

*Draft - Not for Implementation*

## Guidance for Industry

# Preparation of Premarket Notifications for Food Contact Substances: Administrative

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June 2000

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## GUIDANCE FOR INDUSTRY

### I. Introduction

Section 309 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) amends Section 409 of the Federal Food, Drug, and Cosmetic Act (FFDCA) (21 U.S.C. 348) to establish a premarket notification (PMN) procedure as the primary method by which the Food and Drug Administration (FDA) regulates food additives that are food contact substances (FCSs). An FCS is any substance that is intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food if such use of the substance is not intended to have any technical effect in such food.

Notifications for an FCS must contain sufficient scientific information to demonstrate that the substance that is the subject of the notification is safe for the intended use (21 U.S.C 348(h)(1)). Because the safety standard is the same for all food additives, whether subject to the petition process or the PMN process, information in a PMN should be comparable to that recommended for inclusion in a food additive petition.

This guidance has been prepared by the Office of Premarket Approval of the Center for Food Safety and Applied Nutrition (CFSAN) at the Food and Drug Administration in accordance with FDA's "Good Guidance Practices" (62 FR 8961; Feb. 27, 1997). The purpose of this document is to provide general guidance for the format and content of information that should be included in a PMN for an FCS. This guidance represents FDA's current thinking on the format and content of information for a PMN. It does not create or confer any rights for or on any person and does not operate to bind the Agency or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations. For situations not addressed in this guidance, notifiers are advised to consult FDA. Periodically, FDA will update this guidance in light of new information.

## **II. Scope of the PMN Program**

### **A. Who May Notify**

Anyone may submit to FDA a notification for a new use of an FCS. However, a notification for an FCS will be "effective" only for the manufacturer(s) identified in the notification. (See II.E.1.)

### **B. Uses of FCSs that may be the subject of a PMN**

Only "food contact substances" that are food additives require premarket authorization by FDA. An FCS is defined as any substance that is intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food if such use is not intended to have any technical effect in such food (21 U.S.C. 348(h)(6)). FDA believes that the definition of an FCS encompasses a broader range of substances used in contact with food than those that have been regulated as food additives. For example, FDA believes that a substance that is GRAS or prior sanctioned for its intended use in contact with food may also be an FCS, and may be the subject of a PMN, even though authorization under the PMN process is not required for the FCS use.

#### **1. Food additives that are FCSs**

In the past, FDA has informally characterized a food additive as being a "direct additive" if it was intended to have a technical effect in food, a "secondary direct additive" if it was intended to have a technical effect on food during food processing but not in the finished food as consumed, or an "indirect additive" if it was intended to have a technical effect in a food contact material. Even though each of these types of food additives is regulated in a separate section of Title 21 of the Code of Federal Regulations (i.e., direct food additives are listed in 21 CFR Part 172, secondary direct food additives are listed in 21 CFR Part 173, and indirect food additives are listed in 21 CFR Parts 175-178), no definitions for direct, secondary direct, or indirect food additive exist in the codified regulations or the statute. PMNs will be accepted for unapproved uses of food additives that meet the definition of an FCS regardless of the location in

the Code of Federal Regulations of any related codified listing regulation. FDA expects that most PMNs will be submitted for the use of substances that are intended to have a technical effect in food contact materials (so-called indirect additives). However, FDA also expects some substances that are intended to have a technical effect in food during processing (processing aids) but not in the finished food may also be the subject of a PMN.

## **2. Other FCSs**

FCSs that may be the subject of a PMN but that are not food additives include substances that are GRAS or prior sanctioned for their intended use, substances that, under their intended conditions of use may contact food but are not reasonably expected to migrate to food, and substances that FDA has historically considered constituents of food additives. FDA recognizes that accepting a PMN for an FCS that is not a food additive under its intended conditions of use may be valuable in clarifying the conditions of safe use for the FCS. Therefore, FDA expects to accept PMNs for FCSs that are not food additives under the intended conditions of use that are the subject of the notification. FDA recommends that potential notifiers for the use of such substances consult with the Agency prior to the submission of a PMN in order to ensure that the safety of the FCS is adequately addressed in the PMN.

## **3. Notifications requiring FDA consent**

Section II.C.2., below, lists circumstances in which the Agency currently does not believe a PMN is appropriate but that a petition would be required. However, there may be some situations in which a petition would not be required even if one or both of the circumstances in Section II.C.2. are met (proposed § 170.100(c)). For example, FDA may determine that a notification is appropriate for an FCS even if the cumulative estimated dietary intake (CEDI) is >1 ppm. The following are examples of four situations where FDA expects that a notification would be appropriate even if the cumulative estimated dietary intake is > 1 ppm.

- 1) There is an existing acceptable daily intake (ADI) for the FCS and its constituent(s). In such case, the notifier should contact the Agency to determine the applicability of the ADI for the cumulative dietary concentration of the FCS, before submitting a PMN. FDA expects to make publicly available on its internet site ([www.cfsan.fda.gov](http://www.cfsan.fda.gov)) a database of ADIs and CEDIs for regulated, exempted, and notified FCSs to assist potential notifiers in preparing notifications and petitions for FCSs.
- 2) A large database is available on close structural analogs of the FCS and its constituent(s), and the analogs have been regulated by the Agency. In such cases, the following toxicological tests are recommended to demonstrate the degree of toxicological and metabolic similarity between the FDA-regulated analogs and the FCS and its constituent(s): a subchronic oral toxicity study in a rodent or non-rodent species and comparative absorption, distribution, metabolism, and elimination studies.
- 3) The FCS and/or its constituent(s) is poorly absorbed or is not absorbed from the gastrointestinal tract (e.g., the substance is a high molecular weight polymer or is a highly charged substance at gastric pH). Such assertions should be supported by relevant scientific information or data.
- 4) The FCS undergoes chemical or metabolic transformation solely to products known to be of little toxicological concern at the estimated level of cumulative dietary concentration. Such assertions should be supported by relevant *in vivo* or *in vitro* data.

FDA recommends that, prior to submission to the Agency, potential notifiers discuss any other scientific bases for FDA accept a notification rather than a food additive petition.

#### **4. Notification for a mixture of FCSs**

FDA believes that there are two types of mixtures of FCSs that may be the subject of a notification. The first type of mixture is an FCS formulation where all the FCSs in the mixture may be legally marketed for their intended use. Notifications for these formulations are discussed further in Section XII. The second type of mixture is a mixture containing one or more FCSs that may not be legally marketed for their intended use at the time FDA receives the notification for the mixture because one or more of the FCSs are unapproved food additives. FDA believes that a notification for a mixture of FCSs containing only a single new FCS or a single new use of a lawful FCS may be submitted under section 409(h) of the act. A notification for a mixture of FCSs containing one or more new FCSs would be comparable to a FAP for the use of an indirect food additive in combination with a particular polymer or other food contact material. In this case, the types of polymers with which a petitioned substance is regulated for use represent a limitation on the conditions of use for which the petitioned substance is authorized. Therefore, FDA currently believes that the conditions of use for an FCS that is the subject of a PMN could include detailed specifications on the other FCS's that may be used in combination with the notified FCS. FDA is concerned that it could be burdensome for FDA to review within 120 days a notification for more than one new FCS. Thus, FDA believes that a separate notification should be submitted for each new FCS in this second type of mixture. In other words, a mixture containing two or more unauthorized FCSs should be the subject of two or more companion notifications. FDA believes that this approach will permit the Agency to better manage its resources and its statutory obligations concerning the review of notifications for FCSs.

When a food additive petition for an FCS is submitted without prior consultation with the Agency, FDA will conduct a prefilling review of the petition to determine whether the petitioned use should instead be the subject of a PMN. If so, FDA will not file the petition and will so notify the petitioner.

## **C. Uses of substances that should not be the subject of a PMN**

### **1. Regulated and exempted uses**

In accordance with proposed 21 CFR 170.100(b), FDA will prohibit the submission of a PMN for any use of an FCS that is already permitted by a regulation in 21 CFR Parts 173 through 186, or that is the subject of an exemption under 21 CFR 170.39.

### **2. Uses for which a petition is required**

Section 409(h)(3)(A) of the act states that the PMN process shall be utilized for authorizing the marketing of an FCS except where FDA determines that the submission of a food additive petition is necessary to provide adequate assurance of safety.

Section 409(h)(3)(B) authorizes, but does not require, FDA to promulgate regulations describing those circumstances in which a food additive petition would be required prior to marketing an FCS. In making this determination, section 409 of the act states that FDA should consider criteria such as probable consumption and potential toxicity.

