydroquinone and the switching to new products should lower risk from direct discharges of hydroquinone. In summary, given that most of the releases of hydroquinone and hydroquinone monosulfonate are processed through POTW's and should not be released into receiving waters at concentrations likely to pose any unreasonable risk, and that the 40 processors who may be direct dischargers do not appear to represent a major or significant portion of the total discharge, the Agency is not requiring chemical fate and environmental effects testing as part of the hydroquinone final rule.

D. Ongoing Testing

On June 15, 1983, industry representatives notified EPA that they were planning to conduct various health effects tests in the near future. Eastman Kodak Company provides EPA with protocols for testing in the areas of metabolic fate, percutaneous absorption, blood elimination kinetics, mutagenicity, teratology and reproductive effects and requested EPA's comments on the adequacy of these protocols. Having received the Agency's comments, the industry embarked on many of these studies and EPA anticipates that many of these will meet the testing requirements established by the Agency in the hydroquinone final rule. However, since many of these studies have only recently reached completion or are still underway, EPA currently has received in many cases only summary or interim reports. Because EPA has not yet received sufficient raw data and other backup materials relating to the already completed studies and only progress reports in the case of ongoing studies, the Agency presently has insufficient data to reasonably predict or determine the human health effects resulting from exposure to hydroquinone.

IV. Final Test Rule for Hydroquinone

A. Findings

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

1. EPA finds that hydroquinone is produced in substantial quantities, and that the processing, distribution and use of hydroquinone may result in substantial human exposure to this chemical.

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 27 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. Although this figure may overestimate the number of workers actually exposed to hydroquinone, even a few percent of the estimate would be substantial.

The Agency believes there are substantial numbers of people in the workplace involved in distributing and processing hydroquinone as it is incorporated into rubber chemicals and other uses.

EPA also believes that there are varying amounts of automation found in the 2,000 photofinishing labs reported by the industry; older operations, and specifically those dealing with large volumes of black and white developing, may result in significant worker exposure.

By industry estimates, there are 800,000 people who use photographic developers in home darkrooms. The Agency believes that included in this group are some hobbyists and

individuals involved in specialty work who, because they are intensively involved in black and white photography, will have more frequent exposures for longer periods to hydroquinone than the "average" photohobbyist.

The Agency believes that these workers and hobbyists may receive both inhalation and dermal exposure to hydroquinone.

2. In addition, EPA has found that the processing and use of hydroquinone may present an unreasonable risk of injury to human health from nervous system, developmentally toxic, reproductive, and carcinogenic effects. The Agency's basis for these findings is presented in the technical support document for the proposed rule and in Unit III.B. of this preamble.

3. EPA finds that existing data and experience are inadequate to reasonably predict or determine the developmental toxicity and nervous system, reproductive and carcinogenic effects of exposures to hydroquinone. The Agency's basis for these findings is presented in the technical support document for the proposed rule and in Unit III.B. of this preamble.

4. EPA also finds that, except in the case of carcinogenicity where adequate testing by NTP is ongoing, testing is necessary for these effects.

Toxicokinetic testing is also necessary for the purpose of reasonably predicting the toxicokinetic behavior of hydroquinone and to help interpret the other testing being required by EPA and performd by NTP. The Agency is requiring 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 and EPA-required studies can be related to doses expected to be received by workers and hobbyists.

EPA does not believe that this 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 the testing being required for this substance will be minimal.

B. Required Testing

EPA is requiring that hydroquinone be tested for reproductive, teratogenic and nervous system effects and that its toxicokinetics be evaluated.

