Contains Nonbinding Recommendations

Preparation of Food Contact Substance Notifications (Administrative): Guidance for Industry

Additional copies are available from:
Office of Food Additive Safety
Division of Food Contact Substances HFS-275
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740
(Tel) 240-402-1175

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Table of Contents

Preparation of Food Contact Substance Notifications (Administrative): Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or we) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance at the phone number listed on the title page.

I. Introduction

Section 409 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) establishes a food contact substance notification (FCN) process as the primary means by which 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 the use is not intended to have any technical effect in such food (section 409(h)(6) of the FD&C Act).

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 (section 409(h) of the FD&C Act). Because the safety standard is the same for all food additives, whether subject to the petition process or the FCN process, information in an FCN should be comparable to that recommended for inclusion in a food additive petition or in a "Threshold of Regulation" submission (see 21 CFR 170.39).

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Office of Food Additive Safety, Division of Food Contact Substances in the Center for Food Safety and Applied Nutrition at the U.S. Food and Drug Administration.

II. Scope of the FCN Program

A. Who May Notify

A manufacturer or supplier of an FCS may submit to FDA a notification for a new use of an FCS. The term "supplier" means any person supplying the FCS, including companies supplying the FCS to themselves for manufacture of a food contact material. However, a notification for an FCS will be "effective" only for the manufacturer(s) identified in the notification. Such manufacturer(s) may include a supplier as defined above. (See II.E.1.)

B. Uses of Substances That May be the Subject of an FCN

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 (section 409(h)(6) of the FD&C Act). Only FCSs that are food additives require premarket authorization by FDA. 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 also may be an FCS, and may be the subject of an FCN, even though authorization under the FCN 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.

FDA will accept FCNs 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 FCNs 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 recognizes that some substances that are intended to have a technical effect in food during processing (processing aids) but not after processing may be included in the definition of an FCS, and thus also may be the subject of an FCN.

2. Other FCSs

FCSs that may be the subject of an FCN, 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 historically has considered constituents of food additives. FDA recognizes that accepting an FCN 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 FCNs 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 us before the submission of an FCN to ensure that the safety of the FCS is addressed adequately in the FCN.

3. Notifications Requiring FDA Consent

Section II.C.2., below lists circumstances in which FDA currently does not believe an FCN is appropriate but that a petition would be required under 21 CFR 170.100(c). However, there may be some situations in which a petition would not be required even if one or both of the circumstances in 21 CFR 170.100(c) are met.

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.

a. There is an existing acceptable daily intake (ADI) for the FCS and its constituent(s). In such a case, the notifier should contact us to determine the applicability of the ADI for the cumulative dietary concentration of the FCS, before submitting an FCN. FDA has made available on its internet site (https://www.fda.gov/food/packaging-food-contact-substances-fcs/cedi-database) a database of CEDIs for regulated, exempted, and notified FCSs to assist potential notifiers/petitioners in preparing notifications or petitions for FCSs.

b. A large database is available on close structural analogs of the FCS and its constituent(s), and the analogs have been regulated by FDA. 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.

c. The FCS and its constituent(s) are poorly absorbed or are 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.

d. 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 us, potential notifiers discuss any other bases for FDA to accept a notification rather than a food additive petition.

4. Food Additive Petition Submitted Without Prior Consultation

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

5. 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 X. 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 FD&C Act. A notification for a mixture of FCSs containing one or more new FCSs would be comparable to an 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 believes that the conditions of use for an FCS that is the subject of an FCN could include detailed specifications on the other FCSs 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 that is a food additive. Thus, FDA believes that a separate notification should be submitted for each new FCS that is a food additive in this second type of mixture. In other words, a mixture containing two or more unauthorized food additives that are FCSs should be the subject of two or more companion notifications. FDA believes that this approach will permit us to manage better our resources and our statutory obligations concerning the review of notifications for FCSs.

C. Uses of Substances That Should Not be the Subject of an FCN

1. Regulated and Exempted Uses

In accordance with 21 CFR 170.100(b), FDA may choose not to accept an FCN for any use of an FCS that already is 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 FD&C Act states that the FCN process must 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) of the FD&C Act 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 FD&C Act states that FDA should consider criteria such as probable consumption and potential toxicity.