Under proposed 21 CFR 170.100(c), FDA would require the submission of a petition in either of the following situations: 1) When the use of the FCS will increase the cumulative estimated daily intake (CEDI) of the FCS from both food and food-contact uses to a level greater than 1 part per million (ppm) (i.e., 3 mg/person/day) or, in the case of a biocide, to a level greater than 200 parts per billion (ppb) (i.e., 0.6 mg/person/day), or 2) When existing data include one or more bioassays on the FCS that the Agency has not already reviewed and such studies are not clearly negative for carcinogenicity.

### **3. Agreement that a petition may be submitted**

Under section 409(h)(3)(A), FDA and a notifier may agree that a petition may be submitted to authorize the use of an FCS. If a notification was submitted prior to this agreement, the notification shall be deemed to be withdrawn in accordance with proposed § 170.103. FDA recommends that persons wishing to submit a petition contact the Agency prior to making such a submission to obtain FDA's agreement.

Under proposed § 171.1(i)(1)(c), FDA will decline to file a food additive petition for a use of an FCS that the Agency believes should be the subject of a PMN.

#### **D. Simultaneous submission of a food additive petition and a PMN**

Section 409(h)(3)(A) of the act states that the notification process shall be utilized for authorizing the marketing of FCSs except where FDA determines that submission and review of a food additive petition is necessary to provide adequate assurance of safety, or where FDA and a sponsor agree that a petition may be submitted. Therefore, simultaneous submission of a food additive petition and a notification for the same use of an FCS by the same person will not be permitted.

#### **E. Scope of an effective premarket notification**

##### **1. For whom is a notification effective?**

Section 409(h)(2)(C) of the act states that a premarket notification is effective for the manufacturer, the FCS, and the conditions of use identified in the notification and not effective for a similar or identical substance produced or prepared by a manufacturer other than a manufacturer identified in the prior notification.<sup>1</sup> Therefore, FDA believes that, for example, a new notification should be submitted in the following situations:

- (1) for a manufacturer other than the manufacturer specified in a prior notification;  
or
- (2) if substantive<sup>2</sup> changes are made in the specifications for the FCS; or
- (3) if changes are made in the manufacturing method that result in substantive

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<sup>1</sup>A PMN may specify more than one manufacturer or supplier of a food contact substance. However, a PMN for an FCS may only address one substance. Also, in addition to the manufacturer or supplier specified in the notification, a PMN is effective for customers of the manufacturer or supplier.

<sup>2</sup>For the purposes of this guidance document, deviations in specifications that are within Good Manufacturing Practice are not considered substantive.

changes in the identity of the product or its impurities, and/or levels of impurities<sup>3</sup> (Notifiers should be aware that identity information in the notification apply to the FCS whether or not they are specifically included in the description of the FCS in an acknowledgement letter or in FDA's inventory of effective notifications); or

(4) for conditions of use or levels of use not included in the prior notification.

## **2. Who may rely on an effective notification?**

Since a PMN is effective only for the manufacturer, substance, and intended use identified in the notification, any person wishing to rely on a PMN will generally need to demonstrate that the FCS being marketed has been manufactured by the manufacturer identified in the PMN and is being used under the conditions that are the subject of the PMN. The following is an example that illustrates how these principles are applied for a particular notification.

There is an effective notification for polymer antioxidant **X** produced by manufacturer **A** and intended for use without limitation in polymer **Y**.

A supplier of antioxidant **X** may rely on that notification if the supplier can establish that the antioxidant was produced by manufacturer **A** and the supplier is marketing antioxidant **X** for the intended use that is the subject of the notification.

A manufacturer of polymer **Y** may rely on the notification to use antioxidant **X** if the polymer manufacturer can establish that the antioxidant **X** was manufactured by manufacturer **A** and the antioxidant **X** is being used under the conditions described in the notification.

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<sup>3</sup>Deviations in a manufacturing process that are within Good Manufacturing Practice are not considered substantive. FDA will consider whether other deviations from an effective notification are substantive or not on a case-by-case basis.

A manufacturer producing food packaging from polymer Y containing antioxidant X may rely on the notification to market such food packaging if the packaging manufacturer can establish that the antioxidant X was produced by manufacturer A and has been used under the conditions described in the notification.

### **3. Conformance with Section 409(a)(3)**

Section 409(a)(3) of the Act states that a food shall not be deemed adulterated by reason of bearing or containing a food additive that is a food contact substance if there is a notification in effect relating to such food additive and such notification has not been revoked pursuant to section 409(i).

Under the food additive petition process for food contact substances, FDA would commonly receive a food additive petition from a chemical manufacturer that produced a chemical used to manufacture a food additive that was a food contact substance. An example of this would be a manufacturer of a chemical intended for use as a monomer in a polymeric food contact material. In the past, in response to such a petition, FDA has regulated the polymeric food contact material as the food additive and has considered the monomeric starting material as a constituent of the food additive. However, FDA currently believes that such a monomeric starting material could be considered an FCS and thus could itself be the subject of a notification.

FDA believes that chemical manufacturers may wish to notify the Agency about the use of monomeric starting materials in order to preserve the proprietary nature of the authorization under the notification process. Therefore, FDA has accepted and expects to continue to accept notifications for monomers and other constituents of food additives where the constituent and the food additive are both FCSs. Under section 409(h)(1), such notifications must demonstrate the safety of the constituent under its intended conditions of use in the production and use of the food additive. In order to demonstrate the safety under the intended conditions of use, the notification must demonstrate the safety of the additive that is manufactured using the notified

constituent.

In cases where FDA does not object to such notifications for a constituent of a food additive and the safety of the food additive under its intended conditions of use has been demonstrated, the Agency believes that the effective notification for the constituent may meet the requirements under section 409(a)(3) of the Act to permit the food additive to be legally marketed. Thus, separate notifications for constituents and food additives produced from constituents will not be necessary.

#### **F. Fiscal requirements**

In accordance with Section 409(h)(5)(i) of the act, the premarket notification program shall not operate in any fiscal year for which the program is not funded as described in section 409(h)(5). FDA currently believes that, in order to use resources effectively, the Agency must be able to object to a notification if any portion of the 120 days after FDA's receipt of the notification falls within a fiscal year for which the program may not operate in accordance with section 409(h)(5) of the act. Accordingly, proposed § 170.104(c)(3) would permit FDA to object to a premarket notification solely on the basis that some portion of the 120-day review period occurs during a period when the PMN program is not in operation.

### **III. Format of a PMN for an FCS**

FDA is requesting that 5 copies of a PMN be submitted. Special instructions for submitting an electronic copy of a notification are presented below. PMNs should be submitted to:

Notifications Control Assistant,  
Office of Premarket Approval, HFS-200  
Center for Food Safety & Applied Nutrition  
Food and Drug Administration

200 C. St., S.W.  
Washington, DC 20204

Because of the short time provided for the Agency to review a PMN, it is important that the PMN be well organized. The Agency recommends the following organizational format for PMNs:

Format items within the PMN should be presented as distinct units or chapters within the submission. This may be accomplished most easily by inserting dividers between the different sections of the submission. In addition, an overall table of contents should be provided identifying each of the required format items within the submission and individual data units within the submission that form the basis for the notifier's safety determination.

A PMN may reference data in a food additive master file. If data have been submitted as a master file by a manufacturer other than the notifier, the notifier may refer to the master file, if and to the extent that the notifier obtains written permission from the manufacturer to do so. The manufacturer may authorize specific reference to the data without disclosure to the notifier.

Notifiers are advised to consult FDA's guidance documents on recommended chemical and toxicological information for PMNs before submitting a PMN. The guidance documents are available on FDA's web site at "[www.cfsan.fda.gov/](http://www.cfsan.fda.gov/)". In addition, notifiers are urged to contact FDA regarding questions not addressed in the guidance. In accordance with proposed § 170.101, a PMN for an FCS should include the information listed below.

#### **A. Comprehensive Summary**

A summary and comprehensive discussion of the basis for the notifier's determination that the use of the FCS is safe within the meaning of Section 409(c)(3)(A) of the act,

including a comprehensive discussion of all information and data submitted in the notification.