TABLE 2—TESTING REQUIREMENTS FOR HYDROQUINONE

Effect or study	ITC recommendation	EPA proposal	Final rule
Mutagenicity	–	x	[1] –
Carcinogenicity	x	[2] x	–
Teratogenicity/ developmental toxicity.	x	x	x
Nervous system effects	–	x	[3] x
Reproductive effects	–	x	[4] x
Epidemiology	x	x	[5] –
Metabolism (toxicokinetics).	x	x	x
Environmental fate	x	x	[6] –
Environmental effects	–	x	[6] –

[1] Data received by EPA since proposal indicates negative results in appropriate tests.
[2] Not proposed because NTP is conducting a 2-year bioassay.
[3] Adequate data on motor activity have been reported but neuropathology and testing in a functional observational battery are still needed.
[4] EPA agrees with commenters that suitable cohorts cannot be identified at this time.
[5] Data provided in response to proposed rule show lack of sufficient environmental concentrations to support testing.

C. Test Substance

EPA is requiring 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 will 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) of TSCA specifies that the activities for which the Agency makes section 4(a) findings (manufacture, processing, distribution, use and/or disposal) determine who bears the responsibilities 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 processing, distribution in commerce, and use of hydroquinone gives rise to substantial human exposure to the chemical and that such activities may present unreasonable risks to human health, EPA is requiring that persons who manufacture or process, or who intend to manufacture or process this chemical, 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 will be 5 years after the final hydroquinone reproductive effects report is submitted. As discussed in the Agency's test rule and exemption procedures (40 CFR Part 790), EPA expects that manufacturers will conduct testing and that processors will ordinarily be exempted from testing.

EPA is, however, exempting from these testing requirements those manufacturers and processors which produce and process hydroquinone only as an impurity. "Impurity" is defined in 40 CFR 790.3 to mean "a chemical substance which is unintentionally present with another chemical substance." The Agency is exempting those manufacturers and processors because the EPA's findings under sections 4(a)(1)(A) and 4(a)(1)(B) are based on exposures to hydroquinone which are a result of intentional processing, distribution in commerce and use and which represent a potential unreasonable risk. The Agency would find it difficult to apply both the exemption and reimbursement processes to those who manufacture and/or process hydroquinone solely as an impurity. In fact, the Agency's reimbursement regulations issued pursuant to section 4(c) state that those manufacture or process chemical substances as impurities will not be subject to test requirements unless the rule specifically states otherwise (40 CFR 791.48b).

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 a test 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. The Agency anticipates that the current manufacturers of hydroquinone will form the reimbursement pool and sponsor the testing required. Manufacturers and processors who are subject to the testing requirements of this rule must comply with the test rule and exemption procedures in 40 CFR Part 790. EPA is not requiring the submission of equivalence data as a condition for exemption from the required testing. As noted in Unit IV. B, EPA is interested in evaluating the effects attributable to hydroquinone itself and has specified a relatively pure substance for testing.

E. Test Rule Development and Exemptions

Elsewhere in today's Federal Register, the Agency is proposing that certain

OTS test guidelines and EPA-approved industry protocols be utilized as test standards for the development of data under this rule for hydroquinone. As discussed in that notice and in previous notices (50 FR 20652), EPA has reviewed the method for development of test rules and has decided that for most section 4 rulemakings, the Agency will utilize single-phase rulemaking. In light of this decision, EPA has reevaluated the process for developing test standards for section 4 rulemakings initiated under a two-phase process and has determined that for certain of these two-phase rules, OTS test guidelines are available for promulgation as relevant test standards. EPA has decided that where OTS or other appropriate test guidelines are available, the Agency in most cases will propose the relevant guidelines as the test standards for those rules.

EPA believes that, in line with its commitment to expedite the section 4 rulemaking process, it is appropriate to propose the applicable OTS test guidelines as test standards at the same as a Phase I final test rule is issued. With regard to the rulemaking for hydroquinone, OTS test guidelines and EPA-approved industry protocols are available for all the testing requirements included in this Phase I final rule. Thus, in the accompanying notice, the Agency is proposing these OTS test guidelines and industry protocols as test standards.

