DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

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

[Docket Nos. 77P–0122 and 92N–0181]

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its food additive regulations 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. Although still a ''food additive,'' a substance exempted from regulation under this process will not be required to be the subject of a food additive listing regulation. Under this process, information about the proposed use of the substance will undergo an abbreviated review by FDA, as opposed to the extensive review normally required for food additives. This final rule also lists the criteria that FDA will use in its review in deciding whether it is necessary to regulate the use of a substance as a food additive and identifies the types of data that it will need to make this determination.

EFFECTIVE DATE: August 16, 1995.

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, 202–418–3085.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of October 12, 1993 (58 FR 52719), the agency proposed 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. The proposal was in response to a number of comments from representatives of the food packaging and processing industries suggesting that FDA establish a threshold of regulation policy whereby those substances used in food-contact articles that result in minimal migration into food would be exempt from regulation as food additives.

The proposal also responded to a citizen petition (Docket No. 77P–0122) submitted by the Society of the Plastics Industry, Inc., requesting that FDA modify § 170.3(e) (21 CFR 170.3(e)), the regulation that defines ''food additive,'' to provide 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 is scientific evidence that the substance presents a significant risk of harm to human health.

Traditionally, FDA had been reluctant to adopt any of these suggestions in the absence of data that clearly show that substances present in the daily diet at concentrations at or below the proposed threshold level would not pose safety concerns. However, data on the toxic effects of a large number of representative compounds have become available over the last 5 to 10 years that have made it possible for FDA to evaluate the feasibility of establishing a threshold of regulation for food-contact articles. These data show that noncarcinogenic and carcinogenic toxic effects usually occur within predictable ranges of dietary exposure. They make it possible to identify a specific level of dietary exposure that is well below the range of dietary exposures that typically induce toxic effects and, therefore, that poses only negligible safety concerns. This level can function as the ''threshold of regulation'' for components of food-contact articles.

A Federal court has addressed the issue of whether the use of a food-contact material that results in migration into food at insignificant levels can be exempted from regulation as a food additive. In *Monsanto* v. *Kennedy,* 613 F.2d 947 (D.C. Cir. 1979), the Monsanto Co. contended that no detectable migration of acrylonitrile copolymer resulted from the use of their beverage bottles that contained the substance, and that, therefore, the copolymer did not have to be regulated as a food additive. In its decision, the court stated that the Commissioner of Food and Drugs (the Commissioner) may determine that the level of migration into food of a particular substance is so negligible as to present no public health or safety 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 (613 F.2d at 956). The court also stated that the Commissioner has the discretion not to exercise this exemption authority (id.).

Based on available toxicological data showing that it is feasible to establish a threshold level below which dietary exposures to substances used in food-contact articles are so negligible as to pose no public health or safety concerns, the discretionary authority of the Commissioner to exempt those substances that present no public health concerns from regulation as food additives, and the agency's consideration of the comments that it received on the October 12, 1993, proposal, FDA is amending the food additive regulations 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 that the substance be regulated as a food additive.

As part of this process, the agency is establishing two types of thresholds for the regulation of substances used in food-contact articles. The first type of threshold will exempt from regulation those substances whose use in food-contact articles results in a dietary concentration of the substance of 0.5 ppb or less. The second type of threshold will exempt regulated direct food additives from regulation when used in food-contact articles at levels that result in a dietary exposure of 1 percent or less of the acceptable daily intake (ADI) for the additive.

II. Comments on the Proposed Rule

The agency provided 60 days for comment on the proposed rule. It received two requests from industry for an extension of the comment period. The agency granted a 60-day extension of the comment period to February 11, 1994, in a notice published in the **Federal Register** of December 13, 1993 (58 FR 65139).

FDA received 20 comments from the food packaging industry and trade associations that represent the plastics and paper industries. One of these comments concerned the economic impact of the proposed action. This comment is discussed in section IV of this document. The other issues raised in the comments, and the agency's response to them, are set forth below.

A. The Exemption

Appropriateness of the 0.5 PPB Threshold Level for Components of Food-Contact Articles

1. Eight comments expressed the opinion that the 0.5 ppb threshold is more conservative and restrictive than is necessary to adequately protect the public health. In general, these comments expressed the view that current scientific data support the

establishment of a dietary concentration higher than 0.5 ppb as the threshold.

The agency does not agree that a 0.5 ppb threshold is unduly conservative, especially in light of the fact that a substance being considered for an exemption may not have been the subject of any toxicological testing. As discussed in the proposed rule, carcinogenic toxic effects in test animals typically occur at lower dietary concentrations than the levels at which noncarcinogenic toxic effects occur. Therefore, FDA's goal has been to establish a threshold that is low enough to ensure that even if an unstudied compound that is exempted from regulation is later shown to be a carcinogen, its use would not have represented any more than a negligible risk to the public health.

Although eight comments were received that expressed the opinion that the 0.5 ppb threshold is more conservative and restrictive than is necessary to adequately protect the public health, no data were provided in any of these comments to show that a threshold significantly higher than 0.5 ppb is adequate to ensure that substances present in the diet at or below the threshold would pose only negligible safety concerns. Therefore, as proposed, this final rule establishes 0.5 ppb as the threshold of regulatory concern for substances used in food-contact articles. We will reconsider this threshold if we receive new data that justify a higher level.

2. One comment objected to the agency's apparent use of a 200-fold safety factor when applying to humans the results of studies showing the noncarcinogenic toxic effects observed in animals subjected to chronic chemical exposure. The comment stated that FDA guidelines employ only a 100-fold safety factor. The comment argued that the use of the 100-fold safety factor would allow FDA to establish a threshold of regulatory concern higher than 0.5 ppb.

The agency emphasizes that it did not base its proposed threshold on noncarcinogenic toxic endpoints, and that, therefore, it did not employ the safety factor approach typically used when applying to humans the results of studies showing the noncarcinogenic toxic effects observed in animals subjected to chronic chemical exposure. Because carcinogenic effects typically occur in test animals at lower dietary concentrations than those at which noncarcinogenic toxic effects occur, as stated above, FDA's goal was to establish a threshold that is low enough to ensure that substances that are exempted from regulation under it will pose only negligible safety concerns even if they are ultimately shown to have carcinogenic effects.

Based on its analysis of the carcinogenic potencies of 477 chemicals, and using the assumptions that the distribution of carcinogenic potencies of the 477 chemicals studied are representative of all known and unknown carcinogens, and that it is very unlikely that an unstudied compound would both: (1) Be a carcinogen and (2) have an intrinsic carcinogenic potency far greater than the typical potency observed for the studied compounds, FDA has determined that, if an exempted substance present in the diet at 0.5 ppb were later found to be a carcinogen, the upper-bound lifetime risk resulting from the use of the substance is likely to be below one in a million. This level of risk is generally regarded as very low (i.e., one that poses only negligible safety concerns). Because carcinogenic effects typically occur at lower dietary concentrations than those at which noncarcinogenic toxic effects occur, an 0.5 ppb threshold would ensure that substances that pass under it pose negligible safety concerns from noncarcinogenic toxic effects as well. However, the fact that a 0.5 ppb threshold level happens to be 200, rather than a 100, times lower than the chronic exposure level at which potent pesticides induce noncarcinogenic toxic effects is merely coincidental and does not reflect the agency's reasoning.[1]

3. One comment expressed the opinion that the threshold should have been based on the mean TD_{50}[2] value of the 477 known carcinogens that were the subject of FDA analysis as opposed to the most probable TD_{50} value. This comment stated that the use of a mean TD_{50} would allow FDA to establish a threshold significantly higher than 0.5 ppb.

FDA does not agree that it is appropriate to establish a threshold level based on the mean TD_{50} value of the 477 known carcinogens that were the subject of FDA's analysis because this approach would give inappropriate weight to carcinogens with high TD_{50} values. Because the carcinogenic potency of a substance is inversely related to its TD_{50} value, this approach would give too much emphasis to carcinogens with low potencies. A more meaningful approach to estimating the likelihood that a substance will pose a potential health hazard at a given dietary concentration is to use the potency that it is most likely to have if it were later found to be a carcinogen. Because such an approach would be based on the frequency distribution of the potencies of a large number of carcinogens (i.e., a distribution showing the number of carcinogens whose potencies occur within particular dietary concentration ranges) and would not be based on the magnitude of the potencies themselves, this approach would not give undue weight to carcinogens with low potencies (i.e., high TD_{50} values).

In arriving at a threshold of regulation, FDA's analysis of the potencies of 477 animal carcinogens consisted in part of grouping them by dietary concentration ranges (Ref. 1). The agency plotted the potencies as a probability distribution on a semilogarithmic scale and found that they formed a bell-shaped distribution curve. Using this probability distribution for carcinogenic potencies, FDA determined that most known carcinogens pose less than one in a million upper-bound lifetime risk if present in the daily diet at 0.5 ppb or less.