The summary should address cumulative dietary exposure to the FCS and any potential impurities, the results of toxicity studies, and any ADI derived from those studies. For such a discussion to be deemed comprehensive it should address all safety data in the notification. Although a notifier's discussion of every study or test need not be exhaustive, a notifier should include a thorough discussion of safety data deemed pivotal to the determination of safety. The comprehensive summary should include the safety narrative (See "Guidance for Industry: Preparation of Premarket Notifications for Food Contact Substances: Toxicology Recommendations") and may reference the comprehensive toxicological profiles for the FCS and its constituents. To ensure a balanced evaluation of existing data, the notifier should include a comprehensive discussion of any information that appears inconsistent with the determination that the use of the FCS is safe. Under this proposed scheme, if FDA determines that a notifier's discussion is not sufficiently comprehensive to show that the notifier has considered all relevant facts, the Agency will object to the notification on the basis that the notification does not demonstrate that the use of the FCS is safe.

### **B. Chemical Identity**

Detailed information on the chemical identity of the FCS and the impurities and residual reactants from the production of the FCS, including the chemical and structural formulas and CAS Registry No. (See Guidance for Industry: Preparation of Premarket Notifications for Food Contact Substances: Chemistry Recommendations)

### **C. Intended Conditions of Use**

Detailed information on the intended conditions of use of the food contact material(s) manufactured with the FCS (e.g., maximum use temperature, type of food that the substance is intended to contact, duration of the contact, and whether the food contact material is intended for repeated or single use application). (See Guidance for Industry:

Preparation of Premarket Notifications for Food Contact Substances: Chemistry Recommendations)

**D. Intended Technical Effect**

A statement of the intended technical effect of the FCS and data to establish the minimum amount of the substance that will achieve the intended technical effect. (See Guidance for Industry: Preparation of Premarket Notifications for Food Contact Substances: Chemistry Recommendations)

**E. Estimation of Intake**

Sufficient data to enable FDA to calculate the estimated daily intake (EDI) resulting from the notified use of the substance, including information on levels of residual reactants and impurities and the notifier's estimate of the CEDI from all food uses of the FCS. (See Guidance for Industry: Preparation of Premarket Notifications for Food Contact Substances: Chemistry Recommendations)

**F. Environmental Information**

Either an environmental assessment (EA) or a claim for categorical exclusion from the requirement of an EA.

A claim of categorical exclusion should be made by completing Part IV. of FDA Form No. 3480. FDA recently published a direct final rule amending 21 CFR part 25 to add the action of allowing a PMN to become effective as an action that would qualify for the categorical exclusions in §§ 25.32 (l), (j), (k), (q), and (r). Until that final rule becomes effective, all PMN actions will require an EA under § 25.40. See attachment 3 for interim guidance for preparing EAs for PMN actions.

**G. FDA Form No. 3480**

A completed and signed FDA Form No. 3480 (see Attachment 2).

The name and address of the notifier should be reported on FDA Form No. 3480, as well as a summary of the chemical, toxicological, and environmental information submitted with the notification.

#### **IV. Electronic submissions**

Electronic copies of notifications must meet the requirements of 21 CFR Part 11. Electronic submissions should be submitted to FDA on a CD-ROM or disk compatible with IBM-clone personal computers. Files should be provided in so-called "portable data file" (PDF) format or in a common word-processor format (e.g. WordPerfect or Word). FDA recommends that information addressing each format item above should be saved as a separate file.

#### **V. Disclosability of information in a PMN**

Under section 409(h) of the act, FDA is not permitted to disclose any information in a PMN for 120 days after receipt of the PMN by FDA. Under proposed § 170.102(c) FDA's conclusion regarding the review of a PMN will be publicly available once the Agency has completed its review. For the purposes of this section, FDA's review will be completed when either 120 days have passed after receipt of a PMN or FDA has issued a letter objecting to the PMN.

Under proposed § 170.102(e), at the completion of FDA's 120-day review period, the information in a PMN, including all safety and functionality data and information incorporated by reference, will be publicly available with the exception of trade secret and confidential commercial information. However, under proposed § 170.102(d), by submitting a notification, a notifier waives any claim to confidentiality of information required to adequately describe the FCS and the intended conditions of use that are the subject of the notification.

For those PMNs that the notifier chooses to withdraw prior to completion of FDA's review, FDA will maintain the confidentiality of the information in the PMN under

proposed § 170.102(b).

FDA recommends that a notifier submit an additional copy of its notification identifying those portions that the notifier considers to be trade secret or confidential business information (i.e., a redacted version of the notification). FDA may not agree that all identified information is protected from disclosure under 21 CFR Part 20.

## **VI. FDA response to a PMN**

### **A. Acknowledgment of a PMN**

FDA intends to acknowledge receipt of a premarket notification in writing within 30 days of receipt. This acknowledgment will serve two purposes. First, the acknowledgment will inform the notifier of the date of receipt of the notification by FDA, and thereby the effective date of the notification if FDA does not object to the marketing of the substance. Second, the acknowledgment will identify the substance and use that is the subject of the notification. Notifiers should review the description of the FCS and intended conditions of use in the acknowledgment letter carefully because this will be the description and intended conditions of use that FDA may ultimately list in its inventory of effective notifications. (Notifiers may wish to provide language for the acknowledgement as part of the information on identity and intended conditions of use.) During the course of review of a PMN, FDA may find it necessary to revise or correct the description of the FCS or intended use. In these cases, FDA will inform the notifier as soon as possible of any changes in the description of the FCS or conditions of use. If the notification becomes effective, FDA will place information on the identity of the substance, manufacturer, and conditions of use that are the subject of the notification in the publicly available inventory of effective notifications.

### **B. Nonacceptance of a PMN**

If any component of a notification required under proposed § 170.101 is missing, FDA will not accept the notification for review. In addition, under proposed § 170.100(b), FDA may choose not to accept a notification for a use of an FCS that is the subject of a

regulation in parts 173 through 186, or that is the subject of an exemption under 170.39. In cases where the Agency does not accept a notification based on deficiencies in information, FDA expects to inform the notifier in writing within 30 days of receipt of the submission.

### **C. Objection by FDA**

The bases for FDA's objection depend in part on the provisions of the final rule implementing Section 409(h) of the Act. Under the proposed rule implementing Section 409(h), FDA may object to a PMN if:

- 1) The notification does not comply with the general criteria for a PMN in §170.100.
- 2) FDA does not agree that the notifier has demonstrated that the substance is safe under the intended conditions of use. In this case, FDA will inform the notifier in writing that FDA objects to the marketing of the substance for the use that is the subject of the notification, and describe the basis for the objection, as well as any additional information that would be required to support the safety of the substance for the intended use.
- 3) A portion of the 120 days after FDA's receipt of the notification occurs within a fiscal year for which the premarket notification program does not operate in accordance with section 409(h)(5) of the act.

### **D. Final letter**

FDA is not required to issue a letter if it does not object to the marketing of the notified substance. However, FDA realizes that such a letter may serve to bring the review process to closure. Therefore, FDA expects to issue a letter to the notifier that includes information identifying the FCS that is the subject of the notification and the date on which the notification became effective.

### **E. Inventory of effective PMNs**

In order to provide for efficient enforcement of the act, FDA maintains an inventory of effective premarket notifications. FDA expects that this inventory will be the primary vehicle for informing the public of effective PMNs. The inventory contains information on the identity of the substance that is the subject of the notification, the conditions of use shown to be safe, any limitations on the use of the substance, specifications for the substance, the manufacturer or supplier for whom the notification is effective, the date on which the notification became effective, and a tracking number. The inventory is publicly available on FDA's internet site at "www.cfsan.fda.gov".

### **VII. Withdrawal without prejudice**

In accordance with proposed § 170.104, a notifier may withdraw a PMN for an FCS, without prejudice to a future submission, at any time prior to the completion of FDA's review. For the purposes of this section FDA's review will be considered complete if either 120 days have passed since receipt of the PMN and FDA has not objected to the notification, or FDA has issued an objection letter. Such withdrawal would be effective when FDA receives written authorization from the notifier.

### **VIII. Determination that a premarket notification is no longer effective**

In accordance with proposed § 170.105(a), FDA may declare that a premarket notification for an FCS is no longer effective if the data available to the Agency no longer demonstrate that the intended use of the substance is safe. FDA may use information other than that submitted by the notifier in determining whether a PMN should continue to be effective. As stated in proposed §170.105(b), if information becomes available that demonstrates that the use of an FCS that is the subject of an effective notification can no longer be considered safe, FDA will inform the notifier in writing of its tentative conclusion and provide the basis for that tentative conclusion. Under proposed § 170.105(b), the notifier would be given an opportunity to adequately address the information raising FDA's concerns. The FDA will establish a time frame for the notifier to respond to the Agency's concerns. If the notifier is not able to

adequately address FDA's concerns within that time, FDA will publish a notice in the Federal Register stating the Agency's conclusion that the notification is no longer effective and the reasons for such conclusion. After publication of such notice, the notification will no longer be effective (proposed § 170.105(c)). Under proposed § 170.105(d), the Agency's determination that a notification is no longer effective shall be final agency action subject to judicial review.