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

During the development of a test rule under the two-phase process, persons subject to the Phase I final rule are normally required to submit proposed study plans within 90 days after the effective date of the Phase I rulemaking. See 40 CFR 790.30(a)(2). However, because EPA is proposing applicable OTS test guidelines as the test standards for the studies required by this Phase I final rule, persons subject to the rule, i.e., manufacturers and processors of hydroquinone, are not required to submit proposed study plans for the required testing at this time. Persons subject to this rule, however, are still required to submit notices of intent to test or exemption applications in accordance with 40 CFR 790.25. For the rule, once the test standards are promulgated, persons who have notified EPA of their intent to test must submit study plans (which adhere to the promulgated test standards) no later than 30 days before the initiation of each required test.

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

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

Because persons subject to this rule for hydroquinone are not required to submit proposed study plans for approval, EPA will grant conditional exemptions under this rule. These exemptions will be granted following EPA's receipt of a letter of intent to conduct the required tests rather than after receipt and approval of a study plan. Notice of EPA's adoption of the proposed test standards and deadlines will be announced in a final Phase II test rule.

In the accompanying **Federal Register** notice, EPA is proposing deadlines for the submission of test data. Such deadlines are required under section 4(b)(1)(C) of TSCA. These proposed data submission deadlines are open for public comment and may be modified, where appropriate, when the final Phase II test rule is promulgated.

F. Reporting Requirements

EPA is requiring that all data developed under this rule be reported in accordance with the EPA Good Laboratory Practice (GLP) standards pursuant to 40 CFR Part 792, published in the **Federal Register** of November 29, 1983 (48 FR 53922).

EPA is required by TSCA section 4(b)(1)(C) to specify the time period during which persons subject to a test rule must submit test data. The Agency is proposing these deadlines elsewhere in today's **Federal Register**.

TSCA section 12(b) requires that persons who export or intend to export to a foreign country any hydroquinone subject to the testing requirements of this rule notify EPA of such exportation or intent to export. While the results of required testing may not be available for some time, a notice to the foreign government that these exported substances are subject to test rules serves to alert them to the Agency's concern about the substances. It gives these governments the opportunity to request such data that the Agency may currently possess plus whatever data may become available as a result of testing activities. Thus, upon the effective date of this rule, persons who export or intend to export hydroquinone must submit notices to the Agency pursuant to TSCA section 12(b)(1) and 40 CFR Part 707. For additional information, see the **Federal Register** of November 19, 1984 (49 FR 45581).

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

G. Enforcement Provisions

The Agency considers failure to comply with any aspect of a section 4 rule to be a violation of section 15 of TSCA. Section 15(1) of TSCA makes it unlawful for any person to fail or refuse to comply with any rule or order issued under section 4. Section 15(3) of TSCA makes it unlawful for any person to fail or refuse to: (1) Establish or maintain records, (2) submit reports, notices, or other information, or (3) permit access to or copying of records required by the Act or any regulation 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 procedures outlined in TSCA section 11 by designated representatives of the EPA for the purpose of

determining compliance with the 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 the TSCA GLP standards and in the test standards proposed rule of this rulemaking.

EPA's authority to inspect a testing facility also derives from section 4(b)(1) of TSCA, which directs EPA to promulgate standards for the development of test data.

These standards are defined in section 3(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 had 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. Intentional violations could lead to the imposition of criminal penalties of up to $25,000 for each day of violation and imprisonment of up to 1 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 16 of TSCA apply to "any person" who violates various provisions of TSCA.

EPA may, at its discretion, proceed against individuals as well as companies themselves. In particular, this includes individuals who report false information or who cause it to be reported. In addition, the submission of false, fictitious, or fraudulent statements is a violation under 18 U.S.C. 1001.

V. Economic Analysis of Rule

To assess the potential economic impact of this proposed rule, EPA has prepared an economic impact analysis that examines the cost 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 economic analysis of this final hydroquinone test rule, which estimates the total testing costs to range from $202,200 to $607,700, 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. The relative magnitude of the test cost is minor. On an annualized unit cost basis, the hydroquinone test costs are estimated to range from 0.19 to 0.57 cents per pound. The unit costs represent 0.10 to 0.29 percent of the current price of technical grade hydroquinone.

