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Part IV

Environmental Protection Agency

Priority List of Chemical Substances Recommended for Testing; Fifth Report of the Interagency Testing Committee to the Administrator, EPA, Receipt of the Report, Request for Comments; and Corrections to the Fourth Report of the Interagency Testing Committee

ENVIRONMENTAL PROTECTION AGENCY

[FRL 1371-3]

Fifth Report of the Interagency Testing Committee to the Administrator, Environmental Protection Agency: Receipt of the Report and Request for Comments Regarding Priority List of Chemicals

AGENCY: Environmental Protection Agency (EPA).

ACTION: This notice requests comments on recent additions to the Interagency Testing Committee's (ITC) priority list of chemical substances recommended for testing under section 4(a) of the Toxic Substances Control Act (TSCA).

SUMMARY: The ITC, established under section 4(e) of TSCA, has transmitted its Fifth Report to the Administrator of EPA. This report revises and updates the Committee's priority list of chemicals. The Report adds two individual chemical substances and three categories to the Committee's list of chemicals for priority consideration by EPA in the promulgation of test rules under section 4(a) of the Act.

The Fifth Report is being published with this Notice. The Agency invites interested persons to submit comments on the Report.

SUPPLEMENTARY INFORMATION:

Background

Section 4(a) of TSCA authorizes the Administrator of EPA to promulgate regulations requiring testing of chemical substances in order to develop data revelant to determining the risks that such chemical substances may present to health and the environment.

Section 4(e) of TSCA established an Interagency Testing Committee to make recommendations of chemical substances to the Administrator of EPA for priority consideration for proposing test rules under section 4(a). The Committee may at any one time designate up to 50 of its recommendations for special priority consideration by EPA. Within 12 months of that designation, EPA must initiate rulemaking to require testing or publish in the **Federal Register** its reasons for not doing so.

The Committee's initial recommendations to the priority list, of four substances and six categories of substances, were published in the **Federal Register** on October 12, 1977 (42 FR 55026). EPA's response to the initial recommendations appeared in the **Federal Register** on October 26, 1978 (43 FR 50134). The ITC's revisions to the initial list appeared in the Committee's Second Report and were published in the **Federal Register** on April 19, 1978 (43 FR 16684). Those revisions were the addition of four substances and four categories of substances to the priority list. EPA responded to the second ITC Report on May 14, 1979 (44 FR 28095). In its Third Report, published in the **Federal Register** on October 30, 1978 (43 FR 50631), the Committee recommended the addition of one chemical substance and two categories of chemical substances to the priority list. In its Fourth Report, the Committee recommended the addition of 11 individual chemicals and one category to its priority list, each designated for priority consideration by EPA. The ITC's Fifth Report was received by the Administrator on November 7, 1979.

Availability

The ITC's Fifth Report follows this Notice.

REQUEST FOR COMMENTS: EPA invites interested persons to submit comments on the ITC's new recommendations. The Agency requests comments be submitted no later than February 5, 1979. All comments received by that date will be considered by the Agency in determining whether to propose test rules in response to the Committee's new recommendations.

Comments should bear the identifying notation OTS–410001 and should be submitted to the Document Control Officer, Chemical Information Division, Office of Pesticides and Toxic Substance (TS–793), Room 447, EPA, 401 M Street SW., Washington, D.C. 20460. All written comments will be available for public inspection in Room 447, East Tower, at the same address, between 8:30 a.m. and 4:30 p.m., weekdays.

Dated: November 28, 1979.

Steven D. Jellinek.

Assistant Administrator for Pesticides and Toxic Substances.

Fifth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency

Toxic Substances Control Act

Interagency Testing Committee

Member agencies—Council on Environmental Quality, Department of Commerce, Environmental Protection Agency, National Cancer Institute, National Institute of Environmental Health Sciences, National Institute for Occupational Safety and Health, National Science Foundation, Occupational Safety and Health Administration

Liaison agencies—Consumer Product Safety Commission, Department of Defense, Department of the Interior, Food and Drug Administration

November 6, 1979.

Hon. Douglas M. Costle,

Administrator, Environmental Protection Agency (A–100), Room 1200 W. 401 M Street, S.W., Washington, D.C.

Dear Mr. Costle: On behalf of the TSCA Interagency Testing Committee I wish to inform you that the Committee now recommends further revision of the Section 4(e) Priority List with the addition and designation of two individual chemicals and three categories of chemical substances. These recommendations and supporting information are presented in the enclosed document, the Fifth Report of the Committee.

This report highlights our recent deliberations on dyes and pigments from which recommendations on certain dyes are made. Essentially, our first recommendation is a generic recommendation for the study of human health effects. I would emphasize the need for scientific investigation rather than routine testing of these materials since great uncertainties regarding the composition of each substance and its complex pharmacodynamics and fate simply preclude isolation upon a specific effect. This recommendation does not imply that testing for mutagenicity, carcinogenicity, teratogenicity and other end-points is inappropriate but that the evaluation of these materials must be a global evaluation to include the parent material, its constituents and metabolites and transformation products.

Our second major recommendation is with respect to the environmental fate and effects of the three categories of dyes. The Committee cannot recommend testing for specific environmental effects at this time. This is because the chemical composition, and hence the environmental fate, of all components of the dyes in each category is not known. Also, both the toxicity and the environmental fate of these dyes will be affected by the metabolic fate of their various components. However the Committee does urge the development of a sequenced approach, in which the results of environmental fate studies are used to determine the environmental compartments in which these chemical substances or their derivatives may be of concern. The organisms, species and effects which are most appropriate for testing can then be determined.

Certainly, the dyes and pigments are a complicated group of chemical substances—from their composition, chemistry and usage to their effective regulation. I personally believe that acceptable use patterns for these materials can only be advanced through a coordinated, comprehensive program of research and testing involving the joint efforts of industry and the Federal Government. And I would suggest that serious consideration be given to finding ways to involve the National Toxicology Program with this effort.

I trust that you will find our recommendations responsive to the intentions of the Toxic Substances Control Act, and I want to assure you that the

Committee continues to regard its mission as a sensitive and serious responsibility.

Sincerely yours,

Carter Schuth,

Chairperson, TSCA Interagency Testing Committee.