#### **IX. Conversion of existing food additive petitions and threshold of regulation requests**

When the PMN program began to operate on October 25, 1999, the Agency had an inventory of pending food additive petitions for the use of FCSs and pending threshold of regulation exemption requests (under § 170.39). Nearly all of these petitions and exemption requests are for uses that would meet the criteria for a food contact substance notification under section 409(h) of the act. On October 25, 1999, FDA issued letters to all submitters of food additive petitions and exemption requests for FCSs, advising them of the possibility of converting their submissions to PMNs.

Existing food additive petitions or threshold of regulation requests for the use of an FCS may be withdrawn and resubmitted as a PMN. If a petitioner does not withdraw the petition and submits a PMN for the same use, the petition would be deemed withdrawn under proposed § 171.7(c) for the use or uses described in the notification. Likewise, if a sponsor does not withdraw the threshold of regulation request and submits a PMN for the same use, the request would be deemed withdrawn. FDA encourages petitioners and requestors under the threshold of regulation process to contact the Agency, prior to withdrawal of a petition or threshold of regulation request, to obtain specific guidance on conversion to a PMN. Petitions and threshold of regulation requests for the use of an FCS not converted to PMNs will continue to be reviewed as petitions or under the threshold of regulation process.

When the notification program began to operate, FDA was awaiting additional

information necessary to the safety determination for some of the food additive petitions and threshold of regulation requests in the Agency's inventory. Any such information is still necessary to establish the safety of the intended use of the FCS even if a petition or request is resubmitted as a notification.

## **X. Presubmission meetings**

If present guidance is not completely applicable to a given situation a presubmission meeting between the notifier and FDA may be advisable. The chemistry and toxicological PMN guidance documents describe certain circumstances under which a presubmission meeting is recommended. Generally there are three circumstances where FDA recommends a presubmission meeting. First, In all cases, FDA recommends that a presubmission meeting be held prior to the submission of a petition for a use of an FCS. Such a meeting may be used to verify that petition is required and that an appropriate level of information is supplied in the petition. Second, FDA recommends a presubmission meeting when there are uncertainties about how scientific data may be interpreted and those uncertainties are of such magnitude that they may affect the outcome of the overall safety determination. For example, if the EDI is close enough to the acceptable daily intake (ADI) that different choices for the no effect level may cause the resulting ADI to be larger or smaller than the EDI, a presubmission meeting is recommended. Third, a presubmission meeting is recommended when different interpretations of available data would result in different conclusions regarding whether a notification or a petition should be submitted. For example, a meeting is recommended if different interpretations of data in a bioassay could change the conclusion regarding the likely carcinogenicity of the substance.

In order to make the most of the usefulness of presubmission meetings, relevant information should be provided to FDA sufficiently in advance of the meeting to permit Agency personnel to familiarize themselves with the information to be discussed.

## **XI. Inquiries concerning FCSs**

Companies that produce, market, and use FCSs are responsible for the compliance of such materials with applicable regulations, exemptions, or notifications. Therefore, such companies should be aware of the regulatory status of any FCS that they produce, market, or use. In addition, Section II.B above specifies that the submission of a PMN for the use of an FCS will be prohibited for any use that is adequately

covered by a regulation or an existing exemption under § 170.39. Information on the regulatory status of an FCS may be obtained by inspection of §§ 170-199 or searching the GPO (Government Printing Office) website at "<http://www.access.gpo.gov/nara/cfr/index.html>". In addition, information on effective PMNs or existing exemptions for an FCS may be obtained through the FDA website. If, after consulting the above information sources, a company is still uncertain about the regulatory status of an FCS, FDA should be consulted by either telephone (202-418-3087 or 202-418-3069), E-mail (OPAPMN@cfsan.fda.gov), or letter (Food and Drug Administration, HFS-215, 200 C Street, SW, Washington, DC 20204).

When contacting FDA concerning the regulatory or notification status of an FCS, the following information is generally pertinent and should be readily available when contacting the FDA by telephone. This information should also be included in a letter or E-mail inquiry to minimize delays in response.

**A. Identity**

Identify the individual FCS, or components of a formulation, by their chemical names, structural formula and CAS Registry No., if available. FCSs are not listed in the regulations or notifications under trade names, nor does FDA maintain a list of such names. Therefore, FDA cannot review materials identified only by trade names. Additionally, give the weight percentages of each component of a formulation.

**B. Use level and conditions of use**

Identify the maximum use levels of the FCS in the food contact article, the most severe anticipated conditions of use of the food contact article (i.e., time-temperature conditions), types of foods to be contacted, and whether the article is intended for single or repeated use. Include information on the intended technical effect of the FCS for each component of a formulation

### **C. Appropriate regulation, exemption, or notification**

List the specific regulation section(s), if known, that are believed to authorize the use of the FCS or formulation under the desired conditions of use. For effective notifications, list the specific notification number, if known, and the identity of the notifier.

In the event that the Agency determines that any of the individual substances, or components of a formulation, are not authorized by a regulation, effective notification, or existing exemption for the proposed use, a PMN or petition will need to be submitted to provide for the proposed use.

## **XII. Format of a notification for food contact substance formulations**

FDA is proposing under 21 CFR 170.106(a) to accept notifications for food contact substance formulations where all of the components of the formulation are already authorized for their intended uses. FDA has serious concerns regarding the potential burden that accepting notifications for formulations could place on the Agency should the number of notifications become unexpectedly high. Therefore, proposed § 170.106(b) states that the Agency may prohibit the submission of notifications for food contact substance formulations at any time by publishing a notice in the Federal Register stating that the Agency does not have sufficient resources to review such notifications.

Such notifications are to be distinguished from PMNs in two ways. First, notifications for food contact substance formulations are for a particular mixture of two or more food contact substances. Second, each of the substances in the formulation is already authorized for its intended use. Thus, FDA's evaluation of such notifications consists of a review of the basis for compliance with section 409 of the act. Because all substances in a notification for a food contact substance formulation should already be authorized for their intended uses, such notifications would not be required under section 409 of the act.

FDA's current view is that notifications for formulations would not require resubmission of the information supporting the safety of the intended use of each food contact substance in the formulation. FDA tentatively believes that a notifier for a formulation would ordinarily submit only a completed FDA form 3479 (attachment 1) and any additional documentation required to establish that each of the components of the formulation is authorized for its intended use. In cases where the basis for compliance of an individual FCS in a formulation is an effective notification, a notifier of the formulation should establish that he could rely on the notification cited and that such notification is effective for the intended use in the formulation.

FDA is requesting that two copies of notifications for formulations for food contact materials be submitted. A notifier may submit the second copy of the notification in an electronic format. Special instructions for submitting an electronic copy of a notification are presented in Section IV. Notifications for food contact substance formulations should be submitted to:

Notification Control Assistant,  
Office of Premarket Approval, HFS-215  
Center for Food Safety & Applied Nutrition  
Food and Drug Administration  
200 C. St., S.W.  
Washington, DC 20204.

**Attachment 1**

U.S. Food and Drug Administration

AGENCY USE ONLY

**NOTIFICATION FOR A FOOD CONTACT SUBSTANCE FORMULATION**

**NOT FOR NEW USES OF FOOD CONTACT SUBSTANCES**

Date of Receipt

When completed send this form and notification to

NOTIFICATION CONTROL ASSISTANT  
OFFICE OF PREMARKET APPROVAL  
HFS-200  
200 C STREET, SW  
WASHINGTON, D.C. 20204

Enter the total number of pages in the Premarket Notification

Date Effective (if effective)

PMF Number

**GENERAL INSTRUCTIONS**

**PMF-**

- This form is intended for use only to ascertain that all components of a food contact substance formulation may be legally marketed for their intended use.
- This form may not be used to request authorization for a new use of a food contact substance under section 409(h) of the Federal Food, Drug, and Cosmetic Act. New uses of food contact substances must be the subject of a notification under section 409(h) including an FDA Form 3480.
- You should include all information necessary to ascertain that each component of the formulation may be legally marketed for its intended use (technical effect). For example, if the basis for compliance is an effective notification, you should provide information establishing that you may rely on that notification.