4. One comment expressed the view that it was unlikely that a given packaging material would be present in the daily diet over the course of a lifetime. It asserted that, therefore, FDA should not have based its threshold on potential lifetime carcinogenic risks.

Because of the changing technology associated with the food-packaging industry, FDA agrees that is not always possible to predict whether a given type of packaging material is likely to be present in the daily diet over the course of a lifetime. However, because many of the substances considered for an exemption from regulation will not have been the subject of any toxicological testing, it is imperative, in establishing a threshold level, to use an approach that is not likely to underestimate the risk associated with the use of such additives. Therefore, the agency used an approach that assumed that a given packaging material would be present in the daily diet for an entire lifetime.

Lifetime upper-bound risks have traditionally been used by FDA to assess the overall safety of packaging materials containing small amounts of carcinogenic impurities, and the agency

[1] The agency typically uses a 100-fold safety factor when applying to humans the results of animal data obtained from long term exposure to a chemical (i.e., 2-year chronic feeding studies). Short term toxicological testing (i.e., 90-day subchronic feeding studies) may not always be long enough to show all of the toxic effects that may be induced by long term exposure to a chemical, and, therefore, in such cases, FDA often uses higher safety factors (1000-fold to 2000-fold).

[2] The TD_{50}, for the purposes of this regulation, is the feeding dose that causes cancer in 50 percent of the test animals when corrected for tumors found in control animals.

believes that it is appropriate to use a similar approach in assessing the likelihood of potential carcinogenic effects associated with substances exempted from regulation. Based on its analysis of the potencies of 477 known carcinogens and the lifetime upper-bound risks that they would pose if present in the daily diet over a lifetime, FDA has determined that a substance present in the daily diet for a lifetime at 0.5 ppb would pose only negligible risk even if it were later shown to be a carcinogen. Because of the conservatisms used by the agency in its approach to determining a threshold level, FDA is confident that an exempted substance present in the daily diet for a lifetime at 0.5 ppb would pose no regulatory concern.

5. Four of the comments recommended that FDA establish a higher threshold for substances that have been shown to be nonmutagenic or to have relatively high LD_{50}[3] values. For example, one comment recommended that for substances that have been shown to be nonmutagenic and to have LD_{50} values greater than 2,000 milligrams per kilogram (mg/kg), the threshold should be raised to 5 ppb.

FDA agrees with these comments that it may be possible to establish separate thresholds for compounds that have been the subject of toxicological tests that show that they are nonmutagenic, or that they have high LD_{50} values. However, a direct correlation will need to be firmly established showing that such compounds, if carcinogenic, are likely to be less potent than those that have been shown to be mutagenic or to have lower LD_{50} values. Such a correlation would provide confirmation that a substance that has been shown to be nonmutagenic or to have a high LD_{50} value poses a significantly lower risk from potential carcinogenic effects when present in the daily diet at the same level than one that has been shown to be mutagenic or to have a low LD_{50} value.

The correlation between mutagenicity or acute toxicity and carcinogenic potency is the subject of ongoing FDA analysis. If the results of FDA's analysis confirm that the likelihood that a substance poses a significant risk from potential carcinogenic effects is significantly lower when that substance has been shown to be nonmutagenic or to have a high LD_{50} value, it may be possible to establish a threshold for such substances that is higher than 0.5 ppb but that still ensures that their use in food-contact articles will pose only negligible health concerns.

6. Three comments suggested that FDA establish a higher threshold for compounds that do not possess structural concerns (i.e., that do not possess structural similarities to known carcinogens).

In general, the principle behind the use of quantitative structure activity relationships is that the analysis of the toxicity of a large number of compounds of known structure enables one to predict the relative toxicity of unstudied compounds based on the degree of similarity in chemical structure to studied compounds. While FDA may use structure activity relationships to ascertain whether there is a basis to suspect that a substance is a carcinogen, knowledge about such relationships is not reliable enough at this time to justify reliance on an analysis of them to establish a higher threshold of regulation for some compounds. The comments did not submit any evidence to support a contrary conclusion.

7. Three comments recommended that the threshold be raised for compounds that have been shown to be noncarcinogenic. For example, one comment recommended that the threshold be raised to 100 ppb for substances that have been shown to be negative in 2-year bioassays.

FDA agrees that it may be possible in the future to establish a threshold higher than 0.5 ppb for substances that have been shown to be noncarcinogenic based on results obtained from appropriate 2-year bioassays. As discussed above, carcinogenic effects in test animals typically occur at lower dietary concentrations than do noncarcinogenic toxic effects. Therefore, FDA proposed to establish 0.5 ppb as the dietary concentration threshold because this level is low enough to preclude the likelihood of all but negligible risk even if an unstudied compound is later shown to be a carcinogen. In the case of noncarcinogens, however, the threshold of regulation could be based solely on the level at, and below which, noncarcinogenic toxic effects are unlikely to occur.

As stated in the proposed rule (58 FR 52719 at 52722), FDA's 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. 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, and that all 5 of these chemicals were pesticides, compounds that are expected to be more toxic than most substances. Even for these five pesticides, none exhibited toxic effects at dietary concentrations below 100 ppb. These results suggest that it may be feasible to establish a separate threshold for substances that have been appropriately tested and found not to be carcinogens. Such a threshold would likely be well below the level at which noncarcinogenic toxic effects are likely to occur but higher than the 0.5 ppb threshold that FDA is establishing to minimize the risk from potential carcinogens. FDA is not establishing a separate threshold for noncarcinogenic substances at this time, however, because the number of chemicals, particularly pesticides, that have been analyzed is not sufficient to ensure that the results of this analysis are representative of substances used in the manufacture of food-contact articles. An analysis of the dietary concentrations at which a large number and a wide variety of potent toxicants, such as pesticides, exhibit noncarcinogenic toxic effects is needed before FDA can determine whether establishment of a threshold significantly higher than 0.5 ppb for noncarcinogenic substances is justified.

Appropriateness of the 1-Percent ADI Threshold for Regulated Direct Additives

8. One comment recommended that once the final rule has been established, and the policy has been put into practice for a time, FDA should reassess the 1 percent of the ADI threshold for regulated direct food additives used in food-contact articles to see whether this threshold can be raised.

As stated in the proposal, a 1-percent ADI threshold for regulated direct food additives used in food-contact articles is appropriate because this level of dietary exposure will contribute only a small fraction of the ADI of a substance and, therefore, will 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 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. It would, therefore, not significantly affect the cumulative dietary exposure, even in the event that a particular substance is granted exemptions for several different types of uses in food-contact articles.

The agency would like to emphasize that no comments were received that expressed any safety concern about the 1 percent of the ADI threshold. As for raising this threshold above the 1-

[3] The LD_{50} is the dose in acute feeding studies that causes lethality in 50 percent of the test animals.

percent ADI level, FDA's main concern is with those cases in which a particular substance may be granted exemptions for a number of different types of new uses, each of which results in a dietary exposure at or near the threshold level. In such cases, the dietary exposure resulting from all of the exempted uses could represent a significant increase in the cumulative dietary exposure for the substance and, in cases where the estimated dietary intake from currently regulated uses is close to the ADI, may not be supported by existing safety data. It is possible, however, that once the threshold of regulation process is put into practice, other factors will surface that mitigate the agency's concerns on this issue. If the latter situation proves to be the case, the agency may find it appropriate to reassess the 1 percent of the ADI threshold for regulated direct food additives used in food-contact articles.

9. One comment recommended that FDA publish or otherwise make available the ADI's for currently regulated direct food additives. In cases where such ADI's are not readily available, FDA should consider other sources (e.g., the European Union's Scientific Committee for Foods) or provide guidelines for the calculation of appropriate ADI's.

FDA agrees that the ADI's for currently regulated direct food additives should be made more readily available. Therefore, FDA plans to incorporate this information into its priority based assessment of food additives (PAFA) data base and make this data base accessible to the public (Ref. 2). In the meantime, requestors can obtain this type of information on a specific substance by submitting a written request to FDA's Office of Premarket Approval (HFS–200, 200 C St. SW., Washington, DC 20204). In some cases, especially for those uses of direct additives that result in low dietary exposures such as flavoring agents, FDA may not have an ADI in its files. Therefore, in those relatively few cases where FDA does not have an appropriate ADI for a regulated direct food additive, the agency would consider the use of an ADI value from another appropriate source, such as the Joint World Health Organization/Food and Agriculture Organization (WHO/FAO), Expert Committee on Food Additives, or the European Union's Scientific Committee for Foods, assuming that the data or other information on which that ADI value is based are also available. FDA is revising proposed § 170.39(a)(2)(ii) to state that FDA may use other appropriate sources for ADI values.