Enclosure
cc: Mr. Jellinek

Fifth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency, November 1979

Contents

Summary

Section 4 of the Toxic Substances Control Act of 1976 (TSCA, Pub. L. 94469) provides for the testing of chemicals in commerce which may pose an unreasonable risk to human health or the environment. This section of the Act also provides for establishment of a Committee, composed of representatives from eight designated Federal agencies, to recommend chemical substances or mixtures to which the Administrator of the U.S. Environmental Protection Agency (EPA) should give priority consideration for the promulgation of testing rules. The Committee makes such revisions in the Section 4(e) Priority List as it determines to be necessary and transmits them to the Administrator, at least every six months.

As a result of its deliberations during the past six months, the Committee is revising the TSCA Section 4(e) Priority List by the addition of 2 individual substances and 3 categories. As provided in the law these substances are designated for action by EPA within twelve months. the Committee considers each newly designated addition to be of equal priority with those previously designated. The additions to the Priority List are presented, together with the types of studies recommended, as follow:

Substances and Categories Designated and Recommended Studies

Benzidine-based dyes—Environmental Fate and Effects
o-Dianisidine-based dyes—Human Health Effects, Environmental Fate and Effects
o-Tolidine-based dyes—Human Health Effects, Environmental Fate and Effects
Hydroquinone—Carcinogenicity, Teratogenicity, Epidemiology, Environmental Fate and Effects
Quinone—Carcinogenicity, Teratogenicity, Environmental Fate and Effects

TSCA Interagency Testing Committee

Statutory Member Agencies

Council on Environmental Quality—Nathan J. Karch
Department of Commerce—Orville E. Paynter, Bernard Greifer, Alternate
Environmental Protection Agency—Warren R. Muir, Amy Rispin, Alternate[1]
National Cancer Institute—James M. Sontag
National Institute of Environmental Health Sciences—Richard R. Bates, Warren T. Piver, Alternate
National Institute for Occupational Safety and Health—Vera W. Hudson,[2] Michael Blackwell, Alternate[3]
National Science Foundation—Carter Schuth, Chair
Occpational Safety and Health Administration—Fred W. Clayton, Vice-Chair, Joseph K. Wagoner, Alternate

Liaison Agencies

Consumer Product Safety Commission—Joseph McLaughlin
Department of Defense—Bernard P. McNamra[4]
Department of the Interior—Charles R. Walker
Food and Drug Administration—Allen H. Heim, Winston deMonsabert, Alternate
Department of Agriculture—Homer E. Fairchild[5]

Committee Staff

Walter G. Rosen, Acting Executive Secretary
Madye B. Cole, Administrative Technician

Fifth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency, October 1979

Chapter 1. Introduction

1.1 *Background.*—The Interagency Testing Committee (Committee) was established under Section 4(e) of the Toxic Substances Control Act of 1976 (TSCA, Pub. L. 94-469). The specific mandate of the Committee is to identify and recommend to the Administrator of the U.S. Environmental Protection Agency (EPA) chemical substances or mixtures in commerce which should be tested to determine their potential hazard to human health and/or the environment. The Act specifies that the Committee's recommendations to the Administrator will be in the form of a list (Section 4(e) Priority List) to be published in the Federal Register. The Committee also is directed to make such revisions in the list as it determines to be necessary and transmit them to the Administrator, at least every six months after submission of its initial list.

The current Committee members, alternates, and liaison representatives are identified in the front of this report. The Committee's chemical review procedures and previous recommendations have been presented elsewhere (References 1-5).

1.2 *Committee Activities in this Reporting Period.*—In August 1979 the Committee completed a second round of scoring of chemicals from its master file (see reference 2 for methodology). Newly scored chemicals will be reviewed for the purpose of making future recommendations to the Administrator.

A significant development since the Committee's last report to the Administrator has been the publication by the EPA of the Toxic Substances Control Act Chemical Substances Inventory. The Committee has begun to utilize the Inventory for production information in its evaluation of chemicals.

Public comments on the Committee's Fourth Report have been reviewed. Based on this review, the Committee does not plan to revise its testing recommendations or alter further the format of its reports.

As in its previous reports, the rationales in this Fifth Report do not contain references to all planned or ongoing studies, although the Committee may be aware of such studies. In this regard, the Committee's reasoning remains the same as stated and explained in Section 3.2 of the Third Report (4):

> The Committee generally does not regard knowledge that studies are planned or ongoing as a sufficient basis to defer consideration of a substance for designation for the effect under investigation or for any other effect. The Committee's judgment as to whether a substance has been adequately tested for health and environmental effects must rest with the data that are presently available. Such data do not exist for planned studies and may be in various stages of generation for ongoing studies.

1.3 *EPA's Response to the Committee's Previous Reports.*—In this Report, twenty one entries appear on the

[1] Dr. Rispin replaced Mr. Joseph Merenda as Alternate on June 29, 1979.
[2] Ms. Hudson replaced Dr. Jean French as Member on August 9, 1979.
[3] Dr. Blackwell replaced Ms. Vera Hudson as Alternate on August 9, 1979.
[4] Dr. McNamara replaced Dr. Seymour Freiss on September 27, 1979.
[5] Dr. Fairchild joined the Committee on September 21, 1979.

Section 4(e) Priority List with designations for EPA action by October 1978, April 1979, and October 1979. Although these chemicals were designated for action by the Administrator in the Committee's previous reports, they are still retained on the Section 4(e) Priority List as shown in Table 1.

1.4 *Liaison Members.*—The Committee continues to rely on input from its liaison agency members and recommends that consideration be given to statutory membership for their agencies.

Chapter 2. Recommendations of the Committee

2.1 *Chemical Substances Designated for Action by EPA Within Twelve Months.*—The Committee is revising its TSCA Section 4(e) Priority List by the designation of an additional 2 individual substances and 3 categories for which initiation of testing rules is recommended. These designations were made after consideration of the factors identified in TSCA Section 4(e)(1)(A), and with the professional judgment of Committee members. The recommended studies deemed appropriate for determining the potential hazard(s) of each new entry and the reasons for such recommendations are described in Section 2.2 of this report and summarized in Table 2. As allowed by Section 4(e)(1)(A) of TSCA, the Committee designates these chemicals and categories for action by EPA within twelve months of the date of this Report.

In previous reports, the Committee has recommended studies for specific health effects. In the present report however, the Committee makes the generic recommendation for human health effects testing of *o*-dianisidine and *o*-tolidine based dyes. Further elaboration can be found in Section 2.2.