**Part I-GENERAL INFORMATION**

A notification may not be submitted for a formulation unless all of the components of the formulation may be legally marketed for their intended use in contact with food. A notification for a food contact substance formulation should include all information necessary to establish that each compound in the formulation may be legally marketed. For example, additional information necessary to establish that each component of the formulation may be legally marketed for the intended use in contact with food should be attached. Any information referenced in a notification must be submitted to FDA prior to your notification. If you reference information from a third party that is located in other FDA files, provide a letter of authorization for such use, if necessary. For example, authorization is not necessary to reference publicly available information in FDA's files. If third party authorization is required, provide the name of the authorizing official for the third party and a mailing address.

Two copies of your complete notification must be submitted, each with a completed and signed original copy.

**Part II — IDENTITY**

Provide complete identity information for all components used to produce the food contact substance formulation. If a component (e.g. a reagent or solvent) is completely removed from the formulation as marketed, indicate so. Provide any relevant specifications in order to establish that all components of the formulation may be lawfully marketed.

**Part III — INTENDED USE**

If possible, use the food types listed in Table 1 of 21 CFR 176.170(c) to describe the types of food the food contact substance formulation will contact in its intended use. If possible, use the time and temperature conditions of use listed in Table 2 of 21 CFR 176.170(c) to describe the time and temperature conditions of use for the food contact substance formulation that is the subject of this notification.

**Part IV — LIST OF ATTACHMENTS**

Attach additional sheets if there is not enough space to answer a question fully. Label each continuation sheet with the corresponding section heading. List these attachments, any test data or other data and any optional information included in the notification.

**OPTIONAL INFORMATION**

You may include any information that you want FDA to consider in evaluating this notification.

**CONFIDENTIALITY OF INFORMATION**

If you are claiming any information in this notification confidential you should submit a redacted copy of the notification. FDA may disagree regarding the disclosability of information claimed confidential.

**SAMPLES**

Provide a sample of the food contact substance formulation as intended for market.

**PUBLIC BURDEN STATEMENT**

Public reporting burden for this collection of information is estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Premarket Approval (0910-0014), 200 C Street, SW (HFS-200), Washington, DC 20204. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number.

**Part I — GENERAL INFORMATION**

1a. Person Submitting Notice

Name of authorized official		Position
[Redacted]		[Redacted]
Company		
[Redacted]		
Mailing address (number and street)		
[Redacted]		
City, State, ZIP Code, Country		
[Redacted]		
Telephone No.	Fax No.	E-Mail Address
[Redacted]	[Redacted]	[Redacted]

Please check here if E-Mail is your preferred method of communication.

B. Agent (if applicable)

Name of authorized official		Position
[Redacted]		[Redacted]
Company		
[Redacted]		
Mailing address (number and street)		
[Redacted]		
City, State, ZIP Code, Country		
[Redacted]		
Telephone No.	Fax No.	E-Mail Address
[Redacted]	[Redacted]	[Redacted]

Please check here if E-Mail is your preferred method of communication.



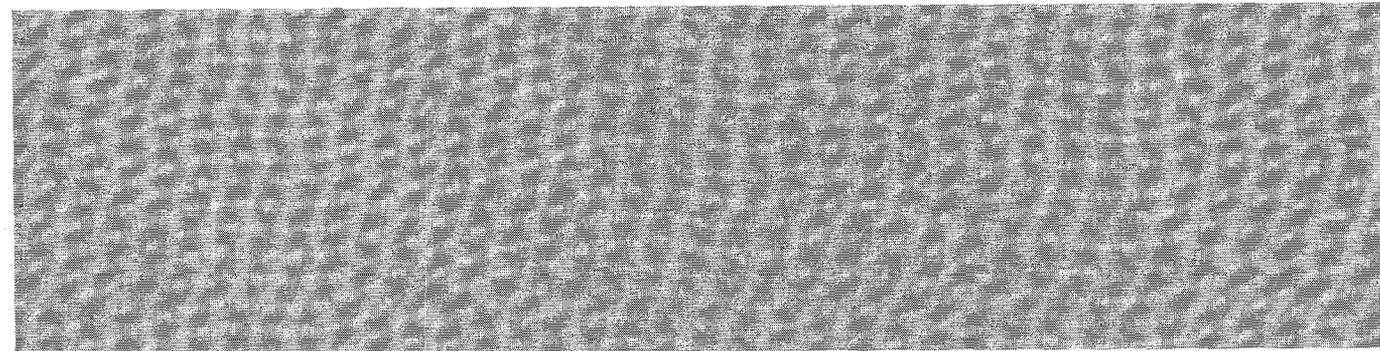
**Part II — INFORMATION ON IDENTITY, USE AND EXPOSURE — Continued**

**Section A - IDENTIFICATION - Continued**

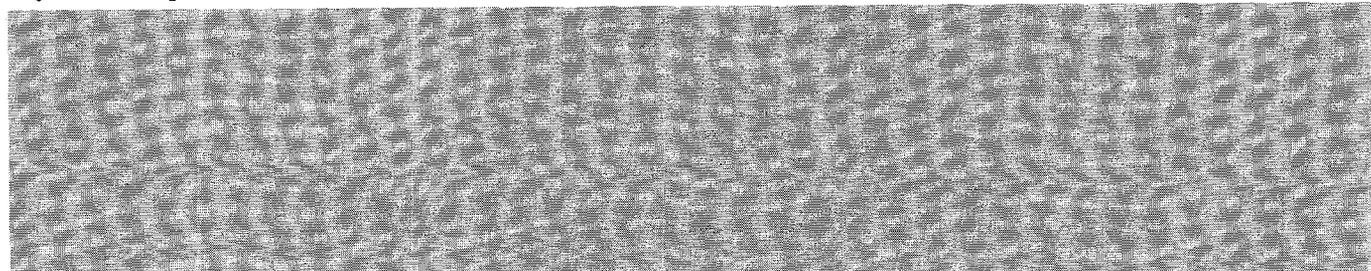
**b. Characterization**

List those characteristics of the formulation necessary to verify that the formulation may be lawfully marketed.

Polymer Properties	Values



c. Describe the manufacturing process, including times and temperatures, and include chemical equations for all synthetic steps and side reactions. Describe any purification steps.



Mark (X) this box if you attach a continuation sheet.

**Part III — INTENDED USE**

1. Describe the intended use of the food contact substance formulation, including maximum use levels (or thickness) in food contact materials, and types of food contact articles in which it is expected to be used (e.g., films, coatings, molded articles). State whether single or repeated use is intended. Provide maximum temperatures and times of food contact, refer to classifications in 21 CFR 176.170© Table 2 when possible.

Please check here if you attach a continuation sheet.

2. List types of food expected to contact the formulation, with examples if known. Refer to classifications in 21 CFR 176.170(c) Table 1 when possible.

Please check here if you attach a continuation sheet.

## PHYSICAL AND CHEMICAL PROPERTIES WORKSHEET

To assist FDA's review of physical and chemical properties data, please complete the following worksheet for data you provide and include it in the notification. Identify the property measured, the page of the notification on which the property appears, the value of the property, and the units in which the property is measured (as necessary). The measured properties should be for the food contact substance formulation. You are not required to submit this worksheet.