FDA disagrees with the comment's suggestion that the agency provide guidelines for the calculation of appropriate ADI's for review under the process specified in this final rule. Regulated direct food additives for which an appropriate ADI does not exist are not suitable candidates for an abbreviated review under the threshold of regulation process. This process is not appropriate for reviewing submissions containing detailed toxicity studies on a substance for the purpose of calculating an ADI value or for verifying an ADI value calculated by the requestor. Such extensive reviews are better handled by the food additive petition process.

10. One comment recommended that FDA expand the proposed threshold of regulation process for regulated direct food additives to include exemptions for direct uses in food, provided the dietary exposures from such uses do not exceed 1 percent of the ADI. The proposed rule limited such exemptions to only those uses that may result in their indirectly becoming components of food (i.e., resulting from their use in food-contact articles).

FDA does not agree that the final rule should be expanded in this manner. There is a fundamental difference in regulatory significance between substances that are deliberately added directly to food to accomplish a technical effect in the food and substances that are used in food-contact articles in a manner such that they may reasonably be expected to become components of food indirectly and to have no technical effect in that food. The purpose of the food additive provisions of the act is to ensure that substances added to food are safe and will have their intended technical effect in the food that is to be consumed (S. Rept. 2422, 85th Cong., August 18, 1958). Thus, given this purpose, there simply would not be circumstances in which a direct additive would be of such little regulatory concern as to justify application to it of the de minimis[4] doctrine that underlies the threshold of regulation concept (see *Monsanto* v. *Kennedy, supra*). For indirect food additives, in contrast, the substance is being used for its technical effect in a food-contact article, not in an article that will itself be consumed.

Moreover, on occasion, it is foreseeable that, while the exact amount of an indirect additive that will get into food is unclear, it will not exceed an extremely small amount. It is in the latter circumstances that it is fair to say that, given the purposes of the Federal Food, Drug, and Cosmetic Act (the act), the use of the substance is of no significant regulatory concern, and thus the use can be exempted from regulation under the food additive provisions of the act. In light of the purposes of the food additive provisions, however, FDA concludes that it is not appropriate to extend the threshold of regulation concept to substances intended for direct use in food.

11. One comment expressed the opinion that the proposed regulation is unduly restrictive for the use of regulated direct food additives in food-contact articles when the direct additive does not have any specific use level restrictions. An example of the type of situation raised by the comment would be flavoring agents where the level of their use in food would be self limiting (i.e., use at high levels would make the food unpalatable, and, therefore, FDA did not find it necessary to impose specific maximum use levels as part of the regulations authorizing the use of such substances). The comment emphasized that, because of the time required to obtain FDA approval (as a result of FDA's current backlog of work), the consumer's access to new packaging technologies is often delayed. Not requiring premarket approval of such substances would save FDA resources, reduce the backlog of work, and enable the consumer to have quicker access to new packaging formulations.

The comment argued that, based on the extremely small levels of dietary exposure that would result from the use of direct additives in food-contact articles, particularly in comparison to the levels of exposure that result from the direct uses of these substances, and based on the fact that direct food additives have been the subject of extensive safety testing, FDA should modify § 174.5(d) (21 CFR 174.5(d)) to allow those direct food additives that are regulated without specific use level limitations to be used as components of food-contact articles. The comment asserted, however, that four restrictions on such use were appropriate: (1) The use of the substance in a food-contact article must not result in a dietary exposure that exceeds 1 percent of the ADI for that substance; (2) the use level must not exceed good manufacturing practice (GMP) or that necessary to accomplish the intended technical effect; (3) the substance must be of a purity suitable for the intended use; and (4) the technical effect for such additives must be as a formulation aid or some other technical effect for which the substance has been listed as a direct

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

food additive (e.g., a substance approved for use as a stabilizer and thickener in food would be allowed to be used as a stabilizer and thickener in the manufacture of food-contact articles). The comment cited FDA's approach to handling generally recognized as safe (GRAS) substances as a precedent for this approach. Under 21 CFR 186.1(a), ingredients affirmed as GRAS for direct use in part 184 (21 CFR part 184) are also affirmed as GRAS for use as indirect human food ingredients in accordance with § 184.1(a).

The agency notes that the issue raised by this comment is outside the scope of the proposed threshold of regulation process. The comment is about whether the uses in question should be approved as food additive uses, not about whether they should be exempted from regulation under the food additive provisions of the act.

Although outside the scope of this rulemaking, FDA would like to comment on the merits of the approach recommended in this comment because the agency is always interested in evaluating ways that may help it to more effectively implement the food additive provisions of the act. FDA's main concern with the recommended approach is that those direct food additives that are regulated without specific use level limitations, and which meet the other restrictions specified in this comment, could be used as components of food-contact articles without any further safety review by FDA. Although it is true that the dietary exposure resulting from the use of a substance added directly to food is usually much higher than that resulting from the use of that substance as a component of a food-contact article, the existing safety data in FDA files used to support the direct additive use may not always be adequate to support even a modest increase in the dietary exposure resulting from its use as an indirect food additive.

Some direct food additives have been regulated for uses in which only a narrow margin exists between the cumulative estimated dietary exposure and the acceptable dietary exposure. Many other direct additives have been regulated for uses for which, initially, the margin between the estimated daily intake and the ADI was reasonably broad, but as the substance has been subsequently regulated for other uses, the margin has become quite narrow. Because existing safety data may not be adequate to support the use of direct additives as components of food-contact articles in all cases, such uses must be evaluated on a case by case basis, either as the subject of a food additive petition (if the dietary exposure is likely to be greater than 1 percent of the ADI) or as a request for an exemption from regulation (if the dietary exposure is likely to be below the 1-percent ADI threshold of regulatory concern).

Another agency concern with the recommended approach is that some of the direct food additives may also have been regulated at a time when FDA did not conduct reviews on the possible environmental effects resulting from such uses. (FDA regulations for considering the environmental effect of its actions in accordance with the National Environmental Policy Act (NEPA) were established on March 15, 1973.) It may be possible that the manufacture, use, and disposal of food-contact articles containing regulated direct food additives may have an adverse impact on the environment. Therefore, the potential environmental effects resulting from the intended use of a direct food additive in a food-contact article need to be evaluated by FDA either as part of a review of a petition or as part of a review of an exemption from regulation request. Further discussion of this issue is found later in this final rule in the agency's response to comments 28 and 29.

For the reasons listed above, FDA has concluded that the use of a regulated direct food additive in a food-contact article should either be the subject of a specific food additive regulation authorizing such use or be exempted from regulation as a food additive by FDA under the procedures specified in this final rule. Application of the Food Additive Definition

12. Two comments expressed the opinion that the *Monsanto* decision gives FDA the flexibility to consider those substances migrating out of food-contact articles in trivial amounts not to be food additives. These comments went on to say that the Delaney Clause (section 409(c)(3)(A) of the act (21 U.S.C. 348(c)(3)(A)), which prohibits the use of known carcinogens as food additives, would therefore not apply.

FDA disagrees with the comments. It is true that *Monsanto* stated that the Commissioner has discretion to implement the statutory scheme established by the Food Additives Amendment, and that this discretion includes the option of declining to define a substance as a food additive (613 F.2d at 956). However, the court also said that the Commissioner's discretion is limited (id.). The Commissioner's exercise of discretion must be consistent with the statutory scheme. He cannot exercise his discretion to vitiate that scheme. Under the Food Additives Amendment, a carcinogenic additive is deemed to be unsafe, no matter how low the exposure to the additive or how low the risk from the additive (see *Public Citizen* v. *Young*, 831 F.2d 1108, 1122 (D.C. Cir. 1987), cert. denied, 485 U.S. 1006 (1988)). Given these facts, FDA has formulated the threshold of regulation regime to exempt substances from regulation as food additives based on the level of dietary exposure but has conditioned that exemption on such substances not having been shown to be carcinogens. No other approach would be consistent with the act.

13. Three comments recommended that FDA clarify whether companies can make their own threshold of regulation determinations. The comments stated that, in those cases where the use of the substance meets the definition of a ''food additive'' in section 201(s) of the act (21 U.S.C. 321(s)), individual manufacturers should be able to make their own determination as to whether the use of a substance in a food-contact article meets the criteria for an exemption from regulation. One of the comments requested that the agency's position on this issue be explicitly stated in the final regulations.