The Committee is recommending environmental fate studies for both of the chemicals and all three of the categories of chemicals which are included in this report. The Committee has refrained from recommending specific environmental effects studies for these chemicals and categories until information concerning their fate is sufficient to establish the identity of metabolities and degradation products and whether significant environmental concentrations are likely to occur. Appropriate tests are conditional on the environmental fate of the chemicals in question.

Although the three categories which are being designated in this report are listed separately, they are closely related to each other and are therefore discussed in a single rationale.

Table 1.—*The TSCA Section 4(e) Priority List*

	Designated for action by
Acetonitrile	April 1980
Acrylamide	April 1979**
Alkyl epoxides	October 1978*
Alkyl phthalates	October 1978*
Aniline and bromo, chloro, and/or nitroanilines.	April 1980
Antimony (metal)	April 1980
Antimony sulfide	April 1980
Antimony trioxide	April 1980
Aryl phosphates	April 1979**
Benzidine-based Dyes	November 1980
Chlorinated benzenes, mono- and di-	October 1978*
Chlorinated benzenes, tri-, tetra- and penta-.	October 1979
Chlorinated naphthalenes	April 1979**
Chlorinated paraffins	October 1978*
Chloromethane	October 1978*
Cresols	October 1978*
o-Dianisidine-based Dyes	November 1980
Dichloromethane	April 1979**
1,2-Dichloropropane	October 1979
Cyclohexanone	April 1980
Glycidol and its derivatives	October 1979
Halogenated alkyl epoxides	April 1979**
Hexachloro-1,3-butadiene	October 1978*
Hexachlorocyclopentadiene	April 1980
Hydroquinone	November 1980
Isophorone	April 1980
Mesityl oxide	April 1980
4,4'-Methylenedianiline	April 1980
Methyl ethyl ketone	April 1980
Methyl isobutyl ketone	April 1980
Nitrobenzene	October 1978*
o-Tolidine-based Dyes	November 1980
Polychlorinated terphenyls	April 1979**
Pyridine	April 1979**
Quinone	November 1980
Toluene	October 1978*
1,1,1-Trichloroethane	April 1979**
Xylene	October 1978*

* Designated by the Committee in its First Report (2) and responded to by the Administrator in 43 FR 50134–50138.
** Designated by the Committee in its Second Report (3) and responded to by the Administrator in 44 FR 28095–28097.

Table II.—*Summary of Studies Recommended in This Report*

Substance or category	Recommended Studies				
	Carcinogenicity	Teratogenicity	Human Health Effects	Epidemiology	Environmental fate and effects
Benzidine-based dyes					X
o-Dianisidine-based dyes			X		X
o-Tolidine-based dyes			X		X
Hydroquinone	X	X		X	X
Quinone	X	X			X

References

1. Preliminary List of Chemical Substances for Further Evaluation, Toxic Substances Control Act Interagency Testing Committee, July 1977.

2. Initial Report to the Administrator, Environmental Protection Agency, TSCA Interagency Testing Committee, October 1, 1977. Published in the Federal Register, Vol. 42, 197, Wednesday, October 12, 1977, pp. 55026–55080. Corrections published in Federal Register Vol. 42, November 11, 1977, pp. 58777–58778. The report and supporting dossiers also were published by the Environmental Protection Agency, EPA 560–10–78/001, January 1978.

3. Second Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency, TSCA Interagency Testing Committee, April 1978. Published in the Federal Register, Vol. 43, No. 76, Wednesday, April 19, 1978, pp. 16684–16688. The report and supporting dossiers also were published by the Environmental Protection Agency, EPA 560–10–78/002, July 1978.

4. Third Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency, TSCA Interagency Testing Committee, October 1978. Published in the Federal Register, Vol. 43, No. 210, Monday, October 30, 1978, pp. 50630–50635.

5. Fourth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency, TSCA Interagency Testing Committee, April 1979. Published in the Federal Register, Vol. 44, No. 107, Friday, June 1, 1979, 31866–31869.

2.2 Rationales

Benzidine-, o-Dianisidine- and o-Tolidine-Based Dyes

Recommended Studies: It is the Committee's view that benzidine-based dyes are an established health hazard. The health effects of *o*-tolidine- and *o*-dianisidine-based dyes, on the other hand, are not as clearly demonstrated. The Committee, therefore, recommends health effects testing for the *o*-tolidine- and *o*-dianisidine-based dyes. These general human health effects recommendations are based on uncertainty about the metabolic fate of each dye in these categories and about the carcinogenic potential of the parent *o*-tolidine and *o*-dianisidine.

The environmental fate and potential environmental effects of these three categories of dyes are largely unknown. This lack of information coupled with their large environmental release causes the Committee to recommend environmental fate and effects testing.

With regard to all three categories of dyes, it is the view of the Committee that specific environmental effects tests cannot be recommended at this time. This is because the chemical composition, and hence the environmental fate, of all components of

the dyes in each category is not known. Also, both toxicity and environmental fate of these dyes will be affected by the metabolic fate of their various components. For these reasons we believe that the evaluation of environmental effects of these three categories of dyes can be most effectively ascertained through a sequenced approach, in which the results of environmental fate studies are used to determine the environmental compartments in which these chemical substances or their derivatives may be of concern. The organisms, species and effects which are most appropriate for testing can then be determined.

The Committee hopes that its recommendation for testing for health or environmental effects does not encourage the premature replacement of the designated dyes with others about which even less test data are available and which might prove hazardous.

The ITC is aware of the fact that considerable attention is being focused on dyes and pigments, including the three categories of dyes which are the subject of this recommendation, by various agencies of the federal government. We believe that the complexity of dye chemistry, the variety of dye uses, the ubiquity of their distribution and the uniqueness of their exposure potential create special problems with regard to their evaluation and effective regulation, possibly exceeding the resources of the EPA under TSCA. Indeed, a coordinated, multi-agency approach to these chemicals may be required.

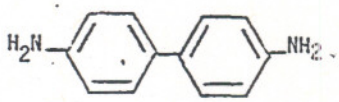
Category Identification. These three categories of dyes which are based on benzidine, *o*-tolidine (3,3'-dimethylbenzidine) and *o*-dianisidine (3,3'-dimethoxybenzidine). The three parent compounds constitute a family of similar synthetic aromatic compounds (see Fig. A) and are referred to in this report as "benzidine and its congeners." The three categories of dyes represent about 90 commercially available dyes in the United States; namely 23 benzidine-based dyes, 37 *o*-dianisidine-based dyes, and 33 *o*-tolidine-based dyes.