Property (a)	Mark (X) if provided	Page number (b)	Value (c)	Measured or Estimate (M or E)
Physical state of the substance	<input type="checkbox"/>		<input type="checkbox"/> (s) <input type="checkbox"/> (l) <input type="checkbox"/> (g)	
Vapor pressure @ Temperature <input type="text"/> °C	<input type="checkbox"/>		<input type="text"/> Torr	
Density/relative density (specify temperature)	<input type="checkbox"/>		<input type="text"/> g/cm <sup>3</sup>	
Solubility @ Temperature <input type="text"/> °C Solvent <input type="text"/>	<input type="checkbox"/>		<input type="text"/> g/L	
Solubility in water @ Temperature <input type="text"/> °C	<input type="checkbox"/>		<input type="text"/> g/L	
Melting Temperature	<input type="checkbox"/>		<input type="text"/> °C	
Boiling/sublimation temperature @ <input type="text"/> torr pressure	<input type="checkbox"/>		<input type="text"/> °C	
Spectra	<input type="checkbox"/>			
Dissociation constant	<input type="checkbox"/>			
Particle size distribution	<input type="checkbox"/>			
Octanol/water partition coefficient	<input type="checkbox"/>			
Henry's Law constant	<input type="checkbox"/>			
pH <input type="text"/> @ concentration <input type="text"/>	<input type="checkbox"/>			
Adsorption/coefficient	<input type="checkbox"/>			
Other - Specify <input type="text"/>	<input type="checkbox"/>			
Polymer specific (If a range is applicable, indicate so) % crystallinity of polymer	<input type="checkbox"/>			
Degree of orientation	<input type="checkbox"/>			
Thermal transitions of polymer (i.e., T <sub>g</sub> , T <sub>m</sub> )	<input type="checkbox"/>			
Density of polymer (specify temperature)	<input type="checkbox"/>			
	<input type="checkbox"/>			



## Attachment 2

U.S. Food and Drug Administration

**AGENCY USE ONLY**

**NOTIFICATION FOR A NEW USE OF  
A FOOD CONTACT SUBSTANCE**

Date of Receipt

**FOR NEW USES OF FOOD CONTACT SUBSTANCES**

When completed send this form and notification to

NOTIFICATION CONTROL ASSISTANT  
OFFICE OF PREMARKET APPROVAL  
HFS-200  
200 C STREET, SW  
WASHINGTON, D.C. 20204

Enter the total number of pages in the Premarket Notification

Date Effective (if effective)

FCN Number

**GENERAL INSTRUCTIONS**

**FCN-**

- You must provide all information requested in this form to the extent that it is known to or reasonably ascertainable by you. You should make reasonable estimates if you do not have actual data.
- Before you complete this form, you should read the appropriate guidance for completion of notification for food contact substances.

**Part I — GENERAL INFORMATION**

Only one new use of an FCS may be the subject of a particular notification. A "new" use is one not otherwise authorized. If authorization is sought for use of multiple FCSs, separate notifications should be submitted for each new use. Any accompanying information for a notification may be provided to FDA in a Food Additive Master File and referenced in a notification. Any information referenced in a notification must be submitted to FDA prior to your notification. If you reference information from a third party that is located in other FDA files, provide a letter of authorization for such use, if necessary. For example, authorization is not necessary to reference publicly available information in FDA's files. If third party authorization is required, provide the name of the authorizing official for the third party and a mailing address.

Completion of this form alone may not constitute a complete notification for a new use of an FCS. A notifier must also submit all data and information that forms the basis of the notifier's safety determination for the use that is the subject of the notification and any data and information required by regulation. Five copies of your complete notification must be submitted, each with a completed and signed original or copy of this form.

**Part II — CHEMISTRY INFORMATION**

Summarize all pertinent information concerning the FCS that is the subject of the notification. This should include: chemical identity, manufacturing process, physical properties and specifications, conditions of use, intended technical effect, and stability data. In addition to the summary information provided, your notification should include all supporting information or data. Also, include sufficient data to enable FDA to determine the estimated daily intake resulting from the intended use of the substance. For information on recommendations on migration testing and presentation of the chemistry information see "Guidance for Industry: Preparation of Premarket Notifications for Food Contact Substances: Chemistry Recommendations."

**Part III — SAFETY INFORMATION**

Include a list of toxicology studies considered key to the safety decision, discuss the potential mutagenicity and carcinogenicity of the notified substance and its constituents, determine the ADI, as appropriate, and state the basis for the safety decision by the notifier. This information should be consistent with the discussion in the Safety Narrative, which is described in the "Guidance for Industry: Preparation of Premarket Notifications for Food Contact Substances: Toxicology Recommendations".

**Part VI — LIST OF ATTACHMENTS**

Attach additional sheets if there is not enough space to answer a question fully. Label each continuation sheet with the corresponding section heading. List these attachments, any test data or other data and any optional information included in the notification.

**OPTIONAL INFORMATION**

You may include any information that you want FDA to consider in evaluating this notification.

**CONFIDENTIALITY OF INFORMATION**

By submitting a notification under section 409(h) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 348(h)), a notifier waives any claim to confidentiality for information necessary to describe the FCS and the intended conditions of use that are the subject of the notification. If you are claiming any information in this notification to be confidential you should submit a redacted copy of the notification. FDA may disagree regarding the disclosability of information claimed confidential.

**PUBLIC BURDEN STATEMENT**

Public reporting burden for this collection of information is estimated to average 20 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Premarket Approval (0910-0014), 200 C Street, SW (HFS-200), Washington, DC 20204. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number.

**Part I — GENERAL INFORMATION**

1a. Person Submitting Notice

Name of authorized official	Position

Company

Mailing address (number and street)

City, State, ZIP Code, Country

Telephone No.	Fax No.	E-Mail Address

Please check here if E-Mail is your preferred method of communication.

B. Agent (if applicable)

Name of authorized official	Position

Company

Mailing address (number and street)

City, State, ZIP Code, Country

Telephone No.	Fax No.	E-Mail Address

Please check here if E-Mail is your preferred method of communication.

2. If you had a prenotification communication (PNC) concerning this notification and FDA assigned a PNC Number to the communication, enter the number.		Mark (X) if none <input type="checkbox"/>
3. If you previously submitted an FCN for this substance that is not effective, enter the FCN number assigned by FDA.		Mark (X) if none <input type="checkbox"/>
4. List all effective notifications for the substance.  FDA maintains a list of effective notifications accessible through its internet site at "www.cfsan.fda.gov".		Mark (X) if none <input type="checkbox"/>

**Part II - INFORMATION ON IDENTITY, USE AND EXPOSURE**

**Section A - IDENTIFICATION OF THE FOOD CONTACT SUBSTANCE**

1. Chemical Identity

a. Chemical Abstracts Service (CAS) name

[Redacted]

b. Other chemical names (IUPAC, etc.)

[Redacted]

c. Trade or common names

[Redacted]

d. CAS Registry Number

[Redacted]

e. Composition

Provide a description of the FCS, including chemical formula(e), structures and molecular weight(s). For substances that cannot be represented by a discrete chemical structure, such as polymers, provide a representative chemical structure(s).

For polymers, submit the M w, Mn, and molecular weight distribution (including method) and, for copolymers, the ratio of monomer units in the copolymers.

[Redacted]

Mark (X) this box if you attach a continuation sheet.

f. Characterization

As appropriate, attach data to characterize the substance, including infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), or mass spectra, or other similar data for identification.

Please check here if any information is attached and list the items below.

[Redacted]

Mark (X) this box if you attach a continuation sheet.

**Part II — INFORMATION ON IDENTITY, USE AND EXPOSURE — Continued**

**Section A - IDENTIFICATION - Continued**

**2. Manufacturing Process**

a. List below all reagents, monomers, solvents, catalyst systems, purification aids, etc. used to manufacture the FCS, their chemical names, CAS Registry Numbers, impurities in each, the typical composition range of each in the total reaction mixture, and the maximum residual of each in the FCS intended to be marketed.

Chemical Name (1)	CAS Reg. No. (2)	Major Impurities (3)	Typical Composition (4)	Maximum Residual (5)
			%	%
			%	%
			%	%
			%	%
			%	%
			%	%
			%	%

b. Describe the manufacturing process, including times and temperatures, and include chemical equations for all synthetic steps and side reactions. Account for the fate of all substances listed in II.A.2.a.(1) that will not remain as residuals under II.A.2.a.(5). Describe any purification steps.

Mark (X) this box if you attach a continuation sheet.

**Part II — INFORMATION ON IDENTITY, USE AND EXPOSURE — Continued**

**Section A - IDENTIFICATION - Continued**

c. List impurities in the FCS including; the chemical name, CAS Registry Number, typical composition (percent weight) in the FCS intended for market, and the maximum residual in the FCS intended for market; for FCS that are polymers include typical and maximum residual monomer concentrations. Some of this data may be duplicated from Section II.A.2.a.

Chemical Name (1)	CAS Reg. No. (2)	Typical Composition (4)	Maximum Residual (5)
			%
			%
			%
			%
			%
			%
			%
			%

**3. Physical Properties and Specifications**

a. Provide physical/chemical specifications for the substance (e.g., maximum impurity levels, melting point) and relevant physical properties (e.g., solubility in food stimulants). Complete, to the extent possible, the "Physical and Chemical Properties Worksheet" included as an attachment to this form.

Properties	Values

Mark (X) this box if you attach a continuation sheet.

b. For polymers, provide relevant information on density range, melt flow indexes, glass transition points, morphology, etc. Provide specification test results for at least three production batches of the substances. Attach methods for establishing compliance with specifications. Indicate the maximum percentage of low molecular weight species, not including residual monomers, reactants or solvents, below 500 daltons and 1000 daltons.