According to *Monsanto*, only the Commissioner has the statutory authority to exempt a substance from regulation as a food additive. A substance that meets the definition of a food additive in section 201(s) of the act must, therefore, either be the subject of a regulation authorizing its use or be exempted from regulation by FDA under the process specified in new § 170.39, unless the use of the substance conforms to an exemption for investigational use issued under section 409(i) of the act.

From a policy standpoint, the procedure outlined in this final rule, whereby FDA makes all exemption decisions, offers a number of advantages over an approach that allows individual manufacturers to make their own threshold of regulation decisions. One advantage is that the agency's determination as to whether a substance used in a food-contact article meets the criteria for an exemption from regulation as a food additive will be binding on the agency. Thus, manufacturers of food-contact articles will be able to rely on these determinations and market their products without fear of regulatory action.

This approach also will result in more consistent decisions. Qualified experts may disagree on what specific assumptions are appropriate for estimating the dietary concentrations resulting from the use of substances in

food-contact articles. Thus, allowing individual manufacturers to make their own determinations would increase the likelihood of inconsistent decisions.

For example, 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, the validated detection limit of the method used to analyze for the substance would need to be considered in order to estimate the dietary concentration from the intended use. Qualified experts may disagree not only on the specific numeric value for this detection limit but also on what percentage of the detection limit should be used in such situations to estimate actual migration (e.g., 100 percent versus 50 percent). Qualified experts may also disagree on the appropriate consumption factor to use in estimating dietary concentrations. Different conclusions on the environmental effects resulting from the use of a food-contact article may also arise from such independent determinations. The agency believes that having all such exemption decisions made by a review team consisting of a small number of agency personnel will help lessen the likelihood of inconsistent decisions on these matters.

Having such determinations made by FDA will also mean that the agency will have more complete information on what materials industry is actually using in food-contact articles. As a result, FDA will be able to make more informed decisions in the event that data become available that raise significant concerns about whether the continued use of a component of a food-contact article is safe.

Although only the Commissioner of FDA has the statutory authority to exempt a substance from regulation as a food additive in those cases where the use of the substance meets the ''food additive'' definition in section 201(s) of the act, FDA emphasizes that nothing in this final rule limits the use of a substance exempted by FDA from regulation to only the manufacturer who submitted the request for an exemption. Other manufacturers may use exempted substances in food-contact articles as long as the conditions of use (e.g., use levels, temperature, type of food contacted, etc.) are those for which the exemption was issued.

Consistent with this fact, FDA plans to give general notice by means of the **Federal Register**, should it ever decide to revoke an exemption. The notice will state that continued use of such a substance would constitute the use of an unapproved food additive, unless a petition is filed, and the substance is listed for use in FDA's regulations. It will also set out the reasons for FDA's decision to revoke the exemption, thereby providing manufacturers with the opportunity to submit relevant data to the agency and to request that the exemption be reinstated.

FDA does not believe, however, that it would be practical to routinely provide notice in the **Federal Register** of its intent to revoke an exemption. Such a process would only unduly delay and burden the revocation process. It would be inconsistent with the intent of the threshold of regulation process to minimize the use of agency and industry resources for those substances whose use in food-contact articles poses only negligible safety concerns. Accordingly, FDA is revising § 170.39(g) to make clear that the agency plans to provide notice in the **Federal Register** after it has decided to revoke an exemption issued for a specific use of a substance in a food contact article.

FDA has decided, however, not to include in § 170.39 a statement that only the Commissioner can make threshold of regulation determinations. It is not the agency's usual practice to enumerate in its regulations those regulatory decisions that are reserved to the agency. Therefore, the agency is not doing so here.

Scope of the Exemption

14. Two comments recommended that FDA expand its proposed threshold of regulation to enable the agency to exempt entire classes of compounds. Under the scheme suggested by these comments, FDA would review one or more compounds within a given class, and, if it determined that these individual chemicals qualified for an exemption, the agency would exempt all of the chemicals within the class. One of these comments expressed the view that many manufacturers do not use their proprietary chemicals for food-contact applications because of FDA's requirement that they be regulated based on their chemical identity, and that the use of such an approach would remove impediments that stifle innovation in the food industry.

FDA disagrees with this approach for a number of reasons. Because the level of migration, and resulting dietary concentration, of the chemical depend on both its molecular weight and chemical properties, it would be impossible to predict whether the use of all compounds within a class would result in dietary concentrations below the threshold based on the migration properties of just one or two sample chemicals. For example, polymeric materials manufactured from the same monomer but having significantly different molecular weights would belong to the same class of chemicals but would be expected to have different migration properties. Similarly, the intrinsic toxic potencies for chemicals within a certain class may vary significantly. For example, the polychlorinated dibenzo-*p*-dioxins are a class of 75 congeners that exhibits a wide range of toxicity depending on the degree of chlorination and the location of the chlorine atoms within the chemical structure. As a result, the likelihood that a substance poses a health hazard is not necessarily determinable based on the information about the toxicity of other chemicals that are in the same class. In addition, it would be difficult to predict the environmental impact that would result from the manufacture, use, and disposal of all substances within a class based on the impact of one or two chemicals. Therefore, FDA does not believe that it is possible, based on the review of one or more compounds within a given class, to justify an exemption for all other chemicals belonging to the same class.

For the foregoing reasons and because the dietary concentration of a specific chemical is dependent on the conditions of its use (e.g., type of use, temperature, food type, and contact time), FDA concludes that to adequately safeguard the public health, it is necessary to limit exemptions under § 170.39 to those conditions of use of a chemical that it has evaluated.

15. One comment recommended that rather than require a submission for each chemical and each proposed use, FDA should publish guidelines based on categories of uses that would provide performance standards that could be used by manufacturers to guide customers on how to stay below the threshold exposure.

As discussed earlier, the dietary concentration resulting from the use of a substance in a food-contact article may vary considerably depending on the type of use and the conditions of use. Therefore, it would not be feasible to establish guidelines for use with respect to all possible food-contact articles under all possible conditions. Interpretation of such complicated guidelines by individual manufacturers and customers would inevitably lead to confusion and inconsistencies.

The process specified in this final rule, as part of which a small team of agency personnel will review each request for an exemption, will result in more consistent decisions. Having all such determinations made by FDA

using the process specified in the final rule should also result in the agency having more complete information on what substances are being used in food-contact articles. This information will permit the agency to take action in the event that data become available that raise significant questions as to whether the continued use of a substance in a food-contact article is safe.

16. One comment stated that the 0.5 ppb threshold was too low for the use of pigments in food-contact articles because such pigments are less toxic than other chemicals. Because these pigments are relatively insoluble, they would also have lower bioavailability.

FDA does not believe that it is feasible to establish specific thresholds of regulation for each of the many types of chemicals used in food-contact articles. Such an approach, with many different thresholds, would be cumbersome. Moreover, as discussed in a previous comment, the toxicological properties of chemicals within a class can vary greatly. Therefore, it would be extremely difficult to establish a single threshold for all the chemicals within a given class. Because of this difficulty, FDA is not taking any action in response to this comment.

The agency believes that it may be feasible in the future to establish a higher threshold based on a substance's toxicological properties rather than based on its type or on the class of chemicals to which it belongs. For example, as discussed in a previous comment, it may be possible in the future to establish separate thresholds for substances that either have been shown to be noncarcinogenic by appropriate 2-year bioassays or, based on the results of short-term toxicity testing (e.g., mutagenicity and acute oral feeding studies), are likely to have a low carcinogenic potency if they are, in fact, carcinogenic.

17. One comment requested that FDA specifically address whether biocides would be eligible for consideration under the threshold of regulation regime. Because such substances must be registered with the Environmental Protection Agency (EPA) in accordance with the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) (7 U.S.C. 136 *et al.*), and must undergo an extensive review for safety and efficacy, the comment stated that biocides are well suited for an abbreviated review under FDA's threshold of regulation process.

As long as the criteria specified in this final rule are met, FDA will grant exemptions from regulation as food additives for biocides that become components of food-contact articles.

18. Two comments requested that FDA clarify how the presence of a ''barrier'' (one that would limit the migration of a packaging substance into food) would be factored into threshold of regulation decisions. In particular, the comment asked whether, in cases where there is a functional barrier, and no migration can be detected, FDA would still consider the validated detection limit of the method used to analyze for the substance in its dietary exposure estimate.

The key factor in FDA's decision to grant an exemption from regulation for a substance used in a food-contact article is whether the dietary concentration of the substance resulting from its use is below the threshold. Thus, if the presence of a functional barrier limits the migration of the substance into food such that the resulting dietary concentration is below the threshold, FDA will grant an exemption for the intended use of that substance, provided that the other criteria specified in this final rule are met.

