GUIDANCE DOCUMENT

Guidance for Industry: Preparing a Claim of Categorical Exclusion or an Environmental Assessment for Submission to CFSAN - Appendix A

MAY 2006

Final

Issued by:

(/regulatory-information/search-fda-guidance-documents/guidance-industry-preparing-claim-categorical-exclusion-or-environmental-assessment-submission-cfsan-6)
Center for Food Safety and Applied Nutrition, Office of Food Additive Safety

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Below are recommendations for the suggested format and types of information to submit to the agency in an environmental assessment. An alternative approach may be used if the approach satisfies the requirements of the applicable statutes and regulations.

1. **Date:** The environmental assessment (EA) should provide the date the EA was prepared.
2. **Name of submitter:** The EA should identify the submitter.
3. **Address:** The EA should provide the business address for the submitter.
4. **Description of the proposed action:** FDA recommends that the EA describe the proposed action by addressing the following:
    a. **Requested approval:** The EA should describe the requested approval by naming the substance that is the subject of the action, by describing the proposed use of the substance, including any limitations, and by providing the use level. The EA should identify the proposed regulation by providing the section(s) of the *Code of Federal Regulations* (*CFR*) to be amended, if known. FDA recommends that the description of the proposed use in the EA is consistent with the use requested and described in other sections of the petition.
    b. **Need for action:** The EA must include brief discussions of the need for the proposal (21 *CFR* 25.40). The description of the proposed action, e.g., the intended technical effect of the food additive, should be consistent with other sections of the petition.

c. **Locations of use:** [1] The EA should describe briefly the locations where the substance will be used. FDA recommends that you describe the sites where the substance will be incorporated into food products, *e.g.*, food-processing plants. For locations where consumers prepare and ingest food products, usually in homes and restaurants, FDA recommends that you state, if applicable, that the product will be consumed as a component of the human diet in patterns corresponding to national population density.

d. **Locations of disposal:** The EA should describe disposal sites for the substance. If appropriate, the following sentence may be used in the EA to describe disposal sites: "Disposal is expected to occur nationwide with the substance, or its excretion products, entering publicly owned treatment works (POTW) or septic tanks following consumption."

5. **Identification of substances that are the subject of the proposed action:** FDA recommends that the EA should identify fully the substance by providing sufficient information to locate accurately data about the substance in the scientific literature and to closely identify related substances. Information presented elsewhere in the petition may be repeated here so that the EA is a complete and independent document. FDA recommends that the EA contain:

   - Complete nomenclature
   - Chemical Abstracts Service (CAS) registry number (if available)
   - Molecular weight
   - Molecular formula
   - Structural (graphic) formula
   - Physical description (*e.g.*, triglyceride, solid at room temperature, etc.)

6. **Introduction of substances into the environment:**

   a. **Introduction of substances into the environment as a result of manufacture:** FDA does not ask routinely that information about environmental introductions resulting from the production of an FDA-regulated article be included in an EA. [2] However, the preparer of an EA should determine if any extraordinary circumstances pertain to the manufacture of the article. Extraordinary circumstances include situations where 1) unique emission circumstances are not addressed adequately 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 associated with a proposed action may affect adversely a species or the critical habitat of a species determined under the Endangered Species Act or the Convention on International Trade in Endangered Species of Wild Fauna and Flora to

be endangered or threatened, or wild fauna or flora that are entitled to special protection under some other Federal law. If extraordinary circumstances apply to the manufacture of the macronutrient replacement substance, such as those outlined above, the EA must discuss any reasonable alternative course of action that offers less environmental risk or that is preferable environmentally to the proposed action (21 *CFR* 25.40(a)). If no extraordinary circumstances apply to the manufacture of the substance, FDA recommends that the EA includes a statement to that effect.

b. **Introductions of substances into the environment as a result of use:** The EA should discuss any introductions into the environment resulting from the use of the substance. CFSAN believes that, in general, introductions of macronutrient replacements into the environment as a result of their use will be minimal. Macronutrient substitutes are intended to be incorporated into food and to remain with food until ingestion by consumers. You may consider using the following statement in the EA, if appropriate: "There will be little or no introduction of (insert name of substance) into the environment as a result of its use because it is incorporated almost completely into food and remains with food through ingestion by consumers." If this statement does not apply, FDA recommends that the EA include an estimate of the quantity and concentration of substances introduced into the environment resulting from the use of the macronutrient replacement. Such substances may include the macronutrient replacement substance, its degradation products, and/or any other substance resulting from the use of the food additive.

c. **Introductions of substances into the environment as a result of disposal:** We recommend that the focus of the environmental review of macronutrient replacements be on the disposal of human waste products containing the substance and/or its products of digestion and metabolism.