Under 21 CFR 170.100(c), FDA requires the submission of a petition in either of the following situations: 1) when the use of the FCS will increase the CEDI of the FCS from both food and food-contact uses to a level equal to or greater than 1 part per million (ppm) (*i.e.,* 3 mg/person/day) for a substance that is not a biocide or, in the case of a biocide (*e.g.*, it is intended to exempt microbial toxicity), to a level equal to or 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 FDA has not reviewed already and such studies are not clearly negative for carcinogenicity.

3. Agreement That a Petition May be Submitted

Under section 409(h)(3)(A) of the FD&C Act, 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 21 CFR 170.103. FDA recommends that persons wishing to submit a petition contact us before making such a submission to obtain FDA's agreement. Under 21 CFR 171.1(i)(1)(iii), FDA will decline to file a food additive petition for a use of an FCS that we believe should be the subject of an FCN under section 409(h) of the FD&C Act.

D. Simultaneous Submission of a Food Additive Petition and an FCN

Section 409(h)(3)(A) of the FD&C Act states that the notification process must 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 is not permitted.

E. Scope of an Effective FCN

1. For Whom is a Notification Effective?

Section 409(h)(2)(C) of the FD&C Act states that an FCN 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. For the purposes of section 409(h)(2)(C) of the FD&C Act, the manufacturer for which the FCN may be effective may be a supplier of the FCS.[(1)] Therefore, FDA believes that, for example, a new notification should be submitted in the following situations:

a. for a manufacturer other than the manufacturer specified in a prior notification; or
b. if substantive[(2)] changes are made in the specifications for the FCS; or
c. if changes are made in the manufacturing method that result in substantive changes in the identity of the product or its impurities, and/or levels of impurities.[(3)] (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
d. for conditions of use or levels of use not included in the prior notification.

2. Who May Rely on an Effective Notification?

Because an FCN is effective only for the manufacturer, substance, and intended use identified in the notification, any person wishing to rely on an FCN generally will need to demonstrate that the FCS being marketed has been manufactured or supplied by the manufacturer identified in the FCN and is being used under the conditions that are the subject of the FCN. 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.

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) of the FD&C Act

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

Under the food additive petition process for FCSs, FDA would commonly receive a food additive petition from a chemical manufacturer that produced a chemical used to manufacture a food additive that was an FCS. 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 any residual 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 us about the use of monomeric starting materials and other starting materials for the production of food additives that are FCSs 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 starting materials for food additives where the starting material and the food additive are both FCSs under section 409(h)(1) of the FD&C Act. Such notifications must demonstrate the safety of the starting material under its intended conditions of use in the production and use of the food additive. 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 starting material.

In cases where FDA does not object to such notifications for a starting material for a food additive and the safety of the food additive under its intended conditions of use has been demonstrated, we believe that the effective notification for the starting material would meet the requirements under section 409(a)(3) of the FD&C Act to permit the food additive to be legally marketed. Thus, separate notifications for starting materials and food additives produced from starting materials will not be necessary.

F. Fiscal Requirements

In accordance with section 409(h)(5)(A)(i) of the FD&C Act, the FCN program must not operate in any fiscal year for which the program is not funded as described in section 409(h)(5) of the FD&C Act. FDA currently believes that, to use resources effectively, we 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 FD&C Act. Accordingly, 21 CFR 170.104(c)(3) would permit FDA to object to an FCN solely on the basis that some portion of the 120-day review period occurs during a period when the FCN program is not funded.

III. Format of an FCN for an FCS

FDA is requesting that a copy of an FCN be submitted. Special instructions for submitting an electronic copy of a notification are presented in Section IV. below. FCNs should be submitted to:

Notifications Control Assistant,
Office of Food Additive Safety, HFS-275
Center for Food Safety & Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740.

Because of the short time provided for us to review an FCN, it is important that the FCN be well organized. We recommend the following organizational format for FCNs:

Format items within the FCN 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.

An FCN 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 FCNs before submitting an FCN. The guidance documents are available on FDA's web site at (Food Ingredients and Packaging guidance documents). In addition, notifiers are urged to contact FDA regarding questions not addressed in the guidance. In accordance with 21 CFR 170.101, an FCN for an FCS should include the information listed below.