In most cases, the effectiveness of a material to act as a barrier to migration will depend not only on the physical and chemical properties of the barrier material and the potential migrant but also on the thickness of the barrier layer and the conditions of use (e.g., temperature, food type, contact time). Therefore, it is usually not possible to draw any conclusions regarding the effectiveness of a barrier material in the absence of migration data. In such cases, requests for exemptions from the food additive regulations would need to contain data showing that the barrier material precludes all but minimal migration of the substance into food (i.e., the resulting dietary concentration is at or below the threshold). FDA will consider the validated detection limit of the method used to analyze for the substance in arriving at its dietary exposure estimate.

There are a number of specific situations, however, where FDA would not require data to show that a barrier material precludes all but minimal migration of the substance into food. For example, some packaging materials such as aluminum foil, when used as the inner layer of laminates, have been generally recognized as being able to provide an effective barrier to migration of the outer layer components into food under a variety of conditions. In such cases, it would not be necessary for the requestor to carry out and submit extraction studies designed to show the effectiveness of the barrier layer. Another example involves those cases in which FDA has reviewed the barrier material and has established specific conditions under which the material would indeed function as a barrier. In these cases, the agency will be able to make decisions on similar constructions in the absence of any additional extraction studies, as long as the conditions of use do not differ significantly from those the agency reviewed.

19. One comment inquired as to whether the final rule establishing a threshold of regulation for substances used in food-contact articles will be applicable to regulated direct animal feed additives that are intended to be used as components of articles that may contact animal feed (i.e., indirect animal feed additives).

This final rule will allow those substances exempted under § 170.39 to be used in articles contacting animal feed as long as the intended conditions of use of the substance are those for which the exemption was issued. This result follows from §§ 174.6 and § 570.14 (21 CFR 570.14) of FDA's regulations. Under § 174.6 *Threshold of regulation for substances used in food-contact articles*, FDA will exempt substances from regulation as food additives whose use in food-contact articles meet the criteria in § 170.39. Authority to use substances exempted under § 174.6 in articles contacting animal feed is set out in § 570.14 *Indirect food additives resulting from packaging materials for animal feed and pet food*, which states that the regulations providing for the use of food-packaging materials in parts 174 through 179 (21 CFR parts 174 through 179) are applicable to packaging materials used in animal feed and pet food.

Moreover, in cases where the exemption request concerns the use of a substance in an article that is used only in contact with animal feed, the criteria used by FDA to determine whether an exemption from regulation is warranted will be those specified in new § 170.39. Because § 570.14 contains a cross-reference that includes § 174.6, in accordance with that provision, FDA can review a request for exemption of a substance used only in contact with animal feed under § 170.39.

Sections 170.39, 174.6, and 570.14, however, will not provide for the use in articles contacting animal feed, at a level that is 1 percent or less of their ADI, of substances that are currently regulated for direct use in animal feed in part 573 (21 CFR part 573). To provide for such a review, FDA will have to adopt a regulation similar to § 170.39 that applies to direct animal feed additives that have not been

regulated for direct addition to human food. However, such a regulation is outside the scope of this rulemaking and would require a separate proceeding.

Application of the Exemption

20. One comment inquired whether exempted substances may be used in contact with all types of food.

Because the dietary concentration resulting from the use of a substance in a food-contact article is dependent on the type of food with which it comes in contact, the use of a substance in an article contacting one type of food may result in a dietary concentration below the threshold, while the use of the same material in contact with another type of food may not. Therefore, FDA will limit exemptions to those conditions of use warranted by the available data.

B. The Regulation

21. One comment recommended that FDA revise the language in § 170.39(a)(1) to make clear whether the phrase ''there is no reason, based on the chemical structure of the substance, to suspect that the substance is a carcinogen'' refers to impurities within the substance or the substance itself.

FDA agrees with this comment and is revising proposed § 170.39(a)(1) to make it clear that the phrase ''there is no reason, based on the chemical structure of the substance, to suspect that the substance is a carcinogen'' refers only to the substance itself.

22. One comment recommended that FDA revise the language in proposed § 170.39(c)(1) to make clear that the description of the chemical composition of the substance for which the request is made should include, whenever possible, the name of the chemical in accordance with current chemical abstracts service (CAS) nomenclature guidelines and a CAS registry number if available.

FDA agrees with this comment and has revised proposed § 170.39(c)(1) accordingly.

23. One comment recommended that the word ''substance'' in proposed § 170.39(c)(4)(ii) and (c)(4)(iii) should refer to the singular case for consistency.

FDA agrees and has made the changes that respond to this comment in this final rule.

24. One comment recommended that the regulation define in detail the types of information required by FDA in submissions requesting exemptions from the food additive regulations.

FDA agrees that a detailed description of the information that needs to be included in a request for an exemption should be readily available to interested parties. However, FDA does not believe that it is necessary or appropriate to include this information in the Code of Federal Regulations (CFR). The agency considers it appropriate to make this information available in a manner similar to that which FDA uses with respect to the contents of food additive petitions. For food additive petitions, FDA generally describes the information that must be submitted in part 171 (21 CFR part 171) of its regulations and maintains more detailed guidelines that are available from the agency upon request. While FDA publishes modifications in the CFR only annually, it can modify guidelines whenever necessary, thereby providing requestors with up-to-date guidance. This flexibility in modifying detailed guidelines is needed to take into account ongoing advances in the development of food-contact articles and in the methodologies used to quantify migration of components of such articles into food.

Therefore, FDA is adding § 170.39(h), which states that guidelines to assist requestors in the preparation of submissions seeking exemptions from the food additive regulations are available from FDA's Office of Premarket Approval (HFS–200), 200 C St. SW., Washington, DC 20204.

Because it is not practical to provide guidelines that would cover all of the possible topics associated with these types of submissions, this final rule encourages interested parties to obtain specific guidance from FDA on the protocols to use in obtaining extraction data, on the validation of the analytical methods used to quantify migration levels, on the procedures to use to relate migration data to dietary exposures, and on any other issue not specifically covered in FDA's guidelines.

FDA formerly proposed to announce the availability of guidelines in § 170.39(c)(4)(v) because the guidelines were meant to focus on questions associated with the dietary concentration resulting from the intended use of a substance in a food-contact article. However, the agency believes it is more appropriate to include such language as part of § 170.39(h) to emphasize that interested parties may seek guidance on any issue involving exemption requests. Therefore, FDA is revising § 170.39 to include this provision and has deleted proposed § 170.39(c)(4)(v).

C. Procedural Issues

Obtaining an Exemption

25. One comment commended FDA for its statement in the preamble that manufacturers may make their own determination as to whether the use of a substance in a food-contact article meets the ''food additive'' definition in section 201(s) of the act and recommended that FDA explicitly state this fact in the final regulation.

In response to this comment, FDA would like to reaffirm its position that nothing in the regulatory scheme presented in this 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'' in section 201(s) of the act. However, as noted in the proposal, companies make such determinations at their 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 meets the ''food additive'' definition, FDA recommends that manufacturers seek a determination under the procedures specified in this rule to avoid the possibility of regulatory action.

FDA does not believe, however, that it is appropriate to address this issue in the regulation. The issue raised by the comment applies generally to FDA's application of the ''food additive'' definition in section 201(s) of the act. This rulemaking concerns only the threshold of regulation process. Therefore, the question of whether, and how, to incorporate into FDA's regulations the statement that the comment seeks is outside the scope of this rulemaking.

26. Seven comments recommended that the agency establish a time limit for reviewing and responding to requests for exemptions from regulation as food additives to ensure timely responses. Two of the comments suggested specific time limits of 60 and 90 days.

The agency agrees that such reviews should be carried out in a timely manner. Timely review will mean that manufacturers and suppliers of substances that are exempted from regulation as food additives will be able to market their products much more quickly than has been the case. Timely review will also mean that manufacturers and suppliers of substances that are not exempted will receive prompt notice of the need to file a food additive petition.

A pilot study carried out by FDA showed that such reviews can usually

be completed within 3 to 4 months as compared to the 1 to 2 years typically required for indirect food additive petitions. The agency is concerned, however, that establishing a formal time limit for completion of such reviews will unduly restrict its ability to allocate its limited resources to projects that may be more critical. Therefore, the agency has decided not to establish a time limit for reviewing and responding to requests for exemptions from regulation as food additives at this time. As the agency gains experience with its threshold of regulation policy, it will consider establishing an appropriate time limit. In the interim, however, the agency is committed to reviewing exemption requests as expeditiously as resources allow.

27. One comment recommended that there be a phase-in process that would allow companies to carefully evaluate products that are on the market and to obtain exemption determinations where, and if, required.

