List of Subjects in 21 CFR Part 176

Food additives, Food packaging.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 176 is amended as follows:

PART 176—INDIRECT FOOD ADDITIVES: PAPER AND PAPERBOARD COMPONENTS

1. The authority citation for 21 CFR Part 176 continues to read as follows:

Authority: Secs. 201, 402, 406, 409, 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 342, 346, 348, 376).

2. Section 176.170 is amended in paragraph (a)(5) by alphabetically adding a new entry to read as follows:

§ 176.170 Components of paper and paperboard in contact with aqueous and fatty foods.

* * * * *

(a) * * *

(5) * * *

List of substances	Limitations
* * * * *	
12-Hydroxystearic acid-polyethylene glycol block copolymers (CAS Reg. No. 70142-34-6) produced by the reaction of polyethylene glycol (minimum molecular weight 1500) with 12-hydroxystearic acid.	For use only as a surfactant for dispersions of polyacrylamide retention and drainage aids employed prior to the sheet forming operation in the manufacture of paper and paperboard.
* * * * *	

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Dated: January 21, 1992.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 92-1990 Filed 1-27-92; 8:45 am]

BILLING CODE 4160-01-M

21 CFR Part 177

[Docket No. 89F-0171]

Indirect Food Additives; Poly(Phenyleneterephthalamide) Resins

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the food additive regulations to provide for the safe use of poly(phenyleneterephthalamide) resins and various adjuvants used in the resin production, when used in repeated contact with food. The additive is the subject of a petition filed by E.I. du Pont de Nemours & Co.

DATES: Effective January 28, 1992; written objections and requests for a hearing by February 27, 1992.

ADDRESSES: Written objections to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Julius Smith, Center for Food Safety and Applied Nutrition (HFF-335), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-472-5690.

SUPPLEMENTARY INFORMATION: In a notice published in the **Federal Register** of June 6, 1989 (54 FR 24264), FDA announced that a food additive petition (FAP 8B4101) had been filed by E.I. du Pont de Nemours & Co., 1007 Market St., Wilmington, DE 19898, proposing that the food additive regulations be amended for the safe use of poly(p-phenyleneterephthalamide) resins intended to produce articles for repeated use in the processing and handling of food. The filing notice announced that the processing and finishing of the resins may include the following optional adjuvant substances:

Diundecylphthalate
Mono-and dipotassium salts of lauryl phosphate
o-Phenylphenol
Poly(oxyethylene/oxypropylene)monobutylether
Polyethylene glycol mono(nonylphenyl)ether
Polyvinylmethyl ether
Poly(oxyethylene) sorbitol monolaurate tetraoleate
Poly(oxyethylene) sorbitol hexaoleate
4,4'-Butylidenebis(6-*tert*-butyl-*m*-cresol)

To be consistent with current acceptable nomenclature, polyethylene glycol mono(nonylphenyl)ether has been changed to read poly(oxyethylene) mono(nonylphenyl)ether and poly(p-phenyleneterephthalamide) resin has been changed to read poly(phenyleneterephthalamide) resin.

I. The Additive

FDA has reviewed the safety of these additives, as well as the starting materials. Four of the additives reviewed, poly(oxyethylene/oxypropylene)monobutylether, poly(oxyethylene) mono(nonylphenyl)ether, poly(oxyethylene) sorbitol monolaurate tetraoleate, and poly(oxyethylene) sorbitol hexaoleate may contain minute amounts of ethylene oxide and 1,4-dioxane as impurities from their production. These chemical impurities have been shown to cause cancer in test animals. Residual amounts of reactants and manufacturing aids, such as ethylene oxide and 1,4-dioxane, are commonly found as contaminants in chemical products, including some food additives.