Polymer Properties	Values

Mark (X) this box if you attach a continuation sheet.

**Part II — INFORMATION ON IDENTITY, USE AND EXPOSURE — Continued**

**Section B - INTENDED USE**

1. Describe the intended use of the FCS, including maximum use levels (or thickness) in food-contact materials, and types of food-contact articles in which it is expected to be used (e.g., films, coatings, molded articles). State whether single or repeated use is intended. Provide maximum temperatures and times of food contact, referring to classifications in 21 CFR 176.170(c) Table 2 when possible.

Please check here if you attach a continuation sheet.

2. List types of food expected to contact the substance, with examples if known. Refer to classifications in 21 CFR 176.170(c) Table 1 when possible.

Please check here if you attach a continuation sheet.

3. State the intended technical effect of the FCS and summarize data establishing the minimum amount of the substance required to achieve the intended technical effect. Attach data demonstrating that the FCS will achieve the intended technical effect.

Please check here if you attach a continuation sheet.

**Section C - STABILITY DATA**

1. Will the FCS degrade, decompose, or undergo any other chemical change under the intended conditions of use?

Yes  No

2. Provide the basis for your conclusion. Attach any supporting data.

Please check here if you attach a continuation sheet.

**Part II — INFORMATION ON IDENTITY, USE AND EXPOSURE — Continued**

**Section C - STABILITY DATA - Continued**

3. If the answer to C.1. above is "yes", list the degradation products for the FCS, and provide structures, CAS Reg. Nos. and molecular weights below.

Please check here if you attach a continuation sheet.

**Section D - ESTIMATED DAILY INTAKE (EDI)**

**1. Migration Testing and/or Calculations**

Note: Summary information on migration testing and/or calculations should be provided here. A full report of all analytical testing, including detailed descriptions of methodology, raw data, and sample instrumental output (spectra, chromatograms, etc.) must be attached. In lieu of conducting migration testing, worst-case migration may be calculated by assuming 100% migration to food, or migration to food may be estimated through the use of different considerations. In such case, provide full details of calculations.

- a. Describe test specimen(s), including full composition (e.g., comonomer composition of base polymer, identities and concentrations of adjuvants), dimensions (thickness and surface area), relevant base polymer properties (e.g., density,  $T_g$ ,  $T_m$ , % crystallinity). For polymers, provide levels of residual monomer(s) in the test specimen(s). Indicate whether specimens were extracted by immersion or exposed on a single side.

- b. Identify food simulants employed, and times and temperatures of extraction.

- c. Summarize results of migration testing. Give average migration values (mg/in) for all analytes in each solvent at all time points. Provide sample calculations relating the instrumental output to values in mg/in<sup>2</sup>. For polymers, provide a measure of polymer migration and, if possible, characterize the individual low-molecular oligomer components. Also, provide a measure of monomer(s) migration.

- d. Provide a summary of method validation results. Give average percent recovery for all analytes, food simulants, and spiking levels. Full details, including description of spiking procedure and calculations, must be included in attached report.

**2. Estimated Daily Intake (EDI)**

The incremental and cumulative EDI must be calculated by the notifier.

- a. Calculate weighted-average migration ( $\langle M \rangle$ ) for each migrant by multiplying values measured in food simulants by appropriate food-type distribution (fT) factors and summing over all for food types.

- b. Calculate concentration of substance(s) in the diet by multiplying  $\langle M \rangle$  value(s) by appropriate consumption factors (CF). Note: If CF values other than those assigned by FDA are used, information supporting derivation and use of such factors must be attached.

- c. Calculate EDI, in milligrams per person per day, by multiplying concentration in the diet (expressed as mg per kg, or parts per million) by 3 kilograms/day average diet. Add the calculated EDI to the existing EDI for FCS, if applicable, to determine the cumulative EDI.



**Part IV — ENVIRONMENTAL IMPACT OF FOOD CONTACT SUBSTANCE (21 CFR part 25)**

All FCN submissions must contain either a claim of categorical exclusion under 21 CFR 25.32 or an environmental assessment (EA) under 21 CFR 25.40.

**A - CLAIM OF CATEGORICAL EXCLUSION**

1. Cite the specific section of the CFR under which the categorical exclusion is claimed (21 CFR 25.32 (i), (j), (k), (q), or (r)  .

2. Does your proposed food-contact use comply with the categorical exclusion criteria?  Yes  No

3. To the best of your knowledge, are there any extraordinary circumstances that would require your submission of an EA?  Yes  No

**B - ENVIRONMENTAL ASSESSMENT**

If an EA is required, state that an EA has been prepared under 21 CFR 25.40, and is attached.

**Part V - CERTIFICATION**

The accuracy of the statements you make in this notice should reflect your best prediction of the anticipated facts regarding the chemical substance described herein. Any knowing and willful misinterpretation is subject to criminal penalty pursuant to 18 U.S.C. 1001.

The notifying party certifies that the information provided herein is accurate and complete to the best of his/her knowledge.

Signature of Authorized Official or Agent

Title

Date

### PHYSICAL AND CHEMICAL PROPERTIES WORKSHEET

To assist FDA's review of physical and chemical properties data, please complete the following worksheet for data you provide and include it in the notification. Identify the property measured, the page of the notification on which the property appears, the value of the property, and the units in which the property is measured (as necessary). The measured properties should be for the food contact substance formulation. You are not required to submit this worksheet.

Property (a)	Mark (X) if provided	Page number (b)	Value (c)	Measured or Estimate (M or E)
Physical state of the substance	<input type="checkbox"/>	[ ]	[ ] (s) [ ] (l) [ ] (g)	[ ]
Vapor pressure @ Temperature [ ] °C	<input type="checkbox"/>	[ ]	[ ] Torr	[ ]
Density/relative density (specify temperature)	<input type="checkbox"/>	[ ]	[ ] g/cm <sup>3</sup>	[ ]
Solubility @ Temperature [ ] °C Solvent [ ]	<input type="checkbox"/>	[ ]	[ ] g/L	[ ]
Solubility in water @ Temperature [ ] °C	<input type="checkbox"/>	[ ]	[ ] g/L	[ ]
Melting Temperature	<input type="checkbox"/>	[ ]	[ ] °C	[ ]
Boiling/sublimation temperature @ [ ] torr pressure	<input type="checkbox"/>	[ ]	[ ] °C	[ ]
Spectra	<input type="checkbox"/>	[ ]	[ ]	[ ]
Dissociation constant	<input type="checkbox"/>	[ ]	[ ]	[ ]
Particle size distribution	<input type="checkbox"/>	[ ]	[ ]	[ ]
Octanol/water partition coefficient	<input type="checkbox"/>	[ ]	[ ]	[ ]
Henry's Law constant	<input type="checkbox"/>	[ ]	[ ]	[ ]
pH [ ] @ concentration [ ]	<input type="checkbox"/>	[ ]	[ ]	[ ]
Adsorption/coefficient	<input type="checkbox"/>	[ ]	[ ]	[ ]
Other - Specify [ ]	<input type="checkbox"/>	[ ]	[ ]	[ ]
Polymer specific (If a range is applicable, indicate so)				
% crystallinity of polymer	<input type="checkbox"/>	[ ]	[ ]	[ ]
Degree of orientation	<input type="checkbox"/>	[ ]	[ ]	[ ]
Thermal transitions of polymer (i.e., T <sub>g</sub> , T <sub>m</sub> )	<input type="checkbox"/>	[ ]	[ ]	[ ]



Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number.

**Attachment 3**

## **Preparing an Environmental Assessment for Premarket Notifications: Interim Guidance**

- I. Environmental assessment (EA) for the types of food contact uses specified in the categorical exclusions under 21 CFR 25.32(i), (j), (k), (q), and (r).