The Dyes Environmental and Toxicology Organization, Inc. (DETO) supplied the Committee with the following definition of dyes:

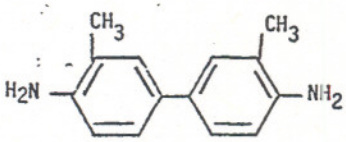
Dyes are intensely colored or fluorescent organic substances which impart color to a substrate by selective adsorption of light. Dyes are water soluble and/or go through an application process which, at least temporarily, destroys any crystal structure of the color substances. Dyes are retained in the substrate by adsorption, solution, and mechanical retention, or by ionic or covalent chemical bonds.

Dyes based on benzidine, *o*-tolidine and *o*-dianisidine are water soluble and non-volatile.

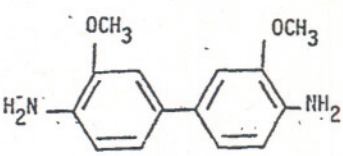
FIGURE A.



Benzidine



o-Tolidine (3,3'-dimethylbenzidine)



o-Dianisidine (3,3'-dimethoxybenzidine)

Production and Importation. According to a 1979 industry survey conducted by DETO for the Committee, benzidine-based dyes in commerce in 1978 from domestic production and imports totaled almost 2 million pounds. *o*-Tolidine-based dyes in commerce totaled at least 1 million pounds and *o*-dianisidine dyes at least 1.3 million pounds for the same year. Not all importers and manufacturers of these dyes contributed to this survey. DETO indicated that the combined production of the companies not contributing to the survey was probably insignificant relative to the totals given although four of the five importers surveyed by DETO did not respond. Since the United States International Trade Commission does not monitor all ports of entry, the Committee does not have an adequate estimate of imports. Currently there is no estimate of quantities of these dyes entering the country in dyed articles of commerce.

Exposure. The dyes derived from benzidine and its congeners are an important class of direct dyes, i.e., dyes which are colorfast without requiring an extra mordant process. Some of them are key dyes for cellulosic fibers. They are used to color textiles, rubber and plastics products, printing inks, paints and lacquers, leathers and paper products.

Dyes derived from *o*-tolidine, *o*-dianisidine, and benzidine are used in consumer products which may result in significant human exposure. Dyes in textiles, leather, paper and fur may rub off by abrasion. Clothing may be subject to perspiration, urine, or saliva. Dyes may be decomposed through the heat of ironing or drying. This exposure may be especially important in the case of fabrics with low attraction between fiber and dye; for example, those derived from batik, tie dyeing or home dyeing rather than from industrial dyeing (Sheldrick et al. 1979).

Exposure to these dyes occurs through three primary paths: inhalation (Genin, 1977; NIOSH, 1979), unintentional ingestion (Yoshida and Miyakawa, 1973) and skin absorption (McKinney, 1979). Industrial workers, professional craft dyers and hobbyists, and individuals using fabric dyes at home or in arts and crafts classes comprise populations of potential high exposure.

Skin absorption as an important route of exposure to both the dyes and their parent compounds is supported by a recent study (McKinney, 1979). This study indicates that Direct Black 38, a

benzidine-based dye, or the benzidine portion of the molecule, is rapidly absorbed from the unbroken skin of experimental animals. The dye, labelled in the benzidine moiety, was painted on the skin of rabbits. By the sixth day after exposure, 90% of the labelled dose had been recovered in the urine and feces.

A NIOSH investigation has examined benzidine levels in the urine of workers exposed to benzidine-based dyes. Four facilities—two benzidine-based dye manufacturing plants, a leather tanning plant, and a papermill—were studied. Samples were collected from the environment to determine the amount of potential exposure to the dyes. There was a good correlation between the amount of benzidine-based dyes in the environment and the occurrence of benzidine in urine. The urinary levels of benzidine was considered to be too high to have come only from impurities in the dye. (NIOSH, 1979).

Human Health Effects. Dyes in these three categories have been reported to undergo reductive cleavage of the azo linkages, resulting in the release of the benzidine or benzidine-congener parent compound in both mammals and anaerobic intestinal bacterial enzyme systems. (Walker, 1970; Chung et al., 1978).

Benzidine is well established as a carcinogen in humans and animals (IARC, 1972). *o*-Tolidine and *o*-dianisidine have been tested for carcinogenicity in rats (IARC, 1974; Pliss, 1965; Pliss and Zabenzbinsky, 1970; Hadidian et al., 1968.) Although there was some indication of carcinogenicity, the protocols used did not permit satisfactory evaluation of the results. *o*-Tolidine and *o*-dianisidine are currently under test for carcinogenicity at the National Center for Toxicological Research.

Two *o*-tolidine-based dyes, commercial grade Evans Blue and Trypan Blue, have been reported to be carcinogenic in rats (Marshall, 1953). There is some question about the purity of the tested compounds. A recent study shows that Trypan Blue contains substantial quantities of monoazo dye impurities (Field et al., 1977). In this study, rats injected with the purified *o*-tolidine-based component of Trypan Blue gave only weak indications of pre-cancerous hepatic changes. Three purified benzidine dyes, Direct Black 38, Direct Brown 95 and Direct Blue 5, were carcinogenic in rats after a treatment period of only 13 weeks (NCI, 1978a).

Epidemiological studies (Meigs et al. 1954; Kiese et al., 1968) show that occupational exposure to benzidine-based dyes is associated with bladder cancer in humans. Yoshida et al. (1973) studied 200 kimono painters who used benzidine-based dyes. Seventeen (8.5%) developed bladder cancer; this was 6.8 times the expected rate. Approximately 47% had ingested dyes by moistening the brushes on their tongues. The workers had used these dyes, Direct Black 38, Direct Green 1, Direct Red 17, and Direct Red 28.

Field et al., (1977) reported the teratogenicity of the pure *o*-tolidine-based component of Trypan Blue. Administration of aqueous solutions of the purified dye to rats on the seventh day of pregnancy resulted in a significantly increased incidence of resorptions and malformations.

o-Tolidine, *o*-dianisidine and benzidine have been reported to be mutagenic in the Ames *Salmonella* assay (Urwin et al., 1976; Ames et al., 1973; Garner et al., 1975; Ferretti et al., 1977).*o*-Tolidine and *o*-dianisidine were weakly mutagenic.