II. Prior Action

Under section 409(c)(3)(A) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348(c)(3)(A), the so-called "general safety clause" of the statute, a food additive cannot be approved for a particular use unless a fair evaluation of the data establishes that the additive is safe for that use. The concept of safety embodied in the Food Additives Amendment of 1958 is explained in the legislative history of the provision: "Safety requires proof of a reasonable certainty that no harm will result from the proposed use of an additive. It does not—and cannot—require proof beyond any possible doubt that no harm will result under any conceivable circumstances." H. Rept. 2284, 85th Cong., 2d Sess. 4 (1958). This definition of safety has been incorporated into FDA's food additive regulations (21 CFR 170.3(i)). The anticancer, or Delaney clause, of the food additive amendment (section 409(c)(3)(A) of the act) provides further that no food additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal.

In the past, FDA has often refused to approve a use of an additive that contained or was suspected of containing even minor amounts of a carcinogenic chemical, even though the additive as a whole had not been shown to cause cancer. The agency now believes, however, that development in scientific technology and experience with risk assessment procedures make it possible for FDA to establish the safety of additives that contain a carcinogenic chemical, but that have not themselves been shown to cause cancer.

In the preamble to the final rule permanently listing D&C Green No. 6, published in the **Federal Register** of April 2, 1982 (47 FR 14138), FDA explained the basis for approving the use of a color additive that had not been shown to cause cancer, even though it contains a carcinogenic constituent. Since that decision, FDA has approved the use of other color additives and food additives on the same basis. An additive that has not been shown to cause cancer, but that contains a carcinogenic constituent, may properly be evaluated under the general safety clause of the statute using risk assessment procedures to determine whether there is a reasonable certainty that no harm will

result from the proposed use of the additive.

The agency's position is supported by *Scott* v. *FDA*, 728 F. 2d 322 (6th Cir. 1984). That case involved a challenge to FDA's decision to approve the use of D&C Green No. 5, which contains a carcinogenic chemical, but has itself not been shown to cause cancer. Relying heavily on the reasoning in the agency's decision to list this color additive, the United States Court of Appeals for the Sixth Circuit rejected the challenge to FDA's action and affirmed the listing regulation.

III. Safety of Petitioned Use

FDA estimates that the petitioned use of the additive poly(phenylene-terephthalamide) resins and its adjuvants diundecylphthalate, mono- and dipotassium salts of lauryl phosphate, *o*-phenylphenol, poly(oxyethylene/oxypropylene) monobutylether, poly(oxyethylene) mono(nonylphenyl)ether, polyvinyl methyl ether, poly(oxyethylene) sorbitol monolaurate tetraoleate, poly(oxyethylene) sorbitol hexaoleate, and 4,4'-butylidenebis (6-*tert*-butyl-*m*-cresol) will result in extremely low levels of exposure to these substances. FDA does not ordinarily consider chronic testing to be necessary to determine the safety of an additive whose use will result in such low exposure levels (Refs. 1 and 2), and the agency has not required such testing here. Because the additive has not been shown to cause cancer, the anticancer clause does not apply.

FDA has evaluated the safety of these additives under the general safety clause, using risk assessment procedures to estimate the upper bound limit of risk presented by the ethylene oxide and 1,4-dioxane that may be present as impurities in the additives. Based on this evaluation, the agency has concluded that the additive is safe under the proposed conditions of use.

The risk assessment procedures that FDA used in this evaluation are similar to the methods that the agency has used to examine the risk associated with the presence of minor carcinogenic impurities in various other food and color additives that contain carcinogenic impurities. (See, e.g., 49 FR 13018 at 13019, April 2, 1984.) This risk evaluation of the carcinogenic impurities has two aspects: (1) Assessment of the worst-case exposure to the impurities from the proposed use of the additive and (2) extrapolation of the risk observed in the animal bioassays to the conditions of probable exposure to humans.

A. 1,4-Dioxane

Based on the fraction of the daily diet that may be in contact with articles containing the four ethoxylated additives, as well as the level of 1,4-dioxane that may be present in these additives, FDA estimated the hypothetical worst-case exposure to 1,4-dioxane from the use of the ethoxylated additives in repeated-use articles would not exceed 7 nanograms (ng) per person per day (Ref. 3). The agency used data in a carcinogenesis bioassay on 1,4-dioxane, conducted for the National Cancer Institute (Ref. 4), to estimate the upper bound level of lifetime human risk from the proposed use of the additives. The results of the bioassay on 1,4-dioxane demonstrated that the material was carcinogenic for female rats under the conditions of the study. The test material caused significantly increased incidence of squamous cell carcinomas and hepatocellular tumors in female rats.