A. Comprehensive Summary

An FCN should include 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 FD&C Act, including a comprehensive discussion of all information and data submitted in the notification. In most cases, the requirement of presenting a comprehensive summary can be addressed by proper completion of FDA Form 3480 and attachment of necessary data.

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 Food Contact Notifications and Food Additive Petitions for Food Contact Substances: Toxicology Recommendations" (see also FDA Form 3480- Part III, Section A)) 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 scheme, if FDA determines that a notifier's discussion is not sufficiently comprehensive to show that the notifier has considered all relevant facts, we 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

(see FDA Form 3480- Part II, Sections A through C, and E)

An FCN should include 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

(see FDA Form 3480- Part II, Section D)

An FCN should include 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 Food Contact Notifications and Food Additive Petitions for Food Contact Substances: Chemistry Recommendations.")

D. Intended Technical Effect

(see FDA Form 3480- Part II, Section D)

An FCN should include 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 Food Contact Notifications and Food Additive Petitions for Food Contact Substances: Chemistry Recommendations.")

E. Estimation of Intake

(see FDA Form 3480- Part II, Sections F and G)

An FCN should include 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 Food Contact Notifications and Food Additive Petitions for Food Contact Substances: Chemistry Recommendations.")

F. Toxicity Information

(See FDA Form 3480- Part III)

A notifier should tabulate information on relevant toxicity studies in FDA Form 3480 and include comprehensive toxicological profiles and complete studies in the attachments to the form. (See "Guidance for Industry: Preparation of Premarket Notifications for Food Contact Substances: Toxicology Recommendations.")

G. Environmental Information

(see FDA Form 3480- Part IV)

FCNs must include 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. Alternatively, an environmental assessment may be included in the notification.

H. FDA Form No. 3480

A completed and signed FDA Form No. 3480.

The name and address of the notifier should be reported on FDA Form No. 3480.

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. FDA is currently developing guidance for submission of electronic versions of FCNs. Further guidance will be made available as it is developed.

V. Disclosure of Information in an FCN

Under section 409(h) of the FD&C Act, FDA is not permitted to disclose any information in an FCN for 120 days after receipt of the FCN by FDA. Under 21 CFR 170.102(c) FDA's

conclusion regarding the review of an FCN will be available publicly once we have completed our review. For the purposes of this section, FDA's review will be completed when either 120 days have passed after receipt of an FCN or FDA has issued a letter objecting to the FCN.

Under 21 CFR 170.102(e), at the completion of FDA's 120-day review period, the information in an FCN, 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 21 CFR 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 FCNs that the notifier chooses to withdraw prior to completion of FDA's review, FDA will maintain the confidentiality of the information in the FCN under 21 CFR 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 an FCN

A. Acknowledgment of an FCN

FDA intends to acknowledge receipt of an FCN 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 carefully the description of the FCS and intended conditions of use in the acknowledgment letter because this will be the description and intended conditions of use that FDA may list in its inventory of effective notifications. (Notifiers may wish to provide language for the acknowledgement letter as part of the information on identity and intended conditions of use.)

During the course of review of an FCN, 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 an FCN

If any component of a notification required under 21 CFR 170.101 is missing, FDA will not accept the notification for review. In most such cases, FDA will provide the notifier a brief

period of time to supply the missing information or withdraw the FCN. If the FCN is not withdrawn and the missing information is not forthcoming, FDA will issue a "Nonacceptance letter" completing review of the submission. If the missing information is submitted before issuance of the nonacceptance letter, the 120-day review period will begin on the date of receipt of the missing information (21 CFR 170.104(b)(1)). In addition, under 21 CFR 170.100(b)(1), 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 21 CFR 170.39. In cases where we do not accept a notification based on deficiencies in information, FDA expects to inform the notifier in writing within 45 days of receipt of the submission.

C. Objection by FDA

Under section 409(h) of the FD&C Act and 21 CFR 170.104(c), FDA may object to an FCN if:

1. The notification is incomplete because it does not comply with the general criteria for an FCN in 21 CFR 170.100.
2. FDA does not agree that the notifier has demonstrated that the substance is safe under the intended conditions of use.
3. A portion of the 120 days after FDA's receipt of the notification occurs within a fiscal year for which the FCN program does not operate in accordance with section 409(h)(5) of the FD&C Act.