2. Market growth for hydroquinone is expected to remain stable.

3. The price elasticity of demand for hydroquinone in its primary uses is relatively inelastic.

For a detailed discussion of hydroquinone markets and the criteria for evaluating the potential for economic impact, see the Economic Impact Analysis of the Final Test Rule for Hydroquinone (Ref. 37).

VI. 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. Copies of the study, "Chemical Testing Industry: Profile of Toxicological Testing," October, 1981, can be obtained through the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161 (PB 82-140773).

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

VII. Public Record

EPA has established a record for this rulemaking (docket number OPTS-42048B). This record includes the basic information the Agency considered in developing this rule, and appropriate Federal Register notices. The Agency will supplement the record with additional information as it is received.

This record includes the following information:

A. Supporting Documentation

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

(a) Notice of final rule on hydroquinone.

(b) Notice of proposed rule on hydroquinone (January 4, 1984, 49 FR 438).

(c) Notice containing the ITC designation of hydroquinone to the Priority List (December 7, 1979, 44 FR 70684).

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

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

(f) Interim final rule for Test Rule Development and Exemption Procedures (May 17, 1985, 50 FR 20652).

(g) Notice of final rule concerning data reimbursement (July 11, 1983, 48 FR 31786).

(2) Support documents consisting of:

(a) Hydroquinone technical support document for proposed test rule.

(b) Economic impact analysis of final test rule for hydroquinone.

(3) Communications consisting of:

(a) Written public comments.

(b) Summaries of telephone conversations.

(c) Meeting summaries including transcript of public meeting on proposed test rule.

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

B. References

(1) Comments on EPA Proposed Test Rule for Hydroquinone, Chemical Manufacturer's Association, April 10, 1984.

(2) Testimony of the National Association of Photographic Manufacturers, Inc.: Proposed Test Rules for Hydroquinone/Quinone: Thomas J. Dufficy, Esq., April 18, 1984.

(3) Eastman Kodak, "Comments by Eastman Kodak Company on EPA's Proposed Test Rules, Hydroquinone 49 FR 438 and Quinone 49 FR 456, April 10, 1984, Appendix B.

(4) Eastman Kodak, "Comments by Eastman Kodak Company on EPA's Proposed Test Rules, Hydroquinone 49 FR 438 and Quinone 49 FR 456, April 10, 1984, Appendix L.

(5) Eastman Kodak, "Comments by Eastman Kodak Company on EPA's Proposed Test Rules, Hydroquinone 49 FR 438 and Quinone 49 FR 456, April 10, 1984.

(6) Chrostek, W.J., Health Hazard Evaluation/Toxicity Determination Report: Instant Copy Service, Philadelphia, PA: NIOSH-TR-HHE-75 84-235, 1975.

(7) Marty, *et al.*, "Pharmacocinetique Percutanee De L'Hydroquinone ^{14}C." *Cong Eur. Biopharm. Pharmacocinet.* 2:221-228, 1981. Translation provided by CMA] Marty, *et al.* "Rate of percutaneous absorption of ^{14}C-hydroquinone." *C.R.* European Congress of Biokinetic Pharmacology IY, 1981, 2 221-8, 1981.

(8) Guest, D., Hamilton, M.L. "Percutaneous absorption of [^{14}C] hydroquinone in dogs," summary report appearing in April 10, 1984 comments of Eastman Kodak on Hydroquinone Proposed Rule (See Ref. 51, 1984. Full report not completed.

(9) Racz, G., *et al.* "Effect of hydroquinone and phlorizin on the ovarian cycle of rats." *Rev. Med.* (Tirgu-Mures, Rom.) 1959.

(10) Skalka, P. "The influence of hydroquinone on the fertility of male rats "

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(12) Ames, S.R. *et al.* "Effects of DPPD, methylene blue, BHT, and hydroquinone on reproductive process in the rat." *Proc. Soc. Exp. Biol. Med.* 93:39–42. 1956.