The Center for Food Safety and Applied Nutrition's Cancer Assessment Committee (the Committee) has reviewed this bioassay and other relevant data available in the literature and concludes that the findings of carcinogenicity were supported by this information on 1,4-dioxane. The Committee further concludes that an estimate of the upper bound level of lifetime risk from potential exposure to 1,4-dioxane stemming from the proposed use of the four ethoxylated additives in repeated-use articles could be calculated from the bioassay.

The agency used a quantitative risk assessment procedure (linear proportional model) to extrapolate from the dose used in the animal experiment to the very low doses encountered under the proposed conditions of use. This procedure is not likely to underestimate the actual risk from very low doses and may, in fact, exaggerate it because the extrapolation models used are designed to estimate the maximum risk consistent with the data. For this reason, the estimate can be used with confidence to determine, to a reasonable certainty, whether any harm will result from the proposed conditions and levels of use of the four ethoxylated additives.

Based on a worst-case exposure of 7 ng per person per day, FDA estimates that the upper bound limit of individual lifetime risk from the potential exposure to 1,4-dioxane from the use of these ethoxylated additives is 2.5×10^{-10}, or less than 2.5 in 10 billion (Ref. 5). Because of numerous conservatisms in the exposure estimate, lifetime average individual exposure to 1,4-dioxane is expected to be substantially less than the estimated daily intake, and therefore, the calculated upper bound limit of risk would be less. Thus, the agency concludes that there is a reasonable certainty of no harm from exposure to 1,4-dioxane that might result from the proposed use of the four ethoxylated additives.

B. Ethylene Oxide

Based on the fraction of the daily diet that may be in contact with articles containing the four ethoxylated additives, as well as the level of ethylene oxide that may be present in the additives, FDA estimated the hypothetical worst-case exposure to ethylene oxide from the use of the ethoxylated additives in repeated-use articles would not exceed 7 ng per person per day (Ref. 3). The agency used data in a carcinogenesis bioassay on ethylene oxide conducted for the Institute of Hygiene, University of Mainz, Germany (Ref. 6), to estimate the upper bound level of lifetime human risk from the proposed use of the additives. The results of the bioassay on ethylene oxide demonstrated that the material was carcinogenic for female rats under the conditions of the study. The test material caused significantly increased incidence of squamous cell carcinomas of the forestomach and carcinoma in situ of the glandular stomach.

The Committee has reviewed this bioassay and other relevant data available in the literature and concludes that the findings of carcinogenicity were supported by this information on ethylene oxide. The Committee further concludes that an estimate of the upper bound level of lifetime risk from potential exposure to ethylene oxide stemming from the proposed use of the four ethoxylated additives in repeated-use articles could be calculated from the bioassay.

The agency used a quantitative risk assessment procedure (linear proportional model) to extrapolate from the dose used in the animal experiment to the very low doses encountered under the proposed conditions of use. As discussed above, this estimate can be used with the confidence to determine, to a reasonable certainty, whether any harm will result from the proposed conditions and levels of use of the ethoxylated additives.

Based on a worst-case exposure of 7 ng per person per day, FDA estimates that the upper bound limit of individual lifetime risk from the potential exposure to ethylene oxide from the use of the four ethoxylated additives is 1.3×10^{-8}, or less than 1.3 in 100 million (Ref. 5). Because of numerous conservatisms in

the exposure estimate, lifetime averaged individual exposure to ethylene oxide is expected to be substantially less than the estimated daily intake, and therefore, the calculated upper bound limit of risk would be less. Thus, the agency concludes that there is a reasonable certainty of no harm from exposure to ethylene oxide that might result from the proposed use of these additives.