As discussed previously, if the use of a substance results in, or is reasonably expected to result in, migration into food, even at low levels, and is not specifically excluded from the definition of a ''food additive'' in section 201(s) of the act, then the substance is a food additive that must either be the subject of a regulation authorizing its use or be exempted from regulation by FDA under the process specified in this rule. However, if the use of a substance in a food-contact article currently on the market involves low levels of migration into food (i.e., results in a dietary concentration at or below the threshold of regulatory concern), and is the subject of a request for an exemption under the process specified by this final rule, it is unlikely that FDA would take regulatory action during the time needed by the agency to complete its review. Therefore, the agency does not believe it is necessary to establish a phase-in program to allow companies to evaluate food-contact articles currently on the market.

28. One comment recommended that § 170.39 be revised to include an abbreviated review (i.e., one that does not require a review of environmental impact data and toxicological feeding study data) for those exemption requests that deal only with new uses of regulated indirect food additives that involve the same manufacturing process but a different technical effect (e.g., a substance currently regulated as a defoamer in the manufacture of paper and paperboard under § 176.170 that is the subject of an exemption request for its use as a deposit control agent in the manufacture of paper and paperboard).

The agency is currently reevaluating its environmental regulations under NEPA, and is committed to expanding the list of categorical exclusions found in § 25.24 (21 CFR 25.24). However, as indicated earlier, a key factor in FDA's decision to grant an exemption from regulation is whether the substance has a significant impact on the environment. A new use of a regulated indirect food additive that involves the same manufacturing process but a different technical effect may have, as a result of its use or subsequent disposal, a significantly different environmental exposure than any previously regulated use of the substance. Therefore, an abbreviated review (i.e., one that does not include a review of environmental impact data) is not justified for all such substances. Although these types of uses do not currently qualify for a categorical exclusion, some may qualify in the future (the categorical exclusion list is currently under consideration for expansion).

In regard to reducing the requirements for the submission of toxicological feeding studies, FDA emphasizes that § 170.39 requires only that submissions contain the results of an analysis of existing toxicological information on the substance and its impurities. This information is needed 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 potent toxin. FDA also requires this type of information to enable it to determine whether any of the impurities present in the substance have been shown to be carcinogenic, and, if carcinogenic, whether their TD50 value is greater than 6.25 mg/kg bodyweight per day (see § 170.39(a)(1)). To clarify this issue, FDA is revising the language in § 170.39(c)(5) to state that the only toxicological information that must be included in a submission for an exemption from the food additive regulations is an analysis of existing toxicological information on the substance and its impurities.

29. Two comments stated that exempted substances should not be subjected to the environmental impact reviews typically required for food additives. The comments asserted that, instead, exempted substances should come under a newly created ''categorical exclusion'' that would exclude such actions from the requirement that an environmental assessment be prepared.

An FDA decision to exempt a substance from regulation as a food additive is an agency action under the National Environmental Policy Act (NEPA) (42 U.S.C. 4321). Under NEPA, an agency action must include a consideration of the environmental effects resulting from the intended use, unless it is the subject of one of the categorical exclusions listed in 21 CFR 25.24. Actions are made subject to an exclusion either because, as a class, they will not result in the production or distribution of any substance and, therefore, will not result in the introduction of any substance into the environment, or because they meet specific criteria that are intended to ensure they will not cause significant environmental effects. As stated above, the agency is actively examining its categorical exclusion regulations. However, neither of the subject comments provided information to show that as a class, substances used in food-contact articles would not be introduced into the environment or to support the establishment of a new categorical exclusion. The agency welcomes the submission of data and information that would support the establishment of a categorical exclusion for these substances. At this time, however, all requests for threshold of regulation exemptions must include an abbreviated environmental assessment.

Availability of the Information Submitted

30. Six comments were submitted on the general subject of what types of information contained in submissions under § 170.39 should be made publicly available (i.e., on display at the Dockets Management Branch or released in response to requests submitted under the Freedom of Information Act (FOIA) (5 U.S.C. 552)). Three of these comments were quite general, recommending that FDA handle the confidential information contained in such submissions in the same manner that it has traditionally treated other documents submitted. A more specific comment recommended that the information released under FOIA should be consistent with that released from food additive petitions. One comment expressed the opposite viewpoint, stating that exempted substances should not be considered food additives, and that, therefore, the rules governing the release of information submitted on food additives should not apply. This comment also requested that the final regulation include a statement recognizing the possible trade secret status of information submitted in support of an exemption request. Another comment stated that the names of companies receiving exemption letters are trade secret.

As a general matter, the FOIA requires that agencies make the fullest possible disclosure of records to the public. The procedures that FDA uses to handle the release of public information in accordance with FOIA are described in part 20 (21 CFR part 20). Under these procedures, information submitted to FDA, including that submitted on the use of food additives, is made publicly available to the greatest extent possible.

As for substances that become components of food below the threshold that FDA is establishing, they will be exempt from the requirement that their use be the subject of a food additive listing regulation. This exemption, like a listing regulation, allows these substances to be used in food contact articles. Given the similarity in effect between a food additive listing and the grant of an exemption, FDA concludes that it is appropriate for it to make publicly available under § 170.39(e) the same type of information that is releasable on regulated food additives. This information includes the name of the company that sought and received authorization to use the substance.

In response to the request that the final regulation include a statement recognizing the possible trade secret status of information submitted in support of an exemption request, FDA is revising § 170.39(e) to state that the agency will respond to all FOIA requests for information submitted under § 170.39 in accordance with part 20. Thus, data and information that are trade secret or confidential commercial or financial information are not available for public disclosure in accordance with § 20.61(c).

31. One comment stated that information contained in submissions under § 170.39 should not be released in response to FOIA requests.

FDA does not agree with this comment. As discussed in the previous comment, FOIA requires that agencies make the fullest possible disclosure of records to the public. The agency, however, recognizes that it has an obligation to protect trade secret and confidential commercial or financial information as defined in § 20.61(a) and (b). Therefore, FDA will not disclose this type of information.

32. Two comments stated that the chemical identities of exempted substances should not be publicly disclosed. One of these comments stated that such information is trade secret and considered by economists as ''circumstantially relevant business information.'' The comment stated that, if the company requesting an exemption regards this information as trade secret, keeping such information confidential is consistent with controlling case law interpretation of the confidentiality standard that is applied to FDA under *Critical Mass Energy Project* v. *NRC,* 975 F. 2d 871 (D.C. Cir. 1992). This comment also stated that, because these substances are exempt from regulation as food additives, FDA is not under any obligation to disclose their chemical identities. The comment stated that release of proprietary information could force companies to make their own determinations as to whether a food additive regulation is needed. This comment suggested that FDA adopt a system whereby the chemical would be identified only by the general class of chemicals to which it belongs. This comment also pointed out that EPA has used this type of system in Pre-Manufacture Notifications submitted under the Toxic Substances Control Act (40 CFR 720.85). One of these comments raised the possibility that exempted substances could be referred to only by their trade names.

FDA disagrees with the suggestion that exempted substances be referred to only by trade names or by reference to the general class of chemicals to which they belong. Two factors underlie FDA's disagreement. First, the provisions of the act added by the 1958 Food Additives Amendment permit any manufacturer to use any regulated food additive as long as the substance meets all applicable specifications, including those associated with the identity of the additive. Second, as previously discussed, FOIA requires that agencies make the fullest possible disclosure of records to the public. Under the procedures used by FDA to determine the releasability of information under FOIA, the agency has traditionally considered the chemical identity of food additives to be disclosable information, and thus, the regulations implementing the 1958 Food Additives Amendment refer to food additives by their chemical names. Because FDA's approach to exempted substances derives from the food additive provisions of the act, and, as stated above, FDA is acquiescing in the use of the substance, FDA concludes that the chemical identities of exempted substances are disclosable under FOIA.

Critical Mass is not to the contrary. While a company has an alternative to making a submission to FDA under § 170.39 (i.e., filing a food additive petition), and thus, the submission is in a sense voluntary, the key question under *Critical Mass* is whether the information is of a kind that would customarily not be released to the public by the person from whom it was obtained (975 F.2d at 879). As stated above, information about the chemical identity of food additives for which listing is sought is routinely disclosed to the public in the **Federal Register**, pursuant to section 409 of the act. Submitters are well aware of this fact. Thus, FDA finds no merit to the suggestion by the comment that the identity of substances subject to § 170.39 must be kept confidential. To provide differently for substances subject to § 170.39 would be to create a special exemption. Clearly, *Critical Mass* does not require such a result.

From a practical standpoint, chemical nomenclature has typically been used to characterize food additives because chemical names are universally recognized and are not subject to change as trade names often are. Moreover, trade names are often used to refer to formulations in which the chemical composition is held confidential. In such cases, referring to regulated food additives by trade names would make it impossible for other manufacturers to determine whether their chemical substances meet applicable regulations. A similar situation would occur if the list of exempted substances made publicly available did not include the chemical identities of such substances.