Sugimura et al. (1977) reported on the mutagenicity of an *o*-tolidine dye (Benzopurpurine 4B), a dianisidine dye (Pontacyl sky blue 4BX) and two benzidine based dyes (Congo red and chlorazol violet N). These dyes were mutagenic to Salmonella TA98 with S–9 mix (liver homogenate with TPNH) in the presence of riboflaving. When tested without riboflavin, the results were negative. Trypan Blue (based on *o*-tolidine) was mutagenic only when pretreated anaerobically with a cell free bacterial extract containing azo-reductase, or when first chemcially reduced with dithionite (Hartman et al., 1978). These results suggest that the mutagenic activity of Trypan Blue is due to release of the *o*-tolidine group from the dye.

Four benzidine-based dyes (Direct Black 38, Direct Blue 6, Direct Brown 95 and Direct Red 28) have been reported to be metabolized to free benzidine in Rhesus monkeys (Rinde and Troll, 1975). Incubation of benzidine-based dyes (Direct Reds 10, 17, 28, Direct Orange 8 and Direct Black 38) with common intestinal bacteria has demonstrated that the azo linkages can be cleaved enzymatically to release the benzidine-derived moiety (Chung et al., 1978; Diekhues, 1961). Studies being conducted at the National Institute of Environmental Health Sciences indicate that benzidine dyes (Direct Blue 2, Direct Black 4, Direct Brown 2, Direct Red 28, Direct Orange 8 and Direct Green 1) are cleaved metabolically in dogs to release free benzidine (Matthews, 1979, Personal Communication.) Preliminary results in these studies also indicate the release in the urine of *o*-tolidine from Direct Red 2 and Direct Red 39, and *o*-dianisidine from Direct Blue 1.

As discussed earlier, metabolism of benzidine based dyes in humans leading to the release of free benzidine was indicated by a study of workers exposed to dyes (NIOSH, 1979).

Structurally, the *o*-dianisidine, and *o*-tolidine based dyes are similar to three benzidine-based dyes known to cause cancer in animals. The teratogenic potential of one *o*-tolidine-based dye has been reported. Although it is not known precisely how these dyes act in the body, the pattern of evidence appears to support initial reductive cleavage of the dyes to release the toxic biphenylamines. The structure-activity relationships of these chemicals are based on the ease of enzymatic cleavage of these dyes with different substituents near the azo groups and the relative biological activity of the benzidine-containing congener.

Environmental Fate. The environmental fate of these three categories of dyes has received virtually no scientific investigation. That benzidine is an environmentally signficant degradation product of benzidine-based dyes is supported by the finding by Takemura et al. (1965) of levels ranging from 0.082 to 0.233 ppm of benzidine in the Sumida River which, at the time, was receiving large quantities of waste waters from dye and pigment plants. Levels of total aromatic amines in the river were reported as 0.205 to 0.562 ppm. The biodegradability of benzidine under carefully controlled conditions has been reported (Tabak and Barth, 1978; Baird et al., 1977); but none of the studies available to the Committee is adequate to determine the

fate of benzidine in the environment. Further, these studies are not applicable to environmental conditions and real-life wastewater treatment conditions. Their main inadequacy is that only the disappearance of parent benzidine was measured, leaving unresolved the identity of intermediates and end-products of the many reactions possible under environmental or use conditions. Possible products of concern include hydroxylated derivatives of benzidine, 4-aminobiphenyl, *o*-toluidine and aniline. Studies on the metabolism of benzidine are not conclusive as to the identity of the ultimate carcinogen, but hydroxylated forms cannot be ruled out (IARC, 1972). 4-Aminobiphenyl is carcinogenic to several species of animals and was strongly associated with human bladder cancer in an epidemiological study of workers (IARC, 1972). *o*-Toluidine and aniline have been reported to be carcinogenic in laboratory animals (NCI, 1978b; NCI, 1979). The Committee reviewed the possible human and environmental health risks associated with aniline in its Fourth Report. The Committee is not aware of studies on the fate and persistence of the benzidine congeners.

The reduction of azo bonds to release the parent amines has been reported to occur via several different reactions, all of which may be applicable to environmental or use conditions. These include photo-degradation (van Beek and Heertges, 1963), heat decomposition (Mel'nikov and Kirillova 1969), enzymatic cleavage in animals (Rinde and Troll, 1975; Miller and Miller, 1953; Radomski, 1974; Radomski and Mellinger, 1962; Fouts et al., 1957) and by bacteria and cell-free extracts (dieckhues, 1961; Hartman et al., 1978; Yoshida et al., 1973; Idaka et al., 1978). Other reactions of dyes include demethylation (Miller et al., 1945), ring hydroxylation (terayama, 1967), N-hydroxylation (Miller, 1970), and N-acetylation and O-conjugation of metabolites (Terayama, 1967). A myriad of other reactions can be postulated based on the typical structure of these dyes: aromatic ring fission following hydroxylation, reduction of nitro groups to amino groups, oxygen- and nitrogen-dealklyation, olefin oxidation, ester hydrolysis, acetylation, aliphatic hydroxylation and oxygen- and nitrogen-conjugation. The Committee is concerned that these dyes may be converted to free amines, substituted anilines and other chemicals that may pose a potential environmental hazard. Games and Hites (1977) have demonstrated the variety of chemicals in a river receiving dye plant effluents. Many dyes may have the same intermediate and final degradation products in the environment. Identification of the common metabolites and products is prerequisite to an understanding of the environmental fate of the parent compounds and their dyes.

Calculation of the environmental release of dyes is problematic. Consideration of annual production and import data on dyestuffs fails to account for the dyes which are part of dyed materials and articles. In addition to wastewaters and sludges containing some proportion of annual production and imports, one must also account for the disposal of all dyed materials, many of which were produced several to many years ago. Yoshida et al., (1973) report that a benzidine-based dye on cotton cloth lost color in 72 hours when incubated with river water, ostensibly releasing free benzidine which resisted further bacterial degradation. Another study shows that these dyes with their high affinity for cellulosic materials are adsorbed to sludges in biological treatment (Hitz et al., 1978). This would likely lead to additional environmental release when the sludges are disposed of, used as a soil supplement or incinerated. Anaerobic digestion of the dye-containing sludge might also release aromatic amines and other degradation products. The classical emphasis on decolorization of dye wastes without attention to the degradation products possible formed is also a serious concern, particularly if these wastes are chlorinated (Gardiner and Borne, 1978). In real world situations of wastewater treatment, the lack of nutrient chemicals in industrial waste streams may lead to incomplete substrate oxidation and the resulting effluent may contain a variety of unexpected chemicals.