C. Need for Specifications

The agency has also considered whether specifications are necessary to control the amounts of 1,4-dioxane and ethylene oxide in the four ethoxylated additives and in the finished poly(phenyleneterephthalamide) resins. The agency finds that specifications are not necessary for the following reasons: (1) Because of the low levels at which 1,4-dioxane and ethylene oxide may be expected to remain as impurities following production of the ethoxylated additives and the finished resin, the agency would not expect these impurities to become components of food at other than extremely low levels; and (2) the upper bound limit of lifetime risk from exposure to these impurities, even under worst-case assumptions, is very low, less than 1.3 in 100 million and 2.5 in 10 billion for ethylene oxide and 1,4-dioxane, respectively.

D. Conclusion of Safety

FDA has evaluated the available toxicity data and the exposure calculations for the intended use of the poly(phenyleneterephthalamide) resin and its adjuvant additives and has determined that they are safe for their proposed use. Accordingly, FDA is amending Part 177 by adding new § 177.1632. In accordance with § 171.1(h) (21 CFR 171.1(h)), the petition and documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Food Safety and Applied Nutrition by appointment with the information contact person listed above. As provided in 21 CFR 171.1(h), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

IV. Environmental Impact

The agency has carefully considered the potential environmental effects of this action. FDA has concluded that the action will not have a significant impact on the human environment, and that an environmental impact statement is not required. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

V. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Carr, G.M., "Carcinogen Testing Programs," in "Food Safety: Where are we?", Committee on Agriculture, Nutrition, and Forestry, United States Senate, p. 59, July 1979.

2. Kokoski, C.J., "Regulatory Food Additive Toxicology," *Chemical Safety Regulation and Compliance*, edited by F. Hombruger and J.K. Marquis, *S. Karger*, New York, NY, pp. 24–33, 1985.

3. Memorandum dated December 30, 1988, from Food And Color Additives Review Section to Indirect Additives Branch "FAP 8B4101—DuPont. Polymer of Terephthaloyl Chloride and *p*-Phenylenediamine," submission of July 7, 1988.

4. "Bioassay of 1,4-Dioxane for Possible Carcinogenicity," National Cancer Institute, NCI–CG–TR–80, 1978.

5. Memorandum dated October 31, 1990, "Report of the Quantitative Risk Assessment Committee."

6. Dunkelber, H., "Carcinogenicity of Ethylene Oxide and 1,2-Propylene Oxide upon Intragastric Administration to Rats," *British Journal of Cancer*, 46:924, 1982.

VI. Objections

Any person who will be adversely affected by this regulation may at any time on or before February 27, 1992 file with the Dockets Management Branch (address above) written objections thereto. Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents shall be submitted and shall be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 177

Food additives, Food packaging.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 177 is amended as follows:

PART 177—INDIRECT FOOD ADDITIVES: POLYMERS

1. The authority citation for 21 CFR part 177 continues to read as follows:

Authority: Secs. 201, 402, 409, 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 342, 348, 376).

2. New § 177.1632 is added to subpart B to read as follows:

§ 177.1632 Poly (phenyleneterephthalamide) resins.

Poly(phenyleneterephthalamide) resins identified in paragraph (a) of this section may be safely used as articles or components of articles intended for repeated contact with food.

(a) *Identity.* For the purpose of this section, the poly(phenylene-terephthalamide) resins (CAS Reg. No. 26125–61–1) are produced by the polymerization of terephthalolyl chloride with *p*-phenylenediamine. The poly(phenyleneterephthalamide) resin fibers and yarns may contain optional adjuvant substances required in their preparation and finishing.

(b) *Optional adjuvant substances.* The poly(phenyleneterephthalamide) resins identified in paragraph (a) of this section may contain the following optional adjuvant substances, subject to any limitation on their use:

(1) Optional adjuvant substances authorized for this use in accordance with § 174.5 of this chapter.

(2) Optional finish components, total weight not to exceed 1 percent by weight of the base polymer, as follows:

List of substances	Limitations
Diundecylphthalate (CAS Reg. No. 3648–20–2).	
Mono- and dipotassium salts of lauryl phosphate (CAS Reg. No. 39322–78–6).	
o-Phenylphenol (CAS Reg. No. 90–43–7).	For use as a fungicide for finish coating materials. Not to exceed 0.01 percent by weight of the base polymer.