Making available the chemical identities of substances exempted from regulation will permit other manufacturers to use these substances as long as the conditions of use are no more likely to result in migration to food than those for which the exemption was originally issued. It will also allow interested persons to determine what substances have been exempted by FDA under the process established by this final rule. FDA believes that, in the interest of open government, it is essential that decisions made under this policy be available to the public. Therefore, for the reasons specified above, FDA will make publicly available the chemical identities of exempted substances.

33. One comment stated that the technical effect or function of the substance should not be made publicly available.

Under the procedures used by FDA to implement FOIA, the agency has not considered information on the technical effect or functionality of a food additive to be trade secret as defined in § 20.61(a) or confidential commercial or financial information as defined in § 20.61(b). Because the dietary exposure resulting from the use of a substance in a food-contact article may vary considerably depending on the technical effect of that additive, it is often necessary to include such information in the regulation authorizing a specific type of use of the food additive in order to restrict the

dietary exposure to levels that can be supported by existing safety data. For example, substances regulated in 21 CFR 178.3400 are restricted to use as emulsifiers and/or surface active agents in the manufacture of articles or as components of articles contacting food. Moreover, the provisions of the act added by the 1958 Food Additives Amendment permit any manufacturer to use any regulated food additive as long as the use of the substance meets all applicable specifications and limitations. Such limitations include those that restrict the use of the additive to a specific technical effect. Therefore, it is often necessary to include this information as part of the conditions of use set forth in the regulation authorizing the use of the additive so that other manufacturers may use the same substance under only those conditions that are safe. In addition to being made available as part of a regulation, the agency has routinely made technical effect information contained in food additive petitions available to the public in response to FOIA requests in accordance with § 171.1(h)(1)(i). Consistent with the explanation above, FDA sees no reason to change this policy with regard to food additives exempted from regulation.

Treatment of the List of Exempted Uses of Substances

34. One comment recommended that in addition to making available a list of exemptions at the Dockets Management Branch, FDA should publish this list in the **Federal Register**.

The public should have ready access to an up-to-date list of those uses of substances that have been exempted from regulation as food additives by FDA. However, maintaining such a list, updated on a regular basis, on display at the Dockets Management Branch, is the most efficient way of achieving this result. FDA anticipates being able to respond to exemption requests within 3 to 4 months. Thus, the list of exempted substances would be continually changing. Monthly updates in the **Federal Register** would be expensive and yearly updates of little value. Therefore, FDA has no plans to publish this list in the **Federal Register**.

However, to ensure that interested persons are aware that FDA is maintaining such a list at its Dockets Management Branch, the agency plans to publish annually a brief notice in the **Federal Register** on the availability of this list. An updated list of exempted substances can also be obtained by contacting FDA's Office of Premarket Approval (address above). FDA is revising § 170.39(e) to reflect this fact.

Revocation

35. One comment recommended that FDA establish timeframes for the revocation process. The comment suggested that the requestor would have 60 days to respond to FDA's tentative decision to revoke an exemption. Once the response is submitted, FDA would have 60 days to reach its final decision.

FDA agrees that in cases in which new information becomes available showing that continued exemption of a substance in a food-contact article from regulation under the food additive provisions cannot be supported in light of existing safety data, the requestor's response to FDA's tentative decision to revoke an exemption, and FDA's subsequent decision, should occur in a timely manner. However, because the complexity of such reviews may vary greatly and require varying amounts of time to complete, FDA does not consider it to be appropriate to establish specific timeframes for such reviews.

III. Other Actions

FDA is revising § 170.39(c) to state that three copies of a request for an exemption from regulation are to be submitted. The agency is requiring three copies to help expedite its review of such requests. To further expedite such reviews, the agency is revising § 170.39(c) to state that if part of the submitted material is in a foreign language, it must be accompanied by an English translation verified to be complete and accurate in accordance with § 10.20(c)(2) (21 CFR 10.20(c)(2)).

IV. Analysis of Impacts

FDA has examined the impacts of this final rule under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96–354). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects; distributive impacts; and equity). Under Executive Order 12866, a regulatory action is economically significant if it meets any one of a number of specified conditions, including having an annual effect on the economy of $100 million or adversely affecting in a material way a sector of the economy, competition, or jobs. A regulation is otherwise considered significant under Executive Order 12866 if it raises novel legal or policy issues. The Regulatory Flexibility Act requires analyzing options for regulatory relief for small businesses. FDA finds that this final rule is not a significant regulatory action as defined by Executive Order 12866. In compliance with the Regulatory Flexibility Act, the agency certifies that this final rule will not have a significant impact on a substantial number of small businesses.

38. One comment suggested that the proposed threshold of regulation process would have an adverse impact on small businesses. FDA disagrees. The regulation that FDA is adopting does not prohibit or restrict any present activity and, therefore, does not generate compliance costs for either large or small firms. In addition, FDA has received no information that the benefits of the proposed action will accrue differentially to large firms. In fact, this approach should minimize the burden on all businesses by providing a procedure that is less burdensome than the food additive petition process. Without this threshold of regulation process, those components of food-contact materials whose use results in low levels of migration into food would require premarket approval through the food additive petition process.

Based on information provided to FDA by representatives of the food packaging and processing industries, the collection of information and preparation of an exemption request for review under the process established by this final rule is estimated to cost anywhere from $1,400 to $25,000 depending on the complexity of the project. If analytical studies are required to be carried out to show that the dietary exposure resulting from the proposed use is below the threshold of regulation, FDA estimates that the additional cost would vary from $10,000 to $50,000 depending on the complexity of the project (e.g., the number of substances or food simulating solvents involved, and the method of analysis). Thus, the agency estimates that the total cost to submit exemption from regulation requests may vary from $1,400 to $75,000.

The time required to prepare such requests would also vary with the type of data needed to estimate the dietary exposure associated with the intended use. A simple request (i.e., one that does not contain any analytical work) would typically contain: (1) Identity and use information; (2) a literature search of the existing toxicological data on the substance and its impurities; and (3) information on the environmental impact resulting from the proposed use of the substance. Based on information provided to FDA by representatives of the food packaging and processing industries, the average time to prepare such requests is estimated to be 68

hours. The average time to prepare requests that include analytical work (e.g., extraction studies carried out using food-simulating solvents, analytical studies to determine the residual level of the substance in the food-contact article) is estimated to be 108 hours.

Although the preparation of requests for exemptions from regulation may cost anywhere from $1,400 to $75,000 and require on average 68 hours to complete (108 hours for submissions requiring analytical data), these estimates demonstrate that there will be a significant decrease in the overall burden to businesses for those components of food-contact articles that are exempted from regulation 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 on average 2,600 hours to prepare and cost anywhere from $85,000 to $100,000.) Whenever possible, FDA will provide assistance to requestors to minimize the likelihood that unnecessary work will be performed. Based on the preceding considerations, FDA finds that the proposed action will not have an adverse impact on small businesses.

In summary, the comments do not provide a basis on which to change the conclusions of the economic analysis prepared for the proposed rule or to establish that another option would provide higher net benefits.

V. Environmental Impact Considerations

The agency has previously reviewed the environmental effects of this rule as announced in the proposal (see 58 FR 52719, October 12, 1993). The agency determined under 21 CFR 25.24(a)(8) that neither an environmental assessment nor an environment impact statement is required. No new information or comments have been received that would affect the agency's previous determination.

The agency is required to consider the environmental impact of each action to exempt a component of a food-contact article from regulation as a food additive. The final rule sets out the type of information that FDA needs to determine the impact on the environment resulting from the intended use. The agency's finding of no significant impact, and the evidence supporting that finding, contained in an environmental assessment, will be made available for public inspection at the Dockets Management Branch (address above) for those substances whose use in food-contact articles has been exempted from regulation by the process established by this rule.

VI. Paperwork Reduction Act

Section 170.39 of this final rule contains information collection requirements that were submitted for review and approval to the Office of Management and Budget (OMB), as required by section 3504(h) of the Paperwork Reduction Act of 1980. The requirements were approved and assigned OMB control number 0910–0298.

VII. Conclusions

Although a number of comments expressed the opinion that the 0.5 ppb threshold is more conservative and restrictive than is necessary to adequately protect the public health, no data were submitted that would justify FDA establishing a threshold of regulatory concern at a dietary concentration level higher than 0.5 ppb. Based on its analysis of the available evidence, FDA concludes that this evidence does not support a threshold significantly higher than 0.5 ppb, especially where the substance being considered for an exemption has not been the subject of any toxicological testing. Therefore, this final rule establishes 0.5 ppb as the threshold of regulatory concern for substances intended for use in food-contact articles. This final rule also establishes the threshold of regulatory concern for regulated direct food additives used in food-contact articles as that dietary exposure that is at or below 1 percent of the ADI for that substance.