The *in vitro* and *in vivo* conversion of dyes to possibly hazardous products in the environment has not been adequately studied. The Committee therefore recommends that EPA give high priority to assessing the environmental behavior of dyes, in all forms which are released to the environment.

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Hydroquinone

Recommended Studies: The Committee recommends the hydroquinone be studied for environmental fate and health effects. The widespread use of the chemical by consumers having little knowledge of safety and environmental control is of particular concern. The formation of the relatively stable semiquinone radical and the reversibility of the oxidation-reduction system of quinone-semiquinone-hydroquinone are further cause for concern. Information is needed on the stability of this entire system within the environment, rather than simply on the loss of a single component. The Committee believes that existing studies are inadequate to evaluate the potential carcinogenicity of hydroquinone in either experimental animals or in human beings. Evaluation of teratogenicity is also needed, especially in view of the apparent increase in fetal resorption in one reproduction study. Thus, the Committee recommends studies of environmental fate, carcinogenicity, and teratogenicity. Epidemiologic studies are recommended if an appropriate cohort can be identified.

Physical and Chemical Identification

CAS number: 123-31-9

Structural formula:

Molecular formula: $C_6H_6O_2$ Molecular weight: 110.11

Melting point: 173–174°C Vapor pressure: 1 mm at 132.4°C

Hydroquinone is a white crystalline solid at room temperature. It discolors upon exposure to air and light. It is very soluble in water, ethanol and actone; and soluble in alkali, ether, chloroform carbon tetrachloride and hot benzene. It acts chemically as a reducing agent, being readily oxidized to quinone (IARC, 1977). This occurs in two steps

through the formation of a relatively stable semiquinone radical. The reaction is reversible (NIOSH, 1978).

Production, Release and Exposure. Production volume in 1977 was at least 11 million pounds as compiled from non-confidential information in the TSCA Inventory. Any production in excess of this figure in 1977 is not publicly available. Hydroquinone has been reported to be present in cigarette smoke (Schlotzhauer et al., 1978), in effluents from chemical plants (IARC, 1977) and as a glucoside in the leaves and bark of many plants (IARC, 1977).

Hydroquinone is used as a photographic developer; as an antioxidant and polymerization inhibitor in fats, oils, turpentine, paints and motor fuels; in dermatologic preparations designed to bleach hyperpigmented skin; and as an intermediate in the production of dyes and other chemicals (IARC, 1977).

The National Institute for Occupational Safety and Health (NIOSH) has estimated that about 475,000 U.S. workers are potentially exposed (NIOSH, 1979).

Review of Published Studies: Carcinogenicity. Bladder carcinomas were induced in 6 of 19 mice with pellets of cholesterol containing 20% hydroquinone implanted into the bladder (Boyland et al, 1964). Topical application 3 times weekly for 1 year of the highest dose that did not damage the skin did not induce skin tumors (Van Duuren and Goldschmidt, 1976). Simultaneous application of hydroquinone and benzo(a)pyrene according to this regimen resulted in a slight inhibition of the carcinogenicity of the hydrocarbon. Hydroquinone had no promoting activity in a two-stage study. Systemic effect of topical application of hydroquinone was not reported by these authors.

A two-year feeding study on Sprague-Dawley rats was performed by Carlson and Brewer (1953). In one experiment of this study, ten rats of each sex were fed 0.0%, 0.1%, 0.5%, or 1% hydroquinone. In another experiment, 16 to 23 rats of each sex were fed 0.0%, 0.1%, 0.25% or 0.5% hydroquinone that had been heated together with lard for 30 minutes at 190°C. In a third experiment, 20 rats of each sex were fed 0.0%, 0.1%, 0.5% or 1.0% hydroquinone along with 0.1% citric acid. In most of the high dose and some other groups, the weights of treated groups were 8–20% reduced at the end of the experiment, but in most groups the difference was not statistically significant. Histological sections were made of liver, omentum, kidney, spleen, heart, lung, bone marrow, stomach, pancreas, adrenal, subperitoneal and intramuscular abdominal fat. Hemoglobin, erythrocyte and differential white blood cell counts were also done. An unspecified number of animals were necropsied at intervals during the course of the experiments. Histopathologic and hematologic findings were reported as "negative," but no data were reported. Another group of rats fed 5% hydroquinone lost 46% weight over 9 weeks and were reported to show aplastic anemia,; atrophy of liver, lymphoid tissue, fat and muscle; and ulceration of the stomach.

Thus, hydroquinone caused bladder tumors by pellet implantation, but this test is not generally recognized as definitive. Other long term studies were negative, but they do not meet current testing or reporting standards.

Mutagenicity. Several studies of the effect of hydroquinone on plant chromosomes have reported gaps and breakage but no rearrangements (Valadaud and Izard, 1971; Sharma and Chaterjee, 1964; Loveless, 1951; Chaterjee and Sharma, 1972). In a test reported to correlate well with mutagenicity and carcinogenicity, hydroquinone did not inhibit testicular DNA systehsis (Seiler, 1977). Hydroquinone did not mutate *Micrococcus (Staphylococcus) aureus* to penicillin or streptomycin resistance (Clark, 1953). An abstract reporting another bacterial mutation study indicated that it was positive in the *E. coli* pol A test, but no data were published (Bilmoria, 1975).

Reproduction and Teratogenicity. One study reported a significant increase in fetal resorption in rats given a total of 0.5 gm hydroquinone in the diet during pregnancy (Telford et al, 1962). Another study reported no effect on litter size or viability from feeding 0.003 or 0.3% hydroquinone in the diet to pregnant rats (Ames et al., 1956). No teratogenicity studies have been found.

Other Toxic Effects. A large number of acute toxicity studies have been done in several kinds of rodents, rabbits, dogs, cats, pigeons and goldfish. Several routes of administration have been used. Acute effects have included vomiting, labored breathing, cyanosis, coma, convulsions and death (NIOSH, 1978). Intravenous administration resulted in acute renal tubular necrosis (Calder et al., 1973). Subacute poisoning caused hemolytic jaundice, anemia, leukocytosis, hypoglycemia and cachexia (Deichmann and Keplinger, 1963). A chronic study in rats was referred to above under "carcinogenicity" (Carlson and Brewer, 1953): These same authors fed 100 mg/Kg/day of hydroquinone to 5 adult dogs for 26 weeks and doses ranging from 1.6 to 40 mg/Kg/day for 80 weeks to 3 dogs beginning at 4 months of age. Hematologic and histopathologic findings were reported to be similar to controls except for reduced "hemosiderosis" in spleen, liver and bone marrow. A study by Woodward (NIOSH 1978), however, indicated that daily administration of 25 or 50 mg/Kg of hydroquinone in gelatin capsules resulted in hyperplasia of the bone marrow and excessive pigment deposits in the spleens of all dogs after 609 days.