> **NOTE: FDA does not believe that further analysis under Format Items 6, 7, and 8 would be necessary if human metabolism data show that the excretion products that result from the ingestion and metabolism of the substance are the same as the metabolic products resulting from the ingestion of human food. If this is the case, FDA recommends that you make a statement to this effect and provide information to support your statement. If this is not the case, FDA recommends that you address these format items as indicated.**

The EA should include an estimate for 1) the maximum yearly market volume of the substance for the proposed use based on total fifth year production estimates, and 2) the expected introduction concentration (EIC) of the substance and its degradation

products present in wastewater effluents and in sewage sludge generated in POTWs. These estimates should consider the volumes of wastewater effluent and the amount of sewage sludge generated in POTWs. FDA recommends that you state all assumptions, provide the basis for the calculations, and show all calculations. If your calculations and the basis for those calculations are protected from disclosure under 18 U.S.C. 1905, 21 U.S.C. 331(j) or 360j(c), such data and information must be submitted separately in a confidential section of the petition and must be summarized, to the extent possible, in the EA (21 *CFR* 25.51(a)). Specific guidance that you may consider for calculating the EICs for the substance in the aquatic, terrestrial, and atmospheric environments is provided below.

i. **Calculating the EIC for the substance in the aquatic environment:** FDA believes that a conservative calculation of the EIC for the substance in the aquatic environment is based on the following assumptions: a) even distribution of the food substance throughout the U.S. per day, b) total consumption of the food substance, and c) no metabolism and depletion mechanisms. An option for calculating the EIC is as follows:

   EIC--Aquatic (ppm) = A x B x C x D, where

   A = kg/year production volume of the substance_

   B = 1/liters per day entering POTWs [3]

   C = year/365 days

   D = 10^6 mg/kg (conversion factor)

   FDA believes that a more realistic calculation of the EIC for the substance in the aquatic environment would consider human metabolism and environmental depletion mechanisms that occur in the wastewater treatment process (*e.g.*, adsorption, biodegradation, and hydrolysis) if such information is available. If you use a different method to calculate the EIC, FDA recommends that you state clearly your assumptions, show your calculations, and provide the basis for these calculations.

ii. **Calculating the EIC for the substance in the terrestrial environment:** The substance may enter the terrestrial environment when sewage sludge from a POTW is applied to land. Substances with an adsorption coefficient (K_{oc}) $\geq$ 1000 might adsorb significantly to sewage sludge. FDA based the sample calculation of the EIC for the terrestrial environment on the following assumptions: a) even distribution of the food substance throughout the U.S. per day, b) total consumption of the food substance, c) no degradation of the substance, and d) all of the substance adsorbs to sewage sludge.

   EIC--Terrestrial (ppm) = A x B x C x D, where

   A = kg/year production volume of the substance_

B = 1/6.4 x 10^9 kg sewage sludge/year [4]

C = 0.555 [5]

D = 10^6 mg/kg (conversion factor)

FDA believes that a more realistic calculation of the EIC for the terrestrial environment would consider human metabolism and environmental depletion mechanisms that occur in the wastewater treatment process (*e.g.*, adsorption, biodegradation and hydrolysis), if such information is available. If you use a different method to calculate the EIC, FDA recommends that you state clearly your assumptions, show your calculations, and provide the basis for these calculations.

Of the 44.5% of sewage sludge that is not land applied, 22% is incinerated, 14% is landfilled, 7.5% is put to other beneficial uses such as daily landfill covers, and 1% is disposed of by other means. [4] Introductions into the environment from these routes of disposal are expected to be minimal and therefore FDA does not generally recommend they be considered.

iii. **Calculating the EIC for the substance in the atmospheric environment:** The concentration expected in the atmospheric environment should be considered for substances that are likely to volatilize significantly from the aquatic or terrestrial environments. We generally do not expect macronutrient replacement substances to be volatile.

FDA recommends that the EIC(s) will be used to calculate the expected environmental concentrations (EEC(s)) [6] of the substances under Format Item 7 and, in combination with information provided under Format Item 8, to determine whether the proposed action has potential for significant environmental effects.

7. **Fate of substances released into the environment:** FDA recommends using the EIC(s) calculated above in Format Item 6, and available information regarding the fate parameters for the substance when estimating the expected environmental concentration(s) (EEC(s)) for the substance and its degradation products. [7] Environmental fate parameters may include the following:

   a. **Physical/chemical properties** such as water solubility, dissociation constants in water, *n*-octanol/water partition coefficient (K_{ow}), and vapor pressure or Henry's Law constant.

   b. **Environmental depletion mechanisms** such as adsorption coefficient (K_{oc}), aerobic and anaerobic biodegradation, hydrolysis, and photolysis. [8]

   When you estimate the EEC in various environmental compartments, FDA recommends that you also consider dilution by water in receiving streams or by soil mixed with sewage sludