DOCUMENT NUMBER: 21739001

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those service bulletins after September 10, 1990 (the effective date of AD 90-16-04, Amendment 39-6613), whichever occurs later, inspect for cracks in accordance with those service bulletins. Repeat these inspections thereafter at the intervals specified in the service bulletins listed in Table 2.1 of the SARD, Revision A or Revision B.

(1) If any crack is found as a result of any inspection, prior to further flight, either accomplish the terminating modification in accordance with the applicable service bulletin, or repair in accordance with a method approved by the Manager, Los Angeles Aircraft Certification Office (ACO), FAA, Transport Airplane Directorate.

Note 3: Detection of any discrepancies other than cracking necessitates appropriate corrective action in accordance with the provisions of Part 43 of the Federal Aviation Regulations (FAR).

(2) Modification in accordance with paragraph (b) of this AD terminates the individual inspection requirements of the applicable service bulletin.

(b) For service bulletins other than those identified in paragraph (c) of this AD, prior to reaching the incorporation thresholds listed in the SARD, Revision A or Revision B, or prior to four years after September 10, 1990, whichever occurs later, accomplish the structural modifications specified in the service bulletins listed under "S/B No. Rev." in Table 2.1 of the SARD, Revision A or Revision B.

Note 4: The service bulletin revision levels listed under "Recommended Modification" in Table 2.1 of the SARD, Revision B, are acceptable revisions for modifications accomplished prior to September 10, 1990.

Note 5: The modifications required by this paragraph do not terminate the inspection requirements of any other AD unless that AD specifies that any such modification constitutes terminating action for the inspection requirements.

(c) For McDonnell Douglas Service Bulletins A30-37, 30-38, 53-16, 53-19, 53-25, 54-11, 54-27, 54-33, 55-2, and 57-7, listed in Table 2.1 of the SARD, Revision A; and for McDonnell Douglas Service Bulletins A30-37, 30-38, 53-16, 53-19, 53-25, 54-11, 54-27, 55-2, and 57-7, listed in Table 2.1 of the SARD, Revision B: Within the threshold for inspections listed under "S/B Change Required" in Table 2.1 of the SARD, Revision A or Revision B, or within one repetitive inspection period specified under "S/B Change Required" in Table 2.1 of the SARD, Revision A or Revision B, after September 10, 1990, whichever occurs later, inspect for cracks in accordance with a method approved by the Manager, Los Angeles Aircraft Certification Office (ACO), FAA, Transport Airplane Directorate. Repeat these inspections thereafter at the intervals specified under "S/B Change Required" in Table 2.1 of the SARD, Revision A or Revision B.

(1) If any crack is found during any inspection, prior to further flight, either accomplish the terminating modification in accordance with the applicable service bulletin, or repair in accordance with a method approved by the Manager, Los Angeles Aircraft Certification Office (ACO), FAA, Transport Airplane Directorate.

(2) Modification in accordance with paragraph (d) of this AD terminates the individual inspection requirements of the applicable service bulletin.

(d) Prior to four years after September 10, 1990, accomplish the structural modifications stipulated in the service bulletins specified in paragraph (c) of this AD.

(e) Within the threshold for inspections specified in the service bulletins listed in Table 2.2 of the SARD, Revision B, or within one repetitive inspection period specified in those service bulletins after the effective date of this AD, whichever occurs later, inspect for cracks in accordance with those service bulletins. Repeat these inspections thereafter at the intervals specified in the service bulletins listed in Table 2.2 of the SARD, Revision B.

(1) If any crack is found during any inspection, prior to further flight, either accomplish the terminating modification in accordance with the applicable service bulletin, or repair in accordance with a method approved by the Manager, Los Angeles Aircraft Certification Office (ACO), FAA, Transport Airplane Directorate.

(2) Modification in accordance with paragraph (f) of this AD terminates the individual inspection requirements of the applicable service bulletin.

(f) Prior to reaching the incorporation thresholds listed in the SARD, Revision B, or within four years after the effective date of this AD, whichever occurs later, accomplish the structural modifications specified in the service bulletins listed in Table 2.2 of the SARD, Revision B.

Note 6: The service bulletin revision levels listed under "Recommended Modification" in Table 2.2 of the SARD, Revision B, are acceptable revisions for modifications accomplished prior to the effective date of this AD.

Note 7: The modifications required by this paragraph do not terminate the inspection requirements of any other AD unless that AD specifies that any such modification constitutes terminating action for the inspection requirements.

(g) An alternative method of compliance or adjustment of the compliance time that provides an acceptable level of safety may be used if approved by the Manager, Los Angeles Aircraft Certification Office (ACO), FAA, Transport Airplane Directorate. Operators shall submit their requests through an appropriate FAA Principal Maintenance Inspector, who may add comments and then send it to the Manager, Los Angeles ACO.

Note 8: Information concerning the existence of approved alternative methods of compliance with this AD, if any, may be obtained from the Los Angeles ACO.

(h) Special flight permits may be issued in accordance with FAR 21.197 and 21.199 to operate the airplane to a location where the requirements of this AD can be accomplished.

Issued in Renton, Washington, on October 5, 1993.

Suzanne Stevens,

Acting Manager, Transport Airplane Directorate, Aircraft Certification Service.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 5, 25, 170, 171, and 174

[Docket No. 92N-0181]

RIN 0905-AD86

Food Additives; Threshold of Regulation for Substances Used in Food-Contact Articles

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to establish a process for determining when the likelihood or extent of migration to food of a substance used in a food-contact article is so trivial as not to require regulation of the substance as a food additive. Under this process, information about the proposed use of a substance will undergo an abbreviated review by FDA, as opposed to the extensive review and formal issuance of a regulation normally required for food additives. In this document, FDA is proposing the criteria that it will use as part of this review in deciding whether to regulate the use of a substance as a food additive, as well as identifying the types of data that it will need to make this determination.

DATES: Written comments by December 13, 1993.

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

FOR FURTHER INFORMATION CONTACT: Edward J. Machuga, Center for Food Safety and Applied Nutrition (HFS-216), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-254-9528.

SUPPLEMENTARY INFORMATION:

I. Background

In 1958, Congress amended the Federal Food, Drug, and Cosmetic Act (the act) to require premarket approval of food additives (sections 201(s), 402(a)(2)(C), and 409 (21 U.S.C. 321(s),

342(a)(2)(C), and 348)). A "food additive," as defined in section 201(s) of the act, is:

> * * * any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; * * *), if such substance is not generally recognized, among experts qualified by scientific training or experience to evaluate its safety, as having been adequately shown through scientific procedures * * * to be safe under the conditions of its intended use * * *.

Under section 409(a) of the act, the use of a food additive is deemed unsafe unless it either conforms to the terms of a regulation prescribing its use or to an exemption for investigational use. Consequently, the safety of the substance under its intended conditions of use must be demonstrated, and a food additive regulation issued, before the substance can be used in food. Petitions submitted to establish that a use of a food additive is safe ordinarily contain or reference data from toxicological studies that demonstrate to a reasonable certainty that there will be no harm resulting from the specific use of the subject additive. In this regard, petitions must include information that will enable FDA to estimate the dietary concentration resulting from the intended use of the substance. They also address the potential for an environmental impact resulting from the manufacture, use, and disposal of the proposed food additive.

A strict interpretation of the definition of "food additive" would make all substances that migrate, or may be expected to migrate, from food-contact materials into food subject to premarket approval as food additives. However, agency personnel, in response to inquiries from manufacturers of food-contact articles, have stated that certain specific uses of substances in food-contact materials did not require regulation under the food additive provisions. Based on these responses, food additive petitions have not been submitted for use of substances that were expected to result in very low levels of migration and that did not raise any safety concerns. However, this system has never been formalized.

In addition to submitting requests for exemptions from the food additive regulations for specific uses of specific substances, representatives of the food-packaging and food-processing industries have suggested that FDA establish a threshold of regulation policy for such substances. For example, the Society of Plastics Industries submitted a citizen petition (Docket No. 77-0122) requesting that FDA modify § 170.3(e) (21 CFR 170.3(e)), the regulation that defines "food additive," so that the use of a substance that does not result in detectable levels of migration into food-simulating solvents (using validated analytical methods sensitive to at least 50 parts per billion (ppb)) would be exempt from regulation as a food additive unless there was scientific evidence to indicate that the substance presents a significant risk of harm to human health. However, FDA has been reluctant to adopt these or any other proposals in the absence of data clearly showing that substances present in the daily diet at concentrations at or below the proposed threshold level would not pose safety concerns.

A Federal court also has addressed the issue of whether the use of a food-contact material involving insignificant migration into food can be exempted from the food additive regulations. In *Monsanto* v. *Kennedy*, 613 F. 2d 947 (D.C. Cir. 1979)), the Monsanto Co. contended that no migration of acrylonitrile copolymer resulted from the use of their beverage bottles that contained the substance, and that, therefore, the bottles did not have to be regulated as food additives. In its decision, the court stated that the Commissioner of Food and Drugs may determine that the level of migration into food of a particular substance is so negligible as to present no public health concerns and, in such cases, may decline to define the substance as a food additive even though it comes within the strictly literal terms of the statutory definition of a food additive (see 613 F. 2d at 955). The court also stated that the Commissioner has the discretion to decline to exercise this exemption authority (id. at 956).

The agency recognizes that, historically, a number of companies have made their own determination that a particular substance effectively does not migrate to food and thus is not a food additive under its conditions of use. They have marketed the products without recourse to the regulatory process. Nothing in the regulatory scheme presented in this proposed rule would prevent a company from making its own determination that a particular use of a substance does not meet the definition of a food additive. However, as always, the company makes such a determination at its own risk. If the agency learns of the use of a substance from, for example, a competitor and reaches a different conclusion than the company, the agency may take regulatory action against the substance as an unsafe food additive or against the company that makes the substance for introducing an adulterated food into interstate commerce. Therefore, in cases where it is not clear whether the use of a food-contact article would meet the food additive definition, FDA recommends that manufacturers seek a determination under the procedures that FDA is proposing to avoid the possibility of regulatory action.

II. Need for a Threshold of Regulation for Substances Used in Food-Contact Articles

The existing informal practice of determining by letter when a petition is needed for a particular use of a substance presents several problems. While agency personnel have been issuing these letters over the past three decades, the analytical methods used to detect migration into food from indirect food additives, such as packaging materials, have become capable of detecting and measuring much smaller quantities. As a result, many of the food-contact uses for which no migration into food was detectable using older analytical methodologies, may now be shown to result in measurable levels of migration. Therefore, the basis for some letters issued for use of a food-contact material showing "no detectable migration" may no longer be valid. This practice, however, provides no mechanism by which the informal opinions rendered by agency employees can be updated to reflect scientific developments.

A second problem with these opinion letters is that scientific laws of diffusion predict that any two substances that are in contact with one another will tend to diffuse into each other (Ref. 1). As a result, even if migration cannot be detected, it is still likely to be occurring at some level below the detection limit. Therefore, one could argue that all food-contact uses may reasonably be expected to result in migration of the food-contact material into food.

A third problem with the current practice is that because the criteria for data needed to evaluate such requests have never been published, the quality of the requests submitted to FDA for review varies considerably. In many cases, the original submission does not contain adequate data, and FDA has to request additional data to complete the review. As a result, many of these requests for informal opinions have to be reviewed several times. These multiple reviews compete for the resources necessary to review food additive petitions.

of toxicological oral feeding studies, it is possible to predict the likely range of toxic potency for an unstudied compound based on an analysis of the toxic potencies of a large number of representative compounds. Analysis of the data on 18,000 acute oral feeding studies in rats and mice found that all of the acute toxic effects occurred above 1,000 ppb (Ref. 4). Because of the large number and wide variety of chemicals used in this analysis, it is representative of the substances used in the manufacture of food-contact articles. Therefore, this analysis can be used to predict the upper-bound dietary concentration at which an unstudied chemical (i.e., one that has not been the subject of toxicological feeding studies) is unlikely to cause acute toxic effects.

The agency also considered the toxic effects that result from chronic exposure to chemical substances. The results of 2-year chronic oral feeding studies on 220 compounds have shown that only 5 of the 220 chemicals exhibited toxic effects below 1,000 ppb. All 5 of the chemicals that were toxic at levels below 1,000 ppb were pesticides, compounds that would, based on their pesticidal activity, be expected to be more toxic than most substances (Ref. 5). However, even among these 5 pesticides, none exhibited toxic effects at dietary concentrations below 100 ppb.

Based on the results of these analyses, the agency believes that it is reasonable to expect that the noncarcinogenic toxic effects caused by the majority of unstudied compounds would be unlikely to occur below 1,000 ppb. To provide an adequate safety margin, however, the dietary concentration chosen as a level that presents no regulatory concern should be well below 1,000 ppb. Therefore, FDA is proposing in § 170.39(a)(2)(i) to establish a dietary concentration of 0.5 ppb as the threshold of regulation for substances used in food-contact articles. A 0.5 ppb threshold is 2,000 times lower than the dietary concentration at which the vast majority of studied compounds are likely to cause noncarcinogenic toxic effects and 200 times lower than the chronic exposure level at which potent pesticides induce toxic effects. FDA believes that these safety margins, which are larger than the 100 fold safety factor that is typically used in applying animal experimentation data to humans (21 CFR 170.22), support a conclusion that substances consumed in dietary concentrations at or below 0.5 ppb are not of regulatory concern. FDA considered the following additional factors in reaching its tentative decision to establish a 0.5 ppb dietary concentration level as the threshold of regulation:

(1) Because it is possible that a substance that has not been tested for carcinogenicity may later be found to be a carcinogen, FDA also has evaluated the likelihood of carcinogenic toxic effects associated with substances present in the diet at 0.5 ppb or less. FDA used potency data on a large number of known carcinogens to estimate the likely risk that could be expected if an unstudied compound were later found to be a carcinogen. These data were obtained from a carcinogenic potency data base, compiled by Gold et al. (Refs. 6 through 8), that included data on more than 3,500 long-term chronic animal studies of 975 chemicals. FDA restricted its analysis to the 477 animal carcinogens that were the subject of oral feeding studies showing a statistically significant increase in the incidence of animals with specific neoplasms ($p<0.01$) (Ref. 9).

FDA limited its analysis to oral feeding studies because the route of exposure to food additives is by ingestion. FDA further restricted its analysis to the 477 animal carcinogens that were the subject of oral feeding studies showing a statistically significant increase in the incidence of animals with specific neoplasms ($p<0.01$) to ensure that it considered only the most reliable studies. In those cases where multiple studies had been carried out on a specific chemical, the carcinogenic potency chosen represented the most sensitive species/sex/organ combination. Finally, in assessing the appropriate dietary concentration level to use as the threshold of regulation level, FDA has assumed that the distribution of carcinogenic potencies of the 477 chemicals studied is representative of all known and unknown carcinogens, and that it is very unlikely that an unstudied compound would both be a carcinogen and have an intrinsic carcinogenic potency far greater than the typical potency observed for the studied compounds.

Based on the range of potencies exhibited by these 477 animal carcinogens, FDA has determined that most known carcinogens pose less than one in a million lifetime risk if present in the daily diet at 0.5 ppb (Ref. 9). Therefore, FDA tentatively finds that establishing a 0.5 ppb dietary concentration level as the "threshold of regulation" for food-contact articles would result in negligible risk, even in the event that a substance that is exempted from regulation as a food additive were later shown to be a carcinogen.

(2) FDA also tentatively concludes that establishing a 0.5 ppb dietary concentration level as the threshold of regulation is appropriate because it corresponds to a migration level that is above the detection limit for many of the analytical methods used to quantify migrants from food-contact materials. Thus, decisions will usually be made based on dietary concentrations that result from measurable migration into food or food-simulating solvents rather than on worst-case estimates of dietary concentration based on the detection limits of the methods used in the analysis. For example, assuming a consumption factor[1] of 5 percent (the minimum value used by FDA in the absence of specific market volume data), a dietary concentration of 0.5 ppb corresponds to a migration level of 10 ppb. Although detection limits can vary considerably, the analytical methods used to detect migration of food-contact materials can seldom reliably quantify migrants below 1 to 2 ppb.

(3) FDA tentatively concludes that exempting from regulation as food additives those food-contact materials whose use results in dietary concentrations of 0.5 ppb or less is also consistent with the latitude given to FDA in the *Monsanto* v. *Kennedy* decision. The court ruled that in order for the "component" element of the food additive definition in section 201(s) of the act to be met, FDA would have to determine (with a fair degree of confidence) that a substance migrates into food in more than insignificant amounts. The court further stated that "* * * the Commissioner may determine, based on the evidence before him, that the level of migration into food of a particular substance is so negligible as to present no public health or safety concerns * * *." This authority derives from the administrative discretion, inherent in the statutory scheme, to deal appropriately with de minimis[2] situations.

Based on the study of the toxicological effects of a large number of chemicals that is discussed above, FDA tentatively concludes that the presence of a substance in the daily diet at or below 0.5 ppb is so negligible as to present no public health concerns. Therefore, FDA is proposing to adopt

[1] The consumption factor for a food packaging material is that fraction of food in the diet that could be in contact with this material.

[2] This doctrine is expressed in Latin as de minimis non curat lex (the law does not concern itself with trifles).

this level as the threshold of regulation in § 170.39.

Known or suspected carcinogens would be excluded from review under the proposed regulation because the use of carcinogens as food additives is prohibited by the Delaney Clause (section 409(c)(3)(A) of the act). However, in *Scott* v. *FDA*, 728 F. 2d 322 (6th Cir. 1984), the court stated that a food 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 if there is reasonable certainty that no harm will result from the use of the substance.

FDA has used risk assessment procedures to determine under what conditions a substance containing a carcinogenic impurity could be used in a food-contact article and pose no safety concerns. A widely used measure of a carcinogenic response in the scientific literature is the so-called "TD_{50}," that is, the feeding dose that causes cancer in 50 percent of test animals. FDA has calculated a theoretical TD_{50} threshold at which carcinogenic impurities would present less than a one in a million risk, a level of risk generally considered to be very low, when present in the diet at 0.5 ppb. In using these risk assessment procedures, FDA assumed a linear relationship between the feeding dose and the carcinogenic response. Based on a linear dose/response relationship, FDA determined that carcinogenic impurities that cause cancer in 50 percent of test animals at feeding levels above 6.25 milligrams (mg) per kilogram (kg) bodyweight per day (i.e., TD_{50} values above 6.25 mg/kg bodyweight/day) will pose less than a one in a million hypothetical upper-bound lifetime risk if present in the daily diet at levels of 0.5 ppb (Ref. 10). If a chemical with a TD_{50} value above 6.25 mg/kg bodyweight/day is present as an impurity in a substance that is exempted from regulation because its dietary concentration is 0.5 ppb or less, the level of the chemical in the diet as a result of the use of the exempted substance would obviously be considerably less than 0.5 ppb. Therefore, the hypothetical upper-bound lifetime risk of cancer from an impurity that is carcinogenic and that has a TD_{50} value greater than 6.25 mg/kg bodyweight/day would be expected to be well below one in a million and to pose effectively no safety concern.

Based on this risk assessment, FDA proposes to limit its review under proposed § 170.39 to those substances that have not been shown to be carcinogens and that do not contain carcinogenic impurities, unless the impurity has a TD_{50} value of more than 6.25 mg/kg bodyweight/day (proposed § 170.39(a)(1)).

FDA's tentative decision to only review substances known to contain carcinogenic impurities under the proposed regulation if the carcinogenic impurity is shown to have a TD_{50} value greater than 6.25 mg/kg bodyweight/day is conservative. However, FDA tentatively concludes that such conservatism is appropriate because of the limited showing that need be made for such substances. It will only be necessary to show that based on results reported in the scientific literature or on results of a chronic feeding study that has been previously reviewed by the agency, the TD_{50} value for the impurity exceeds the specified level. If such a showing is made, that is the end of the inquiry about the impurity. This approach is in marked contrast to FDA's review of petitions for food additives that appear to contain a carcinogenic impurity. In such cases, the agency carries out an in-depth review of the data to determine whether the impurity should be classified as a carcinogen. If FDA concludes that the impurity is a carcinogen, the agency uses risk assessment procedures to determine whether there is reasonable certainty that no harm will result from the use of the food additive containing the impurity. The quantitative risk assessment carried out by the agency is based on the cumulative dietary exposure to the carcinogenic impurity resulting from the intended use of the food additive under review and from other regulated uses of the additive. The carcinogenic potency used in the risk assessment is that estimated by the agency based on a thorough review of the data available on the carcinogenic impurity.

B. Selection of a Threshold of Regulation for the Use of Direct Food Additives in Food-contact Articles

As mentioned above, FDA has tentatively concluded that there are certain limited types of situations in which the use of a substance in a food-contact article that would result in a dietary concentration greater than 0.5 ppb should still qualify for an exemption from regulation as an indirect food additive. If a substance that is currently regulated for direct addition to food is intended to be used in a food-contact article, and if the dietary concentration of the substance resulting from the proposed indirect use is very small compared to the acceptable daily intake (ADI) for the substance based on data in FDA's files, the agency will consider granting an exemption from regulation for this use of the substance even if the dietary concentration will exceed 0.5 ppb. Because these substances will have already been the subject of acceptable safety studies that have established the level of use of the substance that is safe, FDA believes that the threshold for such substances can be established based not on a specific level of dietary concentration but on a specific percentage of the ADI, that is, 1 percent or less of the ADI for the substance (proposed § 170.39(a)(2)(ii)). This level of exposure would contribute only a small fraction of the ADI of a substance and would be well within the margin of safety for those direct food additives with small cumulative dietary exposures. For substances with high cumulative dietary exposures resulting from currently regulated direct food additive uses, a level of exposure that is 1 percent of the ADI would be within the margin of error for the estimated daily intake, which invariably is based on one or more worst-case assumptions, and would, therefore, not significantly affect the cumulative dietary exposure, even in the event that a particular substance has been granted exemptions for several different types of uses in food-contact articles.

IV. Process for Evaluating Requests for Exemption From Regulation as a Food Additive

FDA proposes to establish the following criteria to evaluate requests to exempt substances from regulation as food additives:

1. The substance must not have been shown to be a carcinogen in humans or animals and must not contain a carcinogenic impurity with a TD_{50} value of less than 6.25 mg/kg bodyweight/day, and there must be no reason, based on the chemical structure of the substance, to suspect that the substance is a carcinogen (proposed § 170.39(a)(1)). Known carcinogens would be excluded from review under the proposed regulation because the use of carcinogens as food additives is prohibited by the Delaney Clause (section 409(c)(3)(A) of the act).

2. The substance must: (a) Not migrate, and not be expected to migrate, into food at levels that result in dietary concentrations that are above 0.5 ppb, corresponding to dietary exposures above 1.5 micrograms/person/day (based on a diet of 1,500 grams of solid food and 1,500 grams of liquid food per

person per day)[3], and, therefore, not pose a public health or safety concern;

(b) be currently regulated for direct addition into food and be used in a manner that would result in exposure levels that are less than 1 percent of the ADI as determined by safety data in FDA files (proposed § 170.39(a)(2)).

3. The substance must have no technical effect in or on the food to which it migrates (proposed § 170.39(a)(3)). FDA tentatively finds that there is no basis on which to exempt a substance that is added directly or indirectly to food at a level at which it has a technical effect in that food.

4. The use of the substance must not have a significant adverse impact on the environment (proposed § 170.39(a)(4)).

To have the use of a substance in a food-contact article reviewed under this proposed regulation, a company would submit its request to the Division of Petition Control (HFS–216), Food and Drug Administration, 200 C St. SW., Washington, DC 20204 (proposed § 170.39(d)).

The agency recognizes that it is impossible to foresee all of the safety issues that may be revealed by scientific information not presently available. Therefore, in proposed § 170.39(b), FDA is reserving the right to decline to grant an exemption in any case where available information suggests that the proposed use of the substance may pose a public health risk.

Listed below is the information that FDA will need to determine whether an exemption is appropriate (proposed § 170.39(c)):

1. Information on the chemical composition of the substance (proposed § 170.39(c)(1)). This information is necessary to enable FDA to confirm the identity of the substance.

2. Detailed information on the conditions of use of the substance (e.g., temperature, types of food with which the substance will come into contact and the duration of the contact, repeat versus single use) (proposed § 170.39(c)(2)). Consistent with the legislative history of the Food Additives Amendment (S. Rept. 2422, 85th Cong. 2d sess. 2–3(1958)), any exemption for a specific substance issued under the proposed regulation will be for a specific use.

3. A clear statement of the basis for the request for exemption from regulation as a food additive (i.e., whether the use of the substance in the food-contact article results in a dietary concentration at or below 0.5 ppb, or whether it involves the use of a regulated direct food additive where the dietary exposure is less than 1 percent of the ADI) (proposed § 170.39(c)(3)).

4. Data that will enable FDA to estimate the daily dietary concentration resulting from the proposed use of the substance (proposed § 170.39(c)(4)). These data should be either in the form of: (a) Validated migration data obtained under worst-case (time/temperature) intended use conditions utilizing appropriate food-simulating solvents; (b) amounts of the substances used in the manufacture of the food-contact article; or (c) residual levels of the substances present in the food-contact article. For repeat-use articles, an estimate of the amount of food contacting a specific unit of surface area over the lifetime of the article should also be provided. In cases where data are provided only in the form of manufacturing use levels or residual levels of the substance present in the food-contact article, FDA will calculate a worst-case dietary concentration level assuming 100 percent migration. A detailed description of the analytical method used to quantify the substance should also be submitted along with data used to validate the detection limit.

In cases where there is no detectable migration into food or food simulants, or when no residual level of a substance is detected in the food-contact article by a suitable analytical method, FDA intends, for the purposes of estimating the dietary concentration, to consider the validated detection limit of the method used to analyze for the substance.

Interested persons are encouraged to obtain guidance from FDA on the appropriate protocols to be used for obtaining extraction data on the validation of the analytical methods used to quantify migration levels and on the procedures used to relate migration data to dietary exposures.

5. A literature search for toxicological data on the substance and its impurities (proposed § 170.39(c)(5)). This search is necessary to show whether an animal carcinogen bioassay has been carried out, or whether there is some other basis for suspecting that the substance is a carcinogen or a potent toxin.

6. Information on the environmental impact resulting from the proposed use of the substance (proposed § 170.39(c)(6)). Under the National Environmental Policy Act, FDA must consider the environmental effect of its actions, including each proposed action to exempt a component of a food-contact article from regulation as a food additive and include those considerations in its decisionmaking. This information should be in the form of an abbreviated environmental assessment as specified in § 25.31a (b)(1) or (b)(2) (21 CFR 25.31a (b)(1) or (b)(2)).

Upon completion of its review, FDA will inform the requestor by letter whether it is exempting the specific food-contact article from regulation as a food additive (proposed § 170.39(e)). FDA is proposing that these letters be issued by either the Director of FDA's Center for Food Safety and Applied Nutrition (CFSAN), the Director of CFSAN'S Office of Premarket Approval, or by the Directors of CFSAN's Divisions of Petition Control and Product Policy (proposed § 5.61(h)). FDA is proposing this delegation of authority because it expects a significant number of such requests, and officials other than the Commissioner should be able to respond to these to ensure the appropriate functioning of this system. Moreover, the determination will generally be based on a straightforward determination as to whether the threshold level is exceeded or not. Thus, delegation to officials other than the Commissioner is appropriate. If the request for an exemption from regulation as a food additive is not granted, the requestor may submit a petition to FDA for reconsideration of the decision in accordance with 21 CFR 10.33 *Administrative reconsideration of action* (proposed § 170.39(f)).

Although the uses of substances exempted under the proposed regulation will not be the subject of a regulation published in the **Federal Register** and will not appear in the **Code of Federal Regulations**, FDA is proposing that it will maintain a list of these exempted substances on display at the Dockets Management Branch (address above) (proposed § 170.39(e)). This list will include the name of the company that made the request, the chemical name of the exempted substance, the specific use for which it has been exempted, and any appropriate limitations. It will not include any trade names.

The agency's determination as to whether a substance used in a food-contact article meets the criteria established in the proposed regulation (§ 170.39) for an exemption from regulation as a food additive will be binding on the agency. Thus, manufacturers of food-contact articles can rely on these determinations and market their products without fear of regulatory action. However, if the

[3] A detailed description of FDA's method for calculating dietary exposure is included in "Recommendations for Chemistry Data for Indirect Food Additive Petitions" and can be obtained from the Division of Petition Control, Center for Food Safety and Applied Nutrition, Food and Drug Administration, Washington, DC 20204.

agency receives significant new information that raises questions about the dietary concentration level or the safety of a food-contact use of a substance that it has exempted from regulation, the agency may reconsider its decision (proposed § 170.39(g)). If FDA concludes that the available information no longer supports an exemption of the use of a food-contact material from the food additive regulations, the agency will notify the original requestor of its tentative decision. The requestor will be given an opportunity to show why regulation of the use of the substance as a food additive is not appropriate. If the requestor fails to adequately respond to the new evidence, the agency will advise the requestor that further use of the substance in question for the particular use will require a food additive regulation. This notification will be placed on public display at the Dockets Management Branch along with the file of those uses of substances exempted from regulation as food additives.

Because substances exempted from regulation as indirect food additives under the proposed regulation (§ 170.39) will not be required to undergo premarket approval through the submission of a food additive petition, FDA proposes to amend 21 CFR part 171 (proposed § 171.8) and 21 CFR part 174 (proposed § 174.6) to provide appropriate cross references to the proposed rule establishing a threshold of regulation for substances used in food-contact articles. FDA is also proposing to modify § 170.3(e) *Definitions* by adding new § 170.3(e)(2) to indicate that those food additives exempted from regulation under proposed § 170.39 will not be required to undergo premarket approval via the food additive petition process (21 CFR 171.1).

V. Economic Impact

FDA has examined the economic implications of the proposed rule establishing a threshold of regulation level for components of food-contact articles as required by Executive Order 12291 and the Regulatory Flexibility Act. Executive Order 12291 compels agencies to use cost-benefit analysis when making decisions. The Regulatory Flexibility Act requires regulatory relief for small businesses where feasible. The agency finds that this proposed rule is not a major rule as defined by Executive Order 12291. In accordance with the Regulatory Flexibility Act (Pub. L. 96–354), FDA has also determined that this proposed rule will not have a significant adverse impact on a substantial number of small businesses.

The compliance cost to firms resulting from the proposed rule is zero, because no current activity is prohibited. Total costs are also zero because no increase in the health risks faced by consumers will result from this proposed rule. Benefits consist of agency resources saved by eliminating the need to consider food additive petitions for food-contact articles in cases involving trivial levels of migration from food-contact articles into food. Resources saved by eliminating this activity may be applied to the review of food additive petitions for food-contact articles in cases where significant migration into food may occur. By reducing the time required for the review of these petitions, the return to private investment in developing safe food-contact articles will be increased. This will lead to the more rapid development and utilization of these products. Because costs are zero and benefits are positive, net benefits will occur.

VI. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(8) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Under the National Environmental Policy Act, FDA must consider the environmental effect of its actions and include these considerations in its decisionmaking. This requirement extends to consideration of whether to exempt a component of a food-contact article from regulation as a food additive. The agency believes that almost all of the substances that would be reviewed under the proposed regulation will be minor components of finished food-packaging material that are present at less than 5-percent-by-weight or that will be used as components of food-contact surfaces of permanent or semipermanent equipment or of other food-contact articles intended for repeated use. The approval of a food additive petition for such substances would qualify for an abbreviated environmental assessment under § 25.31a(b)(1) and (b)(2). Because the environmental information needed for such substances is the same whether or not the substances are regulated as food additives, the agency is proposing to amend 21 CFR part 25 to require an abbreviated environmental assessment for substances that are considered for exemption from regulation as a food additive.

VII. Paperwork Reduction Act

This proposed rule contains information collections which are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1980 (44 U.S.C. 3507). Therefore, in accordance with 5 CFR part 1320, the title, description, and respondent description of the proposed collection of information requirements are shown below with an estimate of the annual collection and information burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering necessary information, and completion and submission of the request.

Title: Food additives; threshold of regulation for substances used in food-contact articles.

Description: FDA is proposing a regulation for determining when the likelihood/extent of migration of a component of a food-contact article is so trivial as not to require regulation as a food additive. A substance considered under this proposed rule would undergo an abbreviated review by FDA, as opposed to the extensive review and formal issuance of a regulation required for other food additives. The agency is proposing to establish § 170.39 as the procedural regulation for these types of reviews. This proposed regulation lists the criteria that must be met for a food-contact material to be reviewed under this policy and identifies the types of data that FDA will need for its review. A substance determined by FDA to be below the threshold of regulation would be exempt from regulation as a food additive and, therefore, would not require the submission of a food additive petition.

Description of Respondents: Businesses or other for-profit organizations.

ESTIMATED ANNUAL REPORTING AND RECORDKEEPING BURDEN

Section	Annual number of respondents	Annual frequency	Average burden per response	Annual burden hours
170.39	60	1	88	5,280
Total				5,280

Although requests submitted for review under the proposed regulation require an average burden of approximately 88 person hours, there will be a significant decrease in overall burden for those components of food-contact articles that are exempted by this expedited process but that previously would have required premarket approval via the food additive petition process. (Petitions on these types of issues can require 270 person hours to prepare and cost anywhere from $85,000 to $100,000.) There would also be a significant decrease in burden to FDA because these types of petitions typically require 250 to 500 person hours to review as compared to the 8 person hours that would be required to review a request under the proposed regulation.

In order to determine whether the proposed regulation (21 CFR 170.39) will significantly reduce the amount of resources that will need to be expended on indirect food additives, FDA analyzed the dietary concentration levels of substances that were the subject of indirect food additive petitions submitted over the last 5 years to determine what percent of these petitions would not have been submitted had the proposed provision been in place. Adhesive petitions seeking to amend 21 CFR 175.105 were not included because such uses involve the presence of a functional barrier between the adhesive component and food, and these petitions do not ordinarily contain migration data. FDA's analysis showed that 22 of the 163 petitions, or 13.5 percent involved dietary concentrations at or below 0.5 ppb and, they would have qualified for the exemption. These results suggest that there will be a significant savings in resources to both FDA and industry if this regulation is adopted.

The agency has submitted copies of the proposed rule to OMB for its review of these recordkeeping requirements. Interested persons are requested to send comments regarding this estimated burden, including suggestions for reducing this burden to FDA's Docket Management Branch (address above), and to the Office of Information and Regulatory Affairs, OMB, rm. 3208, New Executive Office Bldg., Washington, DC 20503, Attn: Desk Officer for FDA.

VIII. Request for Comments

FDA invites public comment on all aspects of the agency's proposed regulations and is particularly requesting comments on the following:

1. The 0.5-ppb dietary concentration level that the agency proposes to establish as the threshold of regulation for those substances used in food-contact articles that are not currently regulated for direct addition into food and the 1 percent of the ADI threshold level proposed for regulated direct food additives.

2. The types of information that FDA should make publicly available regarding decisions made under this policy. FDA believes that it is essential that decisions made under this policy be made available to the public to the greatest extent possible. However, FDA recognizes its obligation to protect trade secret information and is interested in comments on how best to inform the public while protecting proprietary information.

Interested persons may, on or before December 13, 1993, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

IX. 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. Briston, J. H., and L. L. Katan, "Plastics in Contact With Food," Food Trade Press Ltd., pp. 432–438, 1974.

2. FDA, "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food," p. 10, 1982.

3. Munro, I., "Safety Assessment Procedures for Indirect Food Additives: An Overview," *Regulatory Toxicology and Pharmacology*, vol. 12, pp. 2–12, 1990.

4. Rulis, A., "Establishing a Threshold of Regulation" in "Risk Assessment in Setting National Priorities," Edited by Bonin, J., and D. Stevenson, Plenum Publishing Corp., pp. 271–278, 1989.

5. Frawley, J. P., "Scientific Evidence and Common Sense as a Basis for Food-Packaging Regulations," *Food and Cosmetic Toxicology*, vol. 5, pp. 293–308, 1967.

6. Gold, L. S. et al., "A Carcinogenesis Potency Database of the Standardized Results of Animal Bioassays," *Environmental Health Perspectives*, vol. 58, pp. 9–319, 1984.

7. Gold, L. S. et al., "Chronological Supplement to the Carcinogenic Potency Database: Standardized Results of Animal Bioassays Published Through December 1982," *Environmental Health Perspectives*, vol. 67, pp. 161–200, 1986.

8. Gold, L. S. et al., "Second Chronological Supplement to the Carcinogenic Potency Database: Standardized Results of Animal Bioassays Published Through December 1984 and by the National Toxicology Program through May 1986," *Environmental Health Perspectives*, vol. 74, pp. 237–329, 1987.

9. Rulis, A., "Threshold of Regulation: Options for Handling Minimal Risk Situations," in "Food Safety Assessment," Edited by Finley, J. W., S. F. Robinson, and D. J. Armstrong, American Chemical Society Symposium Series 484, pp. 132–139, 1992.

10. Machuga, E., "Review of Substances Containing Carcinogenic Impurities Under the Proposed Threshold of Regulation Policy," Memorandum for the File, December 14, 1992.

List of Subjects

21 CFR Part 5

Authority delegations (Government agencies), Imports, Organization and functions (Government agencies).

21 CFR Part 25

Environmental impact statements, Foreign relations, Reporting and recordkeeping requirements.

21 CFR Part 170

Administrative practice and procedure, Food additives, Reporting and recordkeeping requirements.

21 CFR Part 171

Administrative practice and procedure, Food additives.

21 CFR Part 174

Food additives, Food packaging.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 5, 25, 170, 171, and 174 be amended as follows:

PART 5—DELEGATIONS OF AUTHORITY AND ORGANIZATION

1. The authority citation for 21 CFR part 5 continues to read as follows:

Authority: 5 U.S.C. 504, 552, App. 2; 7 U.S.C. 138a, 2271; 15 U.S.C. 638, 1261–1282, 3701–3711a; secs. 2–12 of the Fair Packaging and Labeling Act (15 U.S.C. 1451–1461); 21 U.S.C. 41–50, 61–63, 141–149, 467f, 679(b), 801–886, 1031–1309; secs. 201–903 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321–394); 35 U.S.C. 156; secs. 301, 302, 303, 307, 310, 311, 351, 352, 361, 362, 1701–1706, 2101 of the Public Health Service Act (42 U.S.C. 241, 242, 242a, 242l, 242n, 243, 262, 263, 264, 265, 300u-300u-5, 300aa-1); 42 U.S.C. 1395y, 3246b, 4332, 4831(a), 10007–10008; E.O. 11490, 11921, and 12591.

2. Section 5.61 is amended by adding new paragraph (h) to read as follows:

§ 5.61 Food standards, food additives, generally recognized as safe (GRAS) substances, and color additives.

* * * * *

(h) The following officials are authorized to issue letters concerning substances determined to be below the threshold of regulation under § 170.39 of this chapter:

(1) The Director, Center for Food Safety and Applied Nutrition (CFSAN).

(2) The Director, Office of Premarket Approval, CFSAN.

(3) The Directors of the Divisions of Petition Control and Product Policy, Office of Premarket Approval, CFSAN.

PART 25—ENVIRONMENTAL IMPACT CONSIDERATIONS

3. The authority citation for 21 CFR part 25 continues to read as follows:

Authority: Secs. 201–903 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321–393); secs. 351, 354–361 of the Public Health Service Act (42 U.S.C. 262, 263b-264); 42 U.S.C. 4321, 4332; 40 CFR parts 1500–1508; E.O. 11514 as amended by E.O. 11991; E.O. 12114.

4. Section 25.22 is amended by revising paragraph (a)(10) to read as follows:

§ 25.22 Actions requiring preparation of an environmental assessment.

* * * * *

(a)(10) Approval of food and color additive petitions, approval of requests for exemptions for investigational use of food additives, and granting of requests for exemption from regulation as a food additive.

* * * * *

5. Section 25.31a is amended by revising the introductory text of paragraphs (a), (b)(1), and (b)(2) to read as follows:

§ 25.31a Environmental assessment for proposed approvals of FDA-regulated products-Format 1.