Listed below are the revisions that are being incorporated into this final rule based on comments received in response to the proposal:

(1) FDA is revising § 170.39(a)(1) to make it clear that the phrase ''there is no reason, based on the chemical structure of the substance, to suspect that the substance is a carcinogen'' refers only to the substance itself (see comment 21 of this document).

(2) FDA is revising § 170.39(a)(2)(ii) to state that, for requests seeking an exemption on the basis that the substance is a regulated direct food additive whose use in a food-contact article will result in a dietary exposure at or below 1 percent of the ADI for that substance, FDA's review will not necessarily be restricted to ADI values based on data in FDA files. In particular, in cases where FDA has not calculated an ADI value for a regulated direct food additive, the agency will consider ADI values from other appropriate sources (see comment 9 of this document).

(3) FDA is adding paragraph (h) to § 170.39 to state that guidelines to assist requestors in the preparation of submissions seeking exemptions from the food additive regulations are available from FDA's Office of Premarket Approval (HFS–200, 200 C St. SW., Washington, DC 20204). Because it is not practical to provide guidelines that would cover all of the possible topics associated with these types of submissions, § 170.39(h) encourages interested parties to obtain specific 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, on the procedures used to relate migration data to dietary exposures, and on any other issue not specifically covered in FDA's guidelines (see comment 24 of this document).

(4) FDA is revising § 170.39(c)(1) to state that the description of the chemical composition of the substance for which the request is made should include, whenever possible, the name of the chemical in accordance with current CAS nomenclature guidelines and a CAS registry number, if available (see comment 22 of this document).

(5) For consistency, FDA is revising § 170.39(c)(4)(ii) and (c)(4)(iii) so that the word ''substance'' refers to the singular case (see comment 23 of this document).

(6) FDA is revising the language in § 170.39(c)(5) to state that the only toxicological information that must be included in a submission for an exemption from the food additive regulations is an analysis of existing toxicological data on the substance and its impurities. This information is needed 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 potent toxin. This type of information on the impurities is needed to show whether any of them are carcinogenic and, if carcinogenic, whether their TD_{50} value is greater than 6.25 mg/kg bodyweight per day in accordance with § 170.39(a)(1) (see comment 28 of this document).

(7) FDA is revising § 170.39(e) to state that interested persons may obtain a list of exempted substances by contacting FDA's Office of Premarket Approval (HFS–200), 200 C St. SW., Washington, DC 20204 (see comment 34 of this document).

(8) FDA is also revising § 170.39(e) to state that FDA will handle requests for copies of releasable information contained in submissions requesting exemptions from the food additive

regulations in accordance with FDA's FOIA procedures as described in part 20. In particular, data and information that fall within the definitions of a trade secret or confidential commercial or financial information are not available for public disclosure in accordance with 21 CFR 20.61(c) (see comment 30 of this document).

(9) FDA is revising the language in § 170.39(g) to state that the agency plans to notify manufacturers by means of a notice published in the **Federal Register** of its decision to revoke an exemption issued for a specific use of a substance in a food-contact article (see comment 13 of this document).

(10) FDA is revising § 170.39(c) to state that three copies of a request for an exemption from regulation are to be submitted. If part of the submitted material is in a foreign language, it must be accompanied by an English translation verified to be complete and accurate in accordance with § 10.20(c)(2) (see Section III. of this document: Other Actions). In addition to these changes, FDA is clarifying its definition of TD_{50} in § 170.39(a)(1). This minor change from the October 12, 1993, proposal ensures the scientific soundness of this definition.

VIII. 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. 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.

2. Rulis, A. M., D. G. Hattan, and V. M. Morgenroth III, ''FDA's Priority Based Assessment of Food Additives,'' *Regulatory Toxicology and Pharmacology*, vol. 4, pp. 37–56, 1984.

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, 21 CFR parts 5, 25, 170, 171, and 174 are 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, 354, 361, 362, 1701–1706, 2101, 2125, 2127, 2128 of the Public Health Service Act (42 U.S.C. 241, 242, 242a, 242l, 242n, 243, 262, 263, 263b, 264, 265, 300u–300u–5, 300aa–1, 300aa–25, 300aa–27, 300aa–28); 42 U.S.C. 1395y, 3246b, 4332, 4831(a), 10007–10008; E.O. 11490, 11921, and 12591; secs. 312, 313, 314 of the National Childhood Vaccine Injury Act of 1986, Pub. L. 99–660 (42 U.S.C. 300aa–1 note).

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, color additives, nutrient content claims, and health claims.

* * * * *

(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 and Deputy Directors, Center for Food Safety and Applied Nutrition (CFSAN).

(2) The Director, Office of Policy, Planning and Strategic Initiatives, CFSAN.

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

(4) 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, and there is no reason, based on the chemical structure of the substance, to suspect that the substance is a carcinogen. The substance must also not contain a carcinogenic impurity or, if it does, must 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 (The TD_{50}, for the purposes of this section, is the feeding dose that causes cancer in 50 percent of the test animals when corrected for tumors found in control 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 appropriate TD50 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 at or below 1 percent of the acceptable daily intake as determined by safety data in the Food and Drug Administration's files or from other appropriate sources;

(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 for 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 three copies of the following information (If part of the submitted material is in a foreign language, it must be accompanied by an English translation verified to be complete and accurate in accordance with § 10.20(c)(2) of this chapter):

(1) The chemical composition of the substance for which the request is made, including, whenever possible, the name of the chemical in accordance with current Chemical Abstract Service (CAS) nomenclature guidelines and a CAS registry number, if available;

(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 parts per billion, or on the fact that it involves the use of a regulated direct food additive for which the dietary exposure is at or below 1 percent of the acceptable dietary intake (ADI);

(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 in the form of:

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

(ii) Information on the amount of the substance used in the manufacture of the food-contact article; or

(iii) Information on the residual level of the substance 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 simulants, 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.

(5) The results of an analysis of existing toxicological information on the substance and its impurities. This information on the substance is needed 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 potent toxin. This type of information on the impurities is needed to show whether any of them are carcinogenic, and, if carcinogenic, whether their TD50 values are greater than 6.25 milligrams per kilogram bodyweight per day in accordance with paragraph (a)(1) of this section.

(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 shall be submitted to the Food and Drug Administration's Office of Premarket Approval (HFS–200), 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 section on display 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. Interested persons may also obtain a copy of the list of exempted substances by contacting the Food and Drug Administration's Office of Premarket Approval (HFS–200), 200 C St. SW., Washington, DC 20204. The agency's finding of no significant 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. Requests for copies of releasable information contained in submissions requesting exemptions from the food additive regulations will be handled in accordance with the Food and Drug Administration's Freedom of Information Act procedures, as described in part 20 of this chapter. In particular, data and information that fall within the definitions of a trade secret or confidential commercial or financial information are not available for public disclosure in accordance with § 20.61(c) 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 reevaluate the substance. If the Food and Drug Administration tentatively concludes that the information that is available about the substance no longer supports an exemption for the use of the food-contact material from the food additive regulations, the agency will notify any persons that requested an exemption for the substance of its tentative decision. The requestors will be given an opportunity to show why the use of the substance should not be regulated under the food additive provisions of the act. If the requestors fail to adequately respond to the new evidence, the agency will notify them 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 as part of the file of uses of substances exempted from regulation as food additives. The Food and Drug Administration recognizes that manufacturers other than those that actually made a request for exemption may also be using exempted substances in food-contact articles under conditions of use (e.g., use levels, temperature, type of food contacted, etc.) that are similar to those for which the exemption was issued. Because only requestors will be notified as part of the revocation process described in this section, the Food and Drug Administration plans to notify other manufacturers by means of a notice published in the **Federal Register** of its decision to revoke an exemption issued for a specific use of a substance in a food contact article.

(h) Guidelines to assist requestors in the preparation of submissions seeking exemptions from the food additive regulations are available from the Food and Drug Administration's Office of Premarket Approval (HFS–200), 200 C St. SW., Washington, DC 20204. Interested persons are encouraged to obtain specific guidance from the Food and Drug Administration on the appropriate protocols to be used for obtaining migration data, on the validation of the analytical methods used to quantify migration levels, on the procedures used to relate migration data to dietary exposures, and on any other issue not specifically covered in the Food and Drug Administration's guidelines.

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 use.

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 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 use.

Dated: July 11, 1995.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 95–17435 Filed 7–14–95; 8:45 am]

BILLING CODE 4160–01–P