(13) Boyland, E. *et al.* "Further experiments on implantation of materials into the uninary bladder of mice." *Br. J. Cancer* 18:575–581. 1964.

(14) Litton, "Evaluation of hydroquinone in the *in vitro* transformation of BALB/3T3 cells assay." 1981. (Submitted by W.D. Davis of Goodyear Tire and Rubber Co. on May 27, 1983).

(15) Serva, R.J., Murphy, S.J. "Evaluation of hydroquinone using the *Drosophila melanoganster*/sex-linked recessive lethal test." Submitted as complete study (incomplete version submitted May 27, 1983 by Goodyear) by Goodyear Tire and Rubber Company as part of April 2, 1984 comments to the hydroquinone proposed test rule. 1981.

(16) Gocke, *et al.* "Mutagenicity of cosmetic ingredients licensed by the European communities." *Mutation Research* 90:91–109. 1981.

(17) Krasavage, W.J. "Hydroquinone: A dominant lethal assay in male rats." 1984. Submitted by Eastman Kodak Company on August 24, 1984.

(18) Christian, R.T., *et al.* "The development of a test for the potability of water treated by a direct reuse system." U.S. Army Medical Research and Development Command, Wash. D.C. 20314. Contract No. DADA–17–73–C–3013. University of Cincinnati. 1980.

(19) Anderson, B. "Observation on corneal and conjunctival pigmentation occurring among workers engaged in the manufacture of hydroquinone." *Trans. Am. Ophthalmol. Soc.* 44:345–394. 1946.

(20) Sterner, J.H., Oglesby, F.L., and Anderson, B. "Quinone vapors and their harmful effects. Corneal and conjunctival injuries." *J. Ind. Hyg. Toxicol.* 29:60–73. 1947.

(21) Anderson, B. "Corneal and conjunctival pigmentation among workers engaged in manufacture of hydroquinone." *Arch. Ophthalmol.* 38:812–828. 1947.

(22) Anderson, B., Oglesby, F. "Corneal changes from quinone hydroquinone exposure." *Arch. Ophthalmol.* 59:495–501. 1958.

(23) Friedlander, B.R., Hearne, F.T., and Newman, B.J. "Mortality cancer incidence, and sickness-absence in photographic processors: an epidemiologic study." *JOM* 24 (8), 605–613. 1982.

(24) Greenwald, P. *et al.* "Diagnostic sensitivity bias—An epidemiologic explanation for an apparent brain tumor excess." *JOM* 24 (6), 690–694. 1981.

(25) Harbison, K.G., Belly, R.T. "The biodegradation of hydroquinone." Rochester, NY: Eastman Kodak Company Technical Report, March 10, 1975.

(26) Ambrose, R.T. *et al.* "A survey of photographic processing effluents." Technical Memorandum, Kodak Research Laboratories, Rochester, N.Y. August 1, 1977.

(27) National Association of Photographic Manufacturers. Letter to David Price, Test Rules Development Branch, Office of Toxic Substances, EPA, August 23, 1984.

(28) USEPA. Memorandum from Exposure Evaluation Division to Test Rules Development Branch, July 30, 1984.

(29) USEPA. Conference call between EPA and CMA, Kodak and Goodyear. Discussion of various issues. August 20, 1984.

(30) Eastman Kodak Company. Letter to David Price, Test Rules Development Branch, Office of Toxic Substance. Follow-up discussion of points covered in August 20, 1984 conference call (Ref. 29). Includes appendices A–E and 1983–84 Wolfman Report as appendix B. August 27, 1984.

(31) USEPA. Memorandum from Health and Environmental Review Division to Test Rules Development Branch. September 7, 1984.

(32) Mathtech Inc. Economic impact analysis of proposed test rule for quinone and hydroquinone. Washington, D.C. Office of Pesticides and Toxic Substances, U.S. Environmental Protection Agency. Contract 68–01–6630. December 5, 1983.

(33) Cotruvo, J.A., *et al.* Investigation of mutagenic effects of products of ozonation reactions in water. *Ann. N.Y. Acad. Sci.* 298:124–140. 1977.