(a) For proposed actions to approve food or color additives, drugs, biological products, animal drugs, and class III medical devices, for proposed actions to affirm food substances as generally recognized as safe (GRAS), and for proposed actions to grant requests for exemption from regulation as a food additive, the applicant or petitioner shall prepare an environmental assessment in the following format:

* * * * *

(b)(1) For actions (either to approve food additive petitions or to grant requests for exemption from regulation as a food additive) concerning components of food-contact articles present in the finished food-packaging material at a level not greater than 5-percent-by-weight, the following information is required for the format items specified:

* * * * *

(b)(2) For actions (either to approve food additive petitions or to grant requests for exemption from regulation as a food additive) concerning components of food-contact articles to be used in surfaces of permanent or semipermanent equipment or of other food-contact articles intended for repeated use, the following information is required for the items specified:

* * * * *

PART 170—FOOD ADDITIVES

6. The authority citation for 21 CFR part 170 continues to read as follows:

Authority: Secs. 201, 401, 402, 408, 409, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 341, 342, 346a, 348, 371).

7. Section 170.3 is amended by redesignating paragraph (e) as (e)(1) and by adding new paragraph (e)(2) to read as follows:

§ 170.3 Definitions.

* * * * *

(e)(2) *Uses of food additives not requiring a listing regulation.* Substances used in food-contact articles (e.g., food-packaging and food-processing equipment) that migrate or may be expected to migrate into food at such negligible levels that they have been exempted from regulation as food additives under § 170.39.

* * * * *

8. New § 170.39 is added to subpart B to read as follows:

§ 170.39 Threshold of regulation for substances used in food-contact articles.

(a) A substance used in a food-contact article (e.g., food-packaging or food-processing equipment) that migrates, or that may be expected to migrate, into food will be exempted from regulation as a food additive because it becomes a component of food at levels that are below the threshold of regulation if:

(1) The substance has not been shown to be a carcinogen in humans or animals, does not contain a carcinogenic impurity or, if it does, does not contain a carcinogenic impurity with a TD_{50} value based on chronic feeding studies reported in the scientific literature, or otherwise available to the Food and Drug Administration, of less than 6.25 milligrams per kilogram bodyweight per day, and there is no reason, based on the chemical structure of the substance, to suspect that the substance is a carcinogen. (The TD_{50}, for the purposes of this regulation, is the feeding dose that causes cancer in 50 percent of the test animals. If more than one TD_{50} value has been reported in the scientific literature for a substance, the Food and Drug Administration will use the lowest TD_{50} value in its review.);

(2) The substance presents no other health or safety concerns because:

(i) The use in question has been shown to result in or may be expected to result in dietary concentrations at or below 0.5 parts per billion, corresponding to dietary exposure levels at or below 1.5 micrograms/person/day (based on a diet of 1,500 grams of solid food and 1,500 grams of liquid food per person per day); or

(ii) The substance is currently regulated for direct addition into food, and the dietary exposure to the substance resulting from the proposed use is less than 1 percent of the acceptable daily intake as determined by safety data in the Food and Drug Administration files;

(3) The substance has no technical effect in or on the food to which it migrates; and

(4) The substance use has no significant adverse impact on the environment.

(b) Notwithstanding paragraph (a) of this section, the Food and Drug Administration reserves the right to decline to grant an exemption in those cases in which available information establishes that the proposed use may pose a public health risk. The reasons

or the agency's decision to decline to grant an exemption will be explained in the Food and Drug Administration's response to the requestor.

(c) A request for the Food and Drug Administration to exempt a use of a substance from regulation as a food additive shall include the following information:

(1) The chemical composition of the substance for which the request is made;

(2) Detailed information on the conditions of use of the substance (e.g., temperature, type of food with which the substance will come into contact, the duration of the contact, and whether the food-contact article will be for repeated or single use applications);

(3) A clear statement as to whether the request for exemption from regulation as a food additive is based on the fact that the use of the substance in the food-contact article results in a dietary concentration at or below 0.5 ppb, or on the fact that it involves the use of a regulated direct food additive for which the dietary exposure is less than 1 percent of the acceptable dietary intake;

(4) Data that will enable the Food and Drug Administration to estimate the daily dietary concentration resulting from the proposed use of the substance. These data should be either in the form of:

(i) Validated migration data obtained under worst-case (time/temperature) intended use conditions utilizing appropriate food-simulating solvents;

(ii) Levels of the substances used in the manufacture of the food-contact article; or

(iii) Residual levels of the substances present in the food-contact article. For repeat-use articles, an estimate of the amount of food that contacts a specific unit of surface area over the lifetime of the article should also be provided. (In cases where data are provided only in the form of manufacturing use levels or residual levels of the substance present in the food-contact article, the Food and Drug Administration will calculate a worst-case dietary concentration level assuming 100 percent migration.) A detailed description of the analytical method used to quantify the substance should also be submitted along with data used to validate the detection limit.

(iv) In cases where there is no detectable migration into food or food stimulants, or when no residual level of a substance is detected in the food-contact article by a suitable analytical method, the Food and Drug Administration will, for the purposes of estimating the dietary concentration, consider the validated detection limit of the method used to analyze for the substance.

(v) Interested persons are encouraged to obtain guidance from the Food and Drug Administration on the appropriate protocols to be used for obtaining extraction data, on the validation of the analytical methods used to quantify migration levels, and on the procedures used to relate migration data to dietary exposures;

(5) The existing toxicological data on the substance and its impurities; and

(6) Information on the environmental impact that would result from the proposed use of the substance. Depending on the type of use, this information should be in the form of an abbreviated environmental assessment as specified in § 25.31a(b)(1) or (b)(2) of this chapter.

(d) Data to be reviewed under this section as well as any requests for guidance, shall be submitted to the Division of Petition Control (HFS–216), Food and Drug Administration, 200 C St. SW., Washington, DC 20204.

(e) The Food and Drug Administration will inform the requestor by letter whether the specific food-contact application is exempt from regulation as a food additive or not. Although a substance that migrates to food at a level that results in a dietary concentration at or below the threshold of regulation will not be the subject of a regulation published in the **Federal Register** and will not appear in the Code of Federal Regulations, the Food and Drug Administration will maintain a list of substances exempted from regulation as food additives under this regulation at the Dockets Management Branch. This list will include the name of the company that made the request, the chemical name of the substance, the specific use for which it has received an exemption from regulation as a food additive, and any appropriate limitations on its use. The list will not include any trade names. This list will enable interested persons to see the types of uses of food-contact materials being exempted under the regulation. The agency's finding of no significant environmental impact and the evidence supporting that finding, contained in an environmental assessment, also will be available for public inspection at the Dockets Management Branch in accordance with § 25.41(b)(2) of this chapter.

(f) If the request for an exemption from regulation as a food additive is not granted, the requestor may submit a petition to the Food and Drug Administration for reconsideration of the decision in accordance with the provisions of § 10.33 of this chapter.

(g) If the Food and Drug Administration receives significant new information that raises questions about the dietary concentration or the safety of a substance that the agency has exempted from regulation, the Food and Drug Administration may reconsider its decision. If the Food and Drug Administration concludes that the available information no longer supports an exemption of the use of the food-contact material from the food additive regulations, the agency will notify the original requestor of its tentative decision. The requestor will be given an opportunity to show why regulation of the use of the substance as a food additive is not appropriate. If the requestor fails to adequately respond to the new evidence, the agency will advise the requestor that further use of the substance in question for the particular use will require a food additive regulation. This notification will be placed on public display at the Dockets Management Branch along with the file of those uses of substances exempted from regulation as food additives.