List of substances	Limitations
Poly(oxyethylene/oxypropylene)monobutylether (CAS Reg. No. 9038-95-3).	
Poly(oxyethylene) mono(nonyiphenyl)ether (CAS Reg. No. 9019-45-9).	
Polyvinyl methylether (CAS Reg. No. 9003-09-2).	
Poly(oxyethylene) sorbitol monolaurate tetraoleate (CAS Reg. No. 71243-28-2).	
Poly(oxyethylene) sorbitol hexaoleate (CAS Reg. No. 57171-56-9).	
4,4'-Butylidenebis (6-*tert*-butyl-*m*-cresol) (CAS Reg. No. 85-60-9).	For use only as an oxidation inhibitor for finish coating materials. Not to exceed 0.01 percent by weight of the base polymer.

(c) *Specifications.* (1) Poly(phenyleneterephthalamide) resins in the form of continuous filament yarns or fibers that have been scoured in accordance with paragraph (d)(1) of this section, when refluxed in a 50 percent ethanol/water mixture for 24 hours, yields total extractables not exceeding 0.5 percent by weight of the sample.

(2) Poly(phenyleneterephthalamide) resins in the form of pulp, when refluxed in a 50 percent ethanol/water mixture for 24 hours, yields total extractables not exceeding 0.65 percent by weight of the sample.

(d) *Conditions of use.* (1) Poly(phenyleneterephthalamide) resins in the form of continuous filament yarns and fibers may be used as components of articles intended for repeated use in contact with food at temperatures not to exceed 260 °C (500 °F). All items are scoured prior to use by agitation in a water bath containing 0.5 gram/liter of tetrasodium pyrophosphate and 0.5 percent detergent. The items are agitated at 80 °C (180 °F) for 20 minutes, and then subjected to a cold water rinse.

(2) Poly(phenyleneterephthalamide) resins in the form of pulp may be used as gaskets and packing for food processing equipment at temperatures not to exceed 260 °C (500 °F).

Dated: January 21, 1992.

Michael R. Taylor,

Deputy Commissioner for Policy

[FR Doc. 92-1987 Filed 1-27-92; 8:45 am]

BILLING CODE 4160-01-M

21 CFR Part 177

[Docket No. 89F-0462]

Indirect Food Additives: Polymers

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the food additive regulations to provide for the safe use of polyurethane resins derived from the reaction of diphenylmethane diisocyanate with 1,4-butanediol and polytetramethylene ether glycol as rubber articles intended for repeated use in contact with food. This action is in response to a petition filed by The Dow Chemical Co., E. I. du Pont de Nemours & Co., and B. F. Goodrich.

DATES: Effective January 28, 1992; written objections and requests for a hearing by February 27, 1992.

ADDRESSES: Written objections to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Vir Anand, Center for Food Safety and Applied Nutrition (HFF-335), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-254-9500.

SUPPLEMENTARY INFORMATION: In a notice published in the **Federal Register** of November 17, 1989 (54 FR 47828), FDA announced that a food additive petition (FAP OB4182) had been filed by The Dow Chemical Co., 1803 Bldg., Door 7, Midland, MI 48674, E. I. du Pont de Nemours & Co., 1007 Market St., Wilmington, DE 19898, and B. F. Goodrich, 3925 Embassy Pkwy., Akron, OH 44313, proposing that § 177.2600 *Rubber articles intended for repeated use* (21 CFR 177.2600) of the food additive regulations be amended to provide for the safe use of polyurethane resins derived from the reaction of diphenylmethane diisocyanate with 1,4-butanediol and polytetramethylene ether glycol, as rubber articles intended for repeated use in contact with food.

In its evaluation of the safety of these resins, FDA has reviewed the safety of the proposed additives themselves, their starting materials, and the byproducts of the starting materials used to manufacture the additives. Although polyurethane resins have not been found to cause cancer, some have been found to contain minute amounts of methylenedianiline (MDA) which has been shown to cause cancer in test animals. MDA is produced when diphenylmethane diisocyanate (MDI), a starting material used in the manufacture of polyurethane resins, is reacted with water. Residual amounts of reactants or their reaction products and manufacturing aids are commonly found as contaminants in chemical products, including food additives. Therefore, the agency has evaluated the safety of the use of polyurethane resins that may contain residual amounts of the carcinogenic reaction product MDA and that are intended for repeated use in contact with food.