(34) Bilimoria, M.H. The detection of mutagenic activity of chemicals and tobacco smoke in a bacterial system. *Mutat. Res.* 31:328. 1975.

(35) EMTDP. Environmental Mutagenesis Testing Development Program. Computer Printout. National Toxicology Program. December 3, 1982.

(36) Davis, W.D. The Goodyear Tire and Rubber Company, Akron, Ohio 44316–0001. Letter to D. Price, Office of Toxic Substances, U.S. Environmental Protection Agency, Washington, D.C. 20460. 1983.

(37) Mathtech, Inc. Economic impact analysis of final test rule for quinone and hydroquinone. Final Report. Washington, D.C.: Office of Pesticides and Toxic Substances, U.S. Environmental Protection Agency. Contract 68–01–6630. 1985.

Confidential Business Information (CBI), while part of the record, is not available for public review. A public version of the record, from which CBI has been deleted, is available for inspection from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays, in Rm. E–107, 401 M Street, SW, Washington, D.C.

VIII. Other Regulatory Requirements

A. Classification of Rule

Under Executive Order 12291, EPA must judge whether a regulation is "major" and, therefore, subject to the requirement of a Regulatory Impact Analysis. The regulation for this chemical substance is not major because it does not meet any of the criteria set forth in section 1(b) of the order. First, the annual costs of testing are expected to range from $52,000 to $158,000 over the expected market life of hydroquinone (Ref. 37). Second, because the cost of the required testing will be distributed over a large production volume, the rule will have only very minor effects on producers' costs of 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 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 EPA response to those comments, are included in the public record.

B. Regulatory Flexibility act

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

1. There are no small manufacturers of hydroquinone.

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

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

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

EPA concludes that there will be no significant adverse economic impact of any type as a result of this rule.

C. Paperwork Reduction Act

The information collection requirements contained in this rule have been approved by the Office of Management and Budget (OMB) under the provisions of the Paperwork Reduction Act of 1980, 44 U.S.C. 3501 *et seq.*, and have been assigned OMB control number 2070–0033.

List of Subjects in 40 CFR Part 799

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

Dated: December 20, 1985.

J. A. Moore,

Assistant Administrator for Pesticides and Toxic Substances.

PART 799—[AMENDED]

Therefore, 40 CFR Part 799 is amended as follows:

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

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

2. Section 799.2200 is added, 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, other than as an impurity, from January 13, 1986 to the end of the reimbursement period shall submit letters of intent to test, exemption applications, and shall conduct tests and submit data as specified in this section. Subpart A of this Part and Part 790 of this chapter for two-phase rulemaking.

(2) Persons subject to this section are not subject to the requirements of § 790.30(a) (2), (5), (6), and (b), and § 790.87(a)(1)(ii) of this chapter.

(3) Persons who notify EPA of their intent of conduct tests in compliance with the requirements of this section must submit plans for those tests no later than 30 days before the initiation of each of those tests.

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

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

(ii) *Test standards.* [Reserved]

(iii) *Reporting requirements.* [Reserved]

(2) *Developmental Toxicity*—(i) *Required testing.* Developmental toxicity studies in both a rodent and nonrodent species shall be conducted with hydroquinone. These tests must be conducted using the oral route of exposure.

(ii) *Test standards.* [Reserved]

(iii) *Reporting requirements.* [Reserved]

(3) *Reproductive Effects*—(i) *Required testing.* A two-generation reproductive effects study in a rodent species shall be conducted with hydroquinone. This test must be conducted using the oral route of exposure.

(ii) *Test standard.* [Reserved]

(iii) *Reporting requirements.* [Reserved]

(4) *Neurotoxicity*—(i) *Required testing.* The following neurotoxicity testing shall be conducted for hydroquinone using oral exposure of a rodent species:

(A) A functional observational battery.

(B) A neuropathology test.

(ii) *Test standards.* [Reserved]

(iii) *Reporting requirements.* [Reserved]

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

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