On July 29, 1997, FDA published a final rule revising its policies and procedures for implementing the National Environmental Policy Act (62 FR 40570). This final rule established additional categorical exclusions, two of which apply to food contact substances (§ 25.32(i) and (j)), and three of which may in some cases apply to food contact substances (§ 25.32(r), (k), and (q)). The basis for establishing these exclusions was described in the proposed rule published in the Federal Register of May 1, 1996 (61 FR 19476 at 19481-19482 and 19484-19485). The types of food contact substances and the uses of such substances covered by these categorical exclusions are the same whether a sponsor submits a food additive petition, a request for exemption from regulation as a food additive under 21 CFR § 170.39, or a premarket notification. However, allowing a notification to become effective is not currently one of the enumerated actions listed in the Agency's categorical exclusions. In the Federal Register of May 11, 2000 (65 FR 30352-30355), FDA published a direct final rule, which, if it becomes effective, would amend Part 25 to add allowing a notification to become effective as an action that would qualify for categorical exclusion in § 25.32(i), (j), (k), (q), and (r). Until Part 25 is amended, notifiers should submit an EA for the food contact substance uses covered under these categorical exclusions, following the outline provided below. The information needed for the various types of food contact substances and the uses of such substances is the same, except for information on the potential environmental consequences resulting from the use and disposal of the substances. Item 5.b of the outline delineates the information that should be submitted for the types of substances and the uses of such substances covered by each of the categorical exclusions referred to above.

### **Environmental Assessment**

- 1. Date:** Provide the date the EA was prepared.
- 2. Name of sponsor:** State the name of your company.

**3. Address:** Provide the business address for the company.

**4. Description of the proposed action:** Describe the requested action by naming the food contact substance that is the subject of the notification; describe the proposed use, including any limitations, and state the use level and describe the intended technical effect of the substance. These descriptions should be consistent with the information given elsewhere in the notification.

**5. Environmental consequences of the proposed action:**

**a. Production of the food contact substance:** You need not provide information regarding the production of the food contact substance unless you determine that there are extraordinary circumstances that pertain to its manufacture.

Extraordinary circumstances include such things as (1) unique emission circumstances that are not adequately addressed by general or specific emission requirements (including occupational) promulgated by Federal, State, or local environmental agencies and the emissions may harm the environment; (2) a proposed action threatens a violation of Federal, State, or local environmental laws or requirements (40 CFR 1508.27(b)(10)); and (3) production of the food contact substance may adversely affect a species or the critical habitat of a species determined to be endangered or threatened under the Endangered Species Act or the Convention on International Trade in Endangered Species of Wild Fauna and Flora or of wild fauna and flora that are protected under some other Federal law. If you determine that extraordinary circumstances apply to the manufacture of the food contact substance, discuss any reasonable alternative course of action that offers less environmental risk or that is environmentally preferable to the proposed action (21 CFR 20.40(a)). If you determine that no extraordinary circumstances apply to the manufacture of the food contact substance, then provide a statement to that effect.

**b. Use and disposal of the food contact substance:** The types of food contact substances and the uses of such substances that are described below require only limited environmental information, either because the substances 1) are minor components of food-packaging materials; 2) are components of articles intended for repeated use that have a long service life and small market volume;

3) are added directly to food, are intended to remain with food through use by consumers, and are not macronutrient replacements; 4) are registered by EPA under the Federal Insecticide, Fungicide, and Rodenticide Act for the same use requested in the notification; or 5) are naturally occurring in the environment. You should determine if your notification involves one of these types of uses of a food contact substance, and if so, we recommend that you use the language and information suggested below inserting specific information where indicated:

- 1) If your food-contact substance is intended to be present in finished food-packaging material at not greater than 5-percent-by-weight and is expected to remain with the finished food-packaging material through its use by consumers or when the substance is a component of a coating for a finished food-packaging material, we recommend you use the following language to describe the potential environmental impact of the use and disposal of the substance:

This action involves a food contact substance that is a minor component of finished food-packaging materials present at [insert percent]-by-weight of the finished packaging material and remains with the packaging through its use by consumers [or] is a component of a coating for a finished food-packaging material. [Use either the minor component description or the component of a coating description, as appropriate.] The principal routes of environmental introduction of the food contact substance follow from its disposal in municipal solid waste combustors or in landfills. These disposal routes are governed by Environmental Protection Agency (EPA) regulations in 40 CFR Part 60 (for combustors) and Part 258 (for landfills). Based on the low levels of the food contact substance in the packaging material, the introduction of combustion products or introductions at landfill sites are not environmentally significant. Therefore, we do not expect that any limited increase in environmental introductions resulting from the proposed action will threaten a violation of the EPA regulations governing combustors and landfills or have any other adverse environmental effect.

- 2) If your food contact substance is intended to be used as a component of a food contact surface of permanent or semipermanent equipment or a component of another food contact article intended for repeated use, we recom-

mend that you use the following language to describe the potential environmental impact of the use and disposal of the substance:

This action involves a food contact substance that is a component of a [insert either food contact surface of permanent or semipermanent equipment or repeat use article]. The principal route of environmental introduction of the food contact substance follows from its disposal after use. However, the potential for significant introduction of substances resulting from disposal is very low because of the long service life [insert an estimate of the service life of the article] of [insert food contact equipment or repeat use article] and because of the limited market volume of the substance [insert an estimate of the market volume of the food contact substance for the proposed use<sup>1</sup>.] Therefore, the proposed action will not have a significant environmental effect.

3) If your substance is added directly to food but has no technical effect in the finished food and it is, intended to remain with food through ingestion by consumers and not intended to replace macronutrients in food, one of the following scenarios may apply to the potential environmental impact of the use and disposal of the substance:

- a. The proposed use of the food contact substance will result in very low levels (in the low ppb range or lower) of substances in either effluents and/or sewage sludge from publicly owned wastewater treatment plants and these levels are not toxic to organisms in the environment;
- b. The food contact substance will be digested and/or metabolized by humans such that only products of digestion and metabolism will be excreted and these products are the same as (or very similar to) the products of digestion and metabolism resulting from human food; such products should have no potential for significant environmental effects because wastewater treatment facilities are designed to handle them; and/or

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<sup>1</sup>Data and information that are protected from disclosure under 18 U.S.C.1905, 21 U.S.C. 331(j) or 360 j(c) should be submitted separately in a confidential section of the PMN submission and should be summarized to the extent possible in the EA (21 CFR 25.51).

- c. The food contact substance will be excreted largely intact but will be rapidly degraded into nontoxic products either in wastewater treatment plants or in the environment.

You should identify the scenario that may apply to your proposed use of the food contact substance and briefly explain why that particular scenario is applicable. You should cite any references used to support your explanation.

- 4) If your food contact substance is a substance registered by the EPA under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) for the same use stated in the notification, you should provide a statement to this effect and include a copy of the FIFRA registration label that has the same use requested in the notification.<sup>2</sup> Then we recommend you insert the following statement:

Additional environmental analysis is not needed because the food contact use of [insert the name of the substance] is subsumed under EPA's assessment of the environmental risk of this antimicrobial substance.

- 5) If your proposed food contact substance is a substance that occurs naturally in the environment, you should briefly discuss why the proposed use of the substance will not alter significantly the concentration or distribution of the substance, its metabolites, or degradation products in the environment. You should provide a citation of any references used to support your discussion.
- 6. Alternatives to the proposed action:** If you have identified potential environmental impacts for the proposed action, describe the environmental impact of reasonable alternatives to the proposed action (including no action, and including measures that FDA or another government agency could undertake as well as those you as the notifier could undertake (40 CFR 1502.14 and 1502.16). Describe any reasonable course of action that offers less environmental risk or that is environ-

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<sup>2</sup>By "same use" FDA means that, in a comparison of the use of the food additive use to the pesticide use, the purpose of the use, any components used with the substance for the proposed use, and the amount of the substance and the amounts of any components used with it are substantially identical.

mentally preferable to the proposed action (21 CFR 25.40(a)). Discuss the environmental benefits and risks of the proposed action and of each alternative. If you identify no potential adverse environmental effects based on your review of adequate and complete data and information, we recommend you provide the following statement:

Alternatives to the proposed action need not be considered, because no potential adverse effects have been identified.

**7. List of preparers:** Please list the name, job title, and qualifications (e.g., educational background or professional discipline) for each person contributing to the preparation of the EA (21 CFR 25.40(a)).

**8. Certification:** Provide a signed and dated statement such as the following:

The undersigned official certifies that the information presented is true, accurate, and complete to the best knowledge of [insert company name].

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of responsible official

\_\_\_\_\_  
Name and title of responsible official, printed or typed

II. Environmental assessment for the types of uses of food contact substances **not** specified in 21 CFR 25.32(i), (j), (k), (q), and (r).

FDA is developing an environmental guidance document, which will be made available through a notice published in the Federal Register. This document will contain guidance for preparing an EA for actions involving the types of uses of food-contact substances not covered under the categorical exclusions in § 25.32(i), (j), (k), (q), and (r). Until this guidance is issued, we recommend that you contact the Office of

Premarket Approval for assistance on a case-by-case basis before submitting your notification.

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