I. Determination of Safety

Under section 409(c)(3)(A) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348(c)(3)(A)), the so-called "general safety clause" of the statute, a food additive cannot be approved for a particular use unless a fair evaluation of the data available to FDA establishes that the additive is safe for that use. The concept of safety embodied in the Food Additives Amendment of 1958 is explained in the legislative history of the provision: "Safety requires proof of a reasonable certainty that no harm will result from the proposed use of an additive. It does not—and cannot—require proof beyond any possible doubt that no harm will result under any conceivable circumstance." (H. Rept. 2234, 85th Cong., 2d sess. 4 (1958)). This definition of safety has been incorporated into FDA's food additive regulations (21 CFR 170.3(i)). The anticancer, or Delaney provision of the general safety clause of the Food Additives Amendment of 1958 (section 409(c)(3)(A) of the act) provides further that no food additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal.

In the past, FDA has refused to approve the use of an additive that contained or was suspected of containing even minor amounts of a carcinogenic chemical, even though the additive itself has not been shown to cause cancer. The agency now believes however, that developments in scientific technology and experience with risk assessment procedures make it possible for FDA to establish the safety of additives that contain carcinogenic chemicals but that have not themselves been shown to cause cancer.

In the preamble to the final rule permanently listing D&C Green No. 6, published in the **Federal Register** of April 2, 1982 (47 FR 14138), FDA explained the basis for approving the use of a color additive that had not been shown to cause cancer, even though it contains a carcinogenic impurity. Since that decision, FDA has approved the use

of numerous color additives and food additives on the same basis.

An additive that has not been shown to cause cancer, but that contains a carcinogenic impurity, may properly be evaluated under the general safety clause of the statute using risk assessment procedures to determine whether there is a reasonable certainty that no harm will result from the proposed use of the additive.

This position is supported by *Scott* v. *FDA*, 728 F. 2d 322 (6th Cir. 1984), a case that involved a challenge to FDA's decision to approve the use of D&C Green No. 5, which contains a carcinogenic chemical but has itself not been shown to cause cancer. Relying heavily on the reasoning in the agency's decision to list this color additive, the U.S. Court of Appeals for the Sixth Circuit rejected the challenge to FDA's action and affirmed the listing regulation.

II. Safety of Petitioned Use of the Food Additives

FDA estimates that the petitioned use of the polyurethane resins will result in extremely low levels of exposure to these additives. The agency has calculated the estimated daily intake of the migrants from the additives (polyurethane oligomers and cylic polytetramethylene ether glycol oligomers) under the most severe conditions of the intended use of the additives and the probable concentrations of the migrants in the daily diet from the additives' use in contact with food. The agency estimated the potential daily intakes of the polyurethane oligomers and the cyclic polytetramethylene ether glycol oligomers to be 27 nanograms per person per day and 99 nanograms per person per day, respectively.

FDA does not ordinarily consider chronic toxicological testing to be necessary to determine the safety of an additive whose use will result in such low exposure levels (Refs. 1 and 2) and the agency has not required such testing here. However, the agency has reviewed available data from acute and subacute oral toxicity data in rats. Based on the very low level of exposure to the migrants from the use of these additives and the available toxicity data, the agency concludes that the food contact use of the additives is safe under the proposed conditions of use.

Because polyurethane resins, which may contain MDA, have not been shown to cause cancer, the Delaney anticancer provision of section 409(c)(3)(A) of the act does not apply to them. FDA, therefore, has evaluated the safety of these additives under the general safety clause, considering all available data and using risk assessment procedures to estimate the upper-bound limit of risk presented by the carcinogenic impurity MDA, which may be present in the additives. Based on this evaluation, the agency has concluded that the polyurethane resins are safe under the proposed conditions of use.