If FDA objects to an FCN, we 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. Under 21 CFR 170.104(c)(1), the date of FDA's objection letter is the date of FDA's objection for the purposes of section 409(h)(2)(A) of the FD&C Act.

D. Final Letter

FDA is not required to issue a letter if we do 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 FCNs

To provide for efficient enforcement of the FD&C Act, FDA maintains an inventory of effective FCNs. FDA expects that this inventory will be the primary vehicle for informing the public of effective FCNs. 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 (https://www.accessdata.fda.gov/scripts/fdcc/?set=FCN).

VII. Withdrawal Without Prejudice

In accordance with 21 CFR 170.104, a notifier may withdraw an FCN for an FCS, without prejudice to a future submission, at any time before 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 FCN 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 an FCN No Longer is Effective

In accordance with 21 CFR 170.105(a), FDA may declare that an FCN no longer is effective if the data available to us 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 an FCN should continue to be effective. As stated in 21 CFR 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 21 CFR 170.105(b), the notifier would be given an opportunity to address adequately the information raising FDA's concerns. FDA will establish a time frame for the notifier to respond our concerns. If the notifier is not able to address adequately our concerns within that time, FDA will publish a notice in the *Federal Register* stating our conclusion that the notification no longer is effective and the reasons for such conclusion. After publication of such notice, the notification will no longer be effective (21 CFR 170.105(c)). Under 21 CFR 170.105(d), our determination that a notification is no longer effective is final agency action subject to judicial review.

IX. Prenotification Consultations (PNCs)

FDA encourages prenotification consultations to facilitate the development of a complete FCN. Specifically, in situations where present guidance is not completely applicable to a given situation, a prenotification consultation may be advisable. Generally, there are three circumstances where FDA recommends a prenotification consultation. First, in all cases, FDA recommends a prenotification consultation before the submission of a petition for a use of an FCS. Such a meeting may be used to verify that a petition is required and that an appropriate level of information is supplied in the petition. Second, FDA recommends a prenotification consultation when there are uncertainties about how certain 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 ADI that different choices for the no effect level may cause the resulting ADI to be larger or smaller than the EDI, a prenotification consultation is recommended. Third, a prenotification consultation 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 consultation is recommended if

different interpretations of data in a bioassay could change the conclusion regarding the likely carcinogenicity of the substance.

X. Format of a Notification for an FCS Formulation

Under 21 CFR 170.106(a), FDA will accept notifications for FCS 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 us should the number of notifications become unexpectedly high. Therefore, 21 CFR 170.106(b) states that we may prohibit the submission of notifications for FCS formulations at any time by publishing a notice in the *Federal Register* stating that we do not have sufficient resources to review such notifications.

Such notifications are to be distinguished from FCNs in two ways. First, notifications for FCS formulations are for a particular mixture of two or more FCSs. Second, each of the substances in the formulation must be 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 FD&C Act. Because all substances in a notification for an FCS formulation already should be authorized for their intended uses, such notifications are not required under section 409 of the FD&C 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 FCS in the formulation. A notifier for a formulation would ordinarily submit only a completed FDA form 3479 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 one copy of a notification for an FCS formulation 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 FCS formulations should be submitted to:

Notification Control Assistant,
Office of Food Additive Safety, HFS-275
Center for Food Safety & Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740-3835.

XI. Paperwork Reduction Act of 1995

This guidance contains information collections that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521).

The time required to complete this information collection is estimated to average 25 to 150 hours per response, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to:

Office of Food Additive Safety
Division of Food Contact Substances, HFS-275
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740

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. The OMB control number for this information collection is 0910-0495 (To find the current expiration date, search for this OMB control no. available at https://www.reginfo.gov/public/do/PRAMain).

Document History

- June 2000 – First edition of guidance was issued.
- May 2002 – Second edition of guidance was issued.
- October 2021 – The guidance was updated to include Paperwork Reduction Act information and non-substantive formatting or editorial revisions.

Endnotes

1. An FCN may specify more than one manufacturer or supplier of an FCS. However, an FCN for an FCS may only address one food additive. Also, in addition to the manufacturer or supplier specified in the notification, an FCN is effective for customers of the manufacturer or supplier.

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

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