PART 171—FOOD ADDITIVE PETITIONS

9. The authority citation for 21 CFR part 171 continues to read as follows:

Authority: Secs. 201, 402, 409, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 342, 348, 371).

10. New § 171.8 is added to subpart A to read as follows:

§ 171.8 Threshold of regulation for substances used in food-contact articles.

Substances used in food-contact articles (e.g., food-packaging or food-processing equipment) that migrate or that may be expected to migrate into food at negligible levels may be reviewed under § 170.39 of this chapter. The Food and Drug Administration will exempt substances whose uses it determines meet the criteria in § 170.39 of this chapter from regulation as food additives and, therefore, a food additive petition will not be required for the exempted uses.

PART 174—INDIRECT FOOD ADDITIVES: GENERAL

11. The authority citation for 21 CFR part 174 continues to read as follows:

Authority: Secs. 201, 402, 409, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 342, 348, 371).

12. New § 174.6 is added to read as follows:

§ 174.6 Threshold of regulation for substances used in food-contact articles.

Substances used in food-contact articles (e.g., food-packaging or food-

processing equipment) that migrate or that may be expected to migrate into food at negligible levels may be reviewed under § 170.39 of this chapter. The Food and Drug Administration will exempt substances whose uses it determines satisfy the criteria in § 170.39 of this chapter from regulation as food additives and, therefore, a food additive petition will not be required for the exempted uses.

David A. Kessler,

Commissioner of Food and Drugs.

Dated: August 30, 1993.

Donna E. Shalala,

Secretary of Health and Human Services.

[FR Doc. 93-24940 Filed 10-8-93; 8:45 am]

BILLING CODE 4160-01-P

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21 CFR Part 814

[Docket No. 93N-0047]

Medical Devices; Temporary Suspension of Approval of a Premarket Approval Application

AGENCY: Food and Drug Administration, HHS.

ACTION: *Proposed rule.*

SUMMARY: The Food and Drug Administration (FDA) is proposing to establish procedures to order the temporary suspension of a premarket approval application (PMA) for a medical device. This action implements a new authority granted to the agency by the Safe Medical Devices Act of 1990 (the SMDA). Under this new authority, if, after providing an opportunity for an informal hearing, FDA determines there is a reasonable probability that continued distribution of the device would cause serious, adverse health consequences or death, the agency shall by order temporarily suspend approval of the PMA and proceed expeditiously to withdraw the PMA.

DATES: Written comments by December 13, 1993. FDA intends that the final rule based on this proposal become effective 30 days after publication in the **Federal Register.**

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

FOR FURTHER INFORMATION CONTACT: Joseph M. Sheehan, Center for Devices and Radiological Health (HFZ-84) Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 301-594-4765.

SUPPLEMENTARY INFORMATION:

I. Legislative History

Section 9 of the SMDA (Pub. L. 101-629) amends section 515(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360e(e)) by adding section 515(e)(3) of the act to give the agency emergency authority to order the temporary suspension of approval of a PMA for a medical device pending the outcome of a proceeding to permanently withdraw the PMA.

The legislative history of the SMDA reflects congressional concern about allowing dangerous devices to remain on the market pending the outcome of the potentially time-consuming, permanent withdrawal proceedings under section 515(e)(1) of the act. (See S. Rept. 513, 101st Cong., 2d sess. 18-19 (1990).) To provide the agency with a quick method of removing dangerous devices from the market pending resolution of permanent withdrawal proceedings, Congress amended section 515(e) of the act to allow FDA to order the temporary suspension of a PMA without having to pursue a parallel proceeding in district court (id.).

Under section 515(e)(3) of the act, if, after providing an opportunity for an informal hearing, FDA determines there is "a reasonable probability" that continued distribution of the device would cause serious, adverse health consequences or death, the agency shall by order temporarily suspend approval of the PMA and proceed expeditiously to withdraw the PMA. The legislative history of section 515(e)(3) of the act states that a "reasonable probability" is "one where it is more likely than not that the event will occur." (id.). FDA emphasizes that the application of section 515(e)(3) of the act does not turn on the probability of whether a particular percentage of devices would cause serious adverse health consequences or death, but rather on the judgment that, if distribution of the devices continues, one or more individual devices would be more likely than not to cause serious adverse health consequences or death.

The legislative history also states that the term "serious, adverse health consequences" means:

> any significant adverse experience attributable to a device, including those which may be either life threatening, or involve permanent or long-term injuries, but excluding those non-life-threatening injuries which are temporary and reasonably reversible. In other words, injuries attributable to a device that are not significant in nature and are treatable and reversible by standard medical techniques, proximate in time to the injury, are not included within the term's definition. (id.)

The legislative history clearly indicates congressional intent that FDA will have "considerable discretion" in determining whether the standard required for the issuance of a temporary suspension order has been met (id.).

Under section 515(e)(3) of the act (21 U.S.C. 360e(e)(3)), before FDA may order the temporary suspension of a PMA, the agency must provide the PMA holder with an opportunity for an "informal hearing." The SMDA does not require FDA to issue regulations to implement the temporary suspension provision of section 515(e)(3) of the act. FDA, however, believes that regulations would serve to define certain terms related to temporary suspensions and establish and clarify the procedures the agency intends to follow in exercising its authority under section 515(e)(3) of the act.

II. Contents of the Proposed Regulation

The proposed regulation amends 21 CFR part 814 by adding § 814.3(k) and (l) to include definitions of the terms "reasonable probability" and "serious, adverse health consequences," respectively. The proposed definitions of these two terms conform to the definitions of these terms in the legislative history.

The proposed regulation also adds § 814.47 Temporary suspension of approval of a PMA. Proposed § 814.47 states the scope of the regulation authorizing FDA to issue an order temporarily suspending approval of a PMA, establishes procedures for issuing a temporary suspension order, and sets out the standard for temporarily suspending approval of a PMA.

Proposed § 814.47(a) describes the scope of this proposed rule. FDA would follow the procedures set out in proposed § 814.47 when the agency believes that there is a reasonable probability that continued distribution of the device would cause serious, adverse health consequences or death.

Proposed § 814.47(b) describes the procedures that FDA would follow in providing the PMA holder with an opportunity for a regulatory hearing before the agency decides whether to issue an order temporarily suspending approval of the PMA.

Under proposed § 814.47(b)(1), if FDA believes that there is a reasonable probability that the continued distribution of a device subject to an approved PMA would cause serious, adverse health consequences or death, FDA may initiate and conduct a regulatory hearing to determine whether to temporarily suspend approval of the PMA. Proposed § 814.47(b)(2) makes clear that any regulatory hearing to