The risk assessment procedures that FDA used in this evaluation are similar to the methods that it has used to examine the risk associated with the presence of minor carcinogenic impurities in various other food and color additives that contain carcinogenic impurities (see e.g., 49 FR 13018 at 13019, April 2, 1984). The risk evaluation of the carcinogenic impurity, MDA, has two aspects: (1) Assessment of the worst-case exposure to the impurity from the proposed use of the additives; and (2) extrapolation of the risk observed in the animal bioassays to the conditions of probable exposure to humans.

A. Methylenedianiline (MDA)

Based on the fraction of the daily diet that may be in contact with surfaces containing the polyurethane resins, and on the level of MDA resulting from the hydrolysis of MDI in the resins, FDA estimated the worst-case exposure to MDA from the use of the additive to be 20 picograms (pg) per person per day (Ref. 3). The agency used data in a National Toxicological Program technical report (No. 248; 1983) on a carcinogenesis bioassay on MDA (also referred to as 4,4'-diphenylmethane-diamine in this bioassay) to estimate the upper-bound limit of lifetime human risk stemming from the proposed use of the additives (Ref. 4). The results of the bioassay on MDA demonstrated that MDA was carcinogenic for rats and mice of both sexes. The test material caused a significantly increased incidence of follicular cell tumors of the thyroid in male rats, hepatocellular carcinomas in mice, follicular cell carcinomas in mice and female rats, pheocytochromo-cytomas in male mice, malignant lymphomas in female rats, and neoplastic nodules in the liver of male rats. In addition, several rare tumors (bile duct adenoma in male rats, and ovarian granulosa-cell tumors and urinary bladder transitional cell papillomas in female rats) were observed in this study.

The Center for Food Safety and Applied Nutrition's Cancer Assessment Committee reviewed this bioassay and other relevant data available in the literature and concluded that the findings of carcinogenicity were supported by this information on MDA. The Quantitative Risk Assessment Committee of the Center for Food Safety and Applied Nutrition further concluded that an estimate of the upper-bound human risk from exposure to MDA stemming from the proposed use of the polyurethane resins could be calculated from the MDA bioassay.

The agency used a quantitative risk assessment procedure (linear proportional model) to extrapolate from the dose used in the animal study to the very low doses encountered under the proposed conditions of use of the polyurethane resins. This procedure is not likely to underestimate the actual risk from very low doses and may, in fact, exaggerate it because the extrapolation models used are designed to estimate the maximum risk consistent with the data. For this reason, the estimate can be used with confidence to determine to a reasonable certainty whether any harm will result from the proposed conditions and levels of use of the food additive.

Based on a worst-case exposure of less than 20 pg per person per day, FDA estimates that the upper-bound limit of individual lifetime risk from potential exposure to MDA from the proposed use of the polyurethane resins is 1.6×10^{-11}, or less than 1.6 in 100 billion (Ref. 5). Because of the numerous conservatisms in the exposure estimate, actual lifetime averaged individual exposure to MDA is expected to be substantially less than the estimated daily intake, and therefore, the calculated upper-bound risk would be less. Thus, the agency concludes that there is a reasonable certainty of no harm from exposure to MDA that might result from the proposed use of the polyurethane resins.

B. Need for Specifications

The agency has also considered whether a specification is necessary to control the amount of MDA in the polyurethane resins. The agency finds that specifications are not necessary for the following reasons: (1) Because of the low level at which MDA may be expected to remain as an impurity following production of the additives, the agency would not expect MDA to become a component of food at other than extremely small levels; and (2) the upper-bound limit of lifetime risk from exposure to this impurity, even under worst-case assumptions, is very low, less than 1.6 in 100 billion.

III. Conclusion on Safety

FDA has evaluated data in the petition and other relevant material. The agency concludes that the proposed use of the polyurethane resins as rubber articles intended for repeated use in

contact with food is safe. Based on this information the agency has also concluded that the additives will have their intended technical effect, and, therefore, that § 177.2600 should be amended in paragraph (c)(4) as set forth below.

In accordance with § 171.1(h) (21 CFR 171.1(h)), the petition and the documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Food Safety and Applied Nutrition (address above) by appointment with the information contact person listed above. As provided in 21 CFR 171.1(h), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

IV. Environmental Impact

The agency has carefully considered the potential environmental effects of this action. FDA has concluded that the action will not have a significant impact on the human environment, and that an environmental impact statement is not required. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m, Monday through Friday.

V. Objections

Any person who will be adversely affected by this regulation may at any time on or before February 27, 1992 file with the Dockets Management Branch (address above) written objections thereto. Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents shall be submitted and shall be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

VI. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Carr, G. M., "Carcinogen Testing Programs," in "Food Safety: Where are We?," Committee on Agriculture, Nutrition, and Forestry, U.S. Senate, p. 59, July 1979.

2. Kokoski, C. J., "Regulatory Food Additive Toxicology," *Chemical Safety Regulation and Compliance*, edited by Homburger F., J. K. Marquis, and S. Karger, New York, NY, pp. 24–33, 1985.

3. Memorandum dated February 2, 1990, from the Food and Color Additives Review Section (HFF–415) to the Indirect Additives Branch (HFF–335), FAP OB4182—Dow DuPont, and B. F. Goodrich—Exposure to methylenedianiline.

4. Carcinogenesis bioassay of 4,4'-methylenedianiline dihydrochloride (CAS Reg. No. 1355–44–8) in F344/N Rats an $B6C3F_1$, Mice, National Toxicology Program Technical Report Series, No. NTP TR248, 1983.

5. Memorandum dated April 1, 1991, from the Quantitative Risk Assessment Committee; Upper-Bound Lifetime Risk for Methylenedianiline (MDA) in Polyurethane Resins Used as Rubber Articles, FAP OB4182 (Dow, DuPont, and B. F. Goodrich).

List of Subjects in 21 CFR Part 177

Food additives, Food packaging.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 177 is amended as follows:

PART 177—INDIRECT FOOD ADDITIVES: POLYMERS

1. The authority citation for 21 CFR part 177 continues to read as follows:

Authority: Secs. 201, 402, 409, 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 342, 348, 376).

2. Section 177.2600 is amended in paragraph (c)(4)(i) by alphabetically adding a new entry to read as follows:

§ 177.2600 Rubber articles intended for repeated use.

* * * * *

(c) * * *

(4) * * *

(i) * * *

Polyurethane resins (CAS Reg. Nos. 37383–28–1 or 9018–04–6) derived from the reaction of diphenylmethane diisocyanate with 1,4-butanediol and polytetramethylene ether glycol.

* * * * *

Dated: January 21, 1992.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 92–1986 Filed 1–27–92; 8:45 am]

BILLING CODE 4160–01–M

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21 CFR Part 720

[Docket No. 89P–0180]

Modification in Voluntary Filing of Cosmetic Product Ingredient and Cosmetic Raw Material Composition Statements

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is modifying the program it maintains for cosmetic companies to voluntarily file cosmetic product formulations and raw material compositions. FDA is eliminating the reporting of semiquantitative ingredient information, integrating information on raw materials into cosmetic product formulation statements, and discontinuing the forms for reporting raw material compositions. This action responds to a citizen petition filed by the Cosmetic, Toiletry and Fragrance Association (CTFA). The changes that are being made in the regulations are expected to facilitate participation in the cosmetic filing program.

EFFECTIVE DATE: Effective January 28, 1992.

FOR FURTHER INFORMATION CONTACT: Mary W. Lipien, Center for Food Safety and Applied Nutrition (HFF–444), Food and Drug Administration, 200 C Street SW., Washington, DC 20204, 202–245–1707.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 25, 1990 (55 FR 42993), FDA proposed to modify the program for voluntary filing of cosmetic product formulations and raw material compositions by eliminating the reporting of semiquantitative ingredient information (Forms FDA 2512 and 2512a), integrating raw material composition disclosures into cosmetic product formulation statements and discontinuing the forms for reporting raw material compositions (Forms FDA 2513 and 2513a). The proposal was in response to a citizen petition filed by the CTFA. FDA also proposed clarifying changes to update and to remove references from its regulations that would be obsolete if the proposal