Epidemiology. As would be expected from its pharmaceutic effect, repeated topical exposure with hydroquinone can cause depigmentation of the skin. In addition, prolonged topical exposure has resulted in erythema, hyper-sensitivity, dermatitis, ochronosis and colloid milium. Damage to the cornea and conjunctiva are generally proportional to the amount and time of exposure. Mild effects include conjunctivitis, photophobia, lacrimation and pigmentation. Erosion of the epithelium, changes in thickness and curvature of the cornea and loss of visual acuity were seen in more severe cases. A few reported cases of oral ingestion of acutely toxic amounts of hydroquinone have been characterized by gastroenteritis, cyanosis, tinnitus, convulsions and loss of consciousness (NIOSH, 1978; Hooper et al., 1978).

Environmental Fate and Effects. Hydroquinone has been reported to be readily degraded by algae (Timofeeva, et al, 1975) and readily oxidized in air (IARC, 1977). The principle metabolic products, however, are water soluble conjugates and the relatively insoluble oxidation product, quinone (IARC, 1977). Since hydroquinone and quinone have been reported to reach equilibrium by 90 minutes in tissue culture (Guillerm et al., 1968), a significant portion of the degraded hydroquinone may be in a form available for regeneration to the parent compound. The reversible oxidation-reduction system of hydroquinone and quinone has been reported to involve the formation of a relatively stable semiquinone radical (NIOSH, 1978).

Hydroquinone is rapidly metabolized and excreted by mammals (NIOSH 1978). It is not likely to bioaccumulate. BOD5 has been reported as 0.478 and 1.00 (Verschueren, 1977).

Effects that have been observed experimentally include inhibition of seed germination (Stom and Leonova, 1973), inhibition or stimulation of plant growth depending on dose (Georgiev and Ivanova, 1972), attraction and repellance of beetles (Norris et al., 1970), molluscidal action (El Sebae et al., 1978), inhibition of protoplastic streaming in

algae (Stom et al., 1974) and stimulation of insect feeding (Meyer and Norris et al., 1974).

Summary. There is substantial opportunity for human and environmental exposure to hydroquinone and possibly to its metabolic and oxidation products, semiquinone and quinone. More information is needed on both the environmental fate of hydroquinone and its metabolism in humans in order to estimate the extent of exposure to semiquinone and quinone. Acute and subacute effects of hydroquinone have been well characterized. Such chronic study reports as exist tend to be reassuring, but they do not meet current standards of test design or reporting. No published reports of epidemiologic studies of chronic effects have been found. No teratology studies have been reported. Several mutagenicty studies reported in the literature are negative, but one abstract which provides no data reported hydroquinone to be mutagenic.

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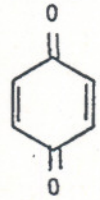
Recommended Studies:

The Committee recommends that quinone be studies for environmental fate and health effects. It is particularly concerned about the formation of the relatively stable semiquinone radical and the reversibility of the oxidation-reduction system of quinone-semiquinone-hydroquinone. Information in needed on the stability of this entire system within the environment, rather than simply on the loss of a single component. The electrophilic nature of quinone is compatible with its being carcinogenic; several bioassays support this possibility. No information on teratogenicity is available, but the inhibition of aggregation of embryonic cells raises concern. Reports of effects in humans are inadequate to assess chronic effects. The Committee recommends that studies of environmental fate, corcinogenicity and teratogenicity be done.

Physical and Chemical Identification:

CAS number: 106-51-4

Structural formula:



Synonym: p-Benzoquinone

Molecular formula: $C_6H_4O_2$

Molecular weight: 108.1

Melting point: 105.7°c

Vapor pressure: 98 mm Hg at 25°C

Quinone is a yellow crystalline solid at room temperature. It is slightly soluble in water, and soluble in ethanol, ether, and hot petroleum ether. It acts as as oxidizing agent while being reduced to hydroquinone (IARC, 1977). This occurs through the formation of a relatively stable semiquinone radical. The reaction is reversible (NIOSH, 1978).

Production, Release and Exposure

Production volume in 1977 was at least 100,00 pounds as compiled from non-confidential information in the TSCA Inventory. Any production in excess of this figure in 1977 is not publicly available. NIOSH (1979) estimates that 3,700 workers may be exposed. It is used as an oxidizing agent, an inhibitor of polymerization, a tanning agent, a photographic chemical and as an intermediate in the synthesis of hydroquinone and other chemicals. It has also been reported to occur naturally in some arthropods (IARC, 1977). Other sources of exposure may result from oxidation of hydroquinone through metabolic or environmental processes (Deichman & Keplinger, 1963) and from ozonation of aromatic amines (Glabisz and Tomaszewska, 1977).

Review of Published Studies

Carcinogenicity

Sugishita (1950) reported results of daily topical application of 0.2% quinone for up to 758 days. Among 14 mice surviving more than 100 days, there was 1 skin cancer, 2 mice with "papillomatous atypical proliferation in the skin", 1 lung cancer, and 6 with "atypical proliferation in their lungs." Sex and strain of mice were not reported, nor was information about control animals. In a similar experiment using 0.2% quinone exposed to light, 5 of 20 mice developed "papillomatosis" of the skin (Takizawa and Sugishita, 1948). Among ten that were necropsied, 1 had "atypical proliferation of the small bronchial tube", 2 had severe atypical proliferation and 1 had "adenomatous carcinoma" of the lung. Again, sex and strain were not specified and no mention was made of controls.

Several studies by Takizawa reported the apparent induction of skin, liver and lung tumors by lifetime topical application to the skin of mice of unspecified strain and sex. In one of these (1940a), among 44 mice receiving 0.25% quinone in benzene and surviving 200 days, 3 had skin papillomas, 1 had skin cancer and 5 had liver cancer. After 0.1% quinone, 6 had skin papillomas, 2 had skin cancer and 10 had liver cancer among 41 survivors. Forty-six benzene-treated controls had 1 papilloma, no skin cancers, and 2 liver cancers. Lung cancer incidence was reported to be increased in quinone-treated mice, but data were not reported. In a subsequent study (Takizawa, 1941), 54.5% of mice surviving topical application of quinone for 200 days had epithelial proliferation in the lung and bronchi compared with 7.1% of benzene treated controls. Three out of 99 of the former had carcinomas and 4 adenomas compared with 0 and 1 respectively among 28 controls. Another study (Takizawa, 1940b) reported 9 mice with skin papillomas, 3 with skin cancer and 8 with lung cancer among 87 mice receiving topical application of quinone and surviving more than 200 days; among 46 benzene-treated controls, 1 had papilloma, none had skin cancer, and 1 had a lung cancer.

In contrast, Tiedemann (1953) applied 1% quinone solution in benzene 6 days a week for 47% days to the skin of albino mice. No skin tumors were seen in these animals or benzene treated controls.

Two local sarcomas were induced in 24 rats by weekly subcutaneous injections for 394 days (IARC, 1977). No lifetime feeding studies appear to have been done, and inhalation studies were inadequate for evaluation (IARC, 1977).

Mutagenicity

Quinone failed to induce chromatid translocations in human leukocyte cultures (Luers and Obe, 1972), *Vicia faba* or *Triturus* (Loveless, 1951), though breaks and gaps did occur. It was not found to be mutagenic by dominant lethal test in mice (Roehrborn and Vogel, 1967) or *Drosophila* (Vogel, 1972), by recessive lethal tests in Drosophila (Luers and Obe, 1972) or in forward or reserve mutation tests in *Neurospora* (Reissig, 1963).

Reproduction and Teratology

No studies of reproductive or teratologic effects of quinone have been found. It has been reported to inhibit aggregation of chick fibroblasts (Jones, 1965) and chick embryo muscle cells (Kemp and Jones, 1970).

Other Toxic Effects

Quinone is readily absorbed through the gastro-intestinal tract and from subcutaneous tissues. In large doses it causes respiratory difficulties, drop in blood pressure and chronic convulsions. Death results from paralysis of medullary centers in the brain (Deichmann and Keplinger, 1963). Intravenous administration is toxic to kidneys (Calder et al, 1973).

Epidemology

Exposure of skin to quinone causes discoloration, severe irritation, erythema, swelling, and formation of papules and vesicles. Prolonged contact leads to necrosis of the skin. Exposure of the eyes to vapors of quinone results in pigmentation of the conjunctiva and cornea, disturbance of vision and corneal ulceration (Deichmann and Keplinger, 1963).

Environmental Fate and Effects

Hydroquinone and quinone are reported to form a reversible oxidation-reduction system through the formation of a relatively stable semiquinone radical (NIOSH, 1978). Quinone can be metabolized to hydroquinone (Deichmann and Keplinger, 1963). Thus, environmental effects of hydroquinone may also be relevant to quinone.

Experimental observations of effects of quinone include breaking dormancy of grass seed (Shimizu and Ueki, 1972), inhibition of oxidation of indoleacetic acid by pea roots (Ugrekhelidze et al, 1972); inhibition of protoplasmic streaming (Stom and Rogozina, 1976), O_2 uptake (Stom and Beim, 1976), and CO_2 fixation (Pristavu, 1975) in algae; and inhibition of growth of plant rootlets (Stom, 1975; Le Thi Muoi et al., 1974). Some of its effects may result from its interaction with sulfhydryl groups (Men'shikova et al., 1975; Stom and Kuzevanova, 1976).

Summary

Although estimates of direct occupational exposure to quinone are relatively small, human and environmental exposure could be significant as a result of oxidation of hydroquinone. More information is needed on metabolism and environmental fate of both hydroquinone and quinone. Quinone has been relatively well studied for mutagenicity and found negative. Carcinogenicity studies are conflicting, raising questions about purity of the chemical administered and quality of experimental observations; better studies are needed. No data are available on teratogenicity.

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Fourth Report of the Interagency Testing Committee; Receipt of the Report and Request for Comments; Corrections

In FR Doc. 79–16820 appearing at page 31866 in the issue of Friday, June 1, 1979, various typographical and editorial errors in the fourth report of the Interagency Testing Committee were published. These errors are corrected as follows:

1. P. 31867, column 1, line 14 of the first complete paragraph is corrected to read: "addition to be of equal priority with those";

2. P. 31868, column 1, line 12 of the first complete paragraph is corrected to read: "basis of their knowledge of scoring";

3. P. 31869, "Table II" is corrected to read "Table 2";

4. P. 31869, column 1 of Table 2, line 11 is corrected to read: "4,4'–Methylenedianiline";

5. P. 31870, column 2, line 13 is corrected to read: "Fassett, D. W. 1963, Cyanides and Nitriles . . .";

6. P. 31878, column 3, 10th line of the final paragraph is corrected to read: "mining, hauling, and smelting of ore,";

7. P. 31878, column 3, 14th line of the final paragraph is corrected to read: "and asphalt concrete . . .";

8. P. 31881, column 2, line 3 of the first complete paragraph is corrected to read: "Weller and Griggs (1973, 1976) and Griggs";

9. P. 31882, column 3, under *Mutagenicity*, line 5 is corrected to read: "liver microsomes (Bonse and Goggleman, 1977),";

10. P. 31885, column 3, line 17 of paragraph is corrected to read: "raw material in the production of QianaR";

11. P. 31886, column 1, line 6 of the first complete paragraph is corrected to read: "[Stienhoff and Grundmann 1970a; . . .";

12. P. 31886, column 1, paragraph 2, line 5 is corrected to read: "compound, 4,4'–diamino-diphenylether on";

13. P. 31886, column 2, the last line of the second complete paragraph is corrected to read: "personal communication reported by McGill and Motto, 1974).";

14. P. 31888, column 2, in alphabetical order, after the eighth entry is added: "Perry, J. J., 1968. Substrate specificity in hydrocarbon utilizing microorganisms. Antonie van Leeuwenhoek J. Microbiol. Serol. 34:27–36.";

15. P. 31888, column 3, line 6 is corrected to read: "Methyl Isobutyl Ketone"; and

16. P. 31889, column 3, line 7 is corrected to read: "1946. Further studies on sensory response".

Dated November 28, 1979.

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Assistant Administrator for Pesticides and Toxic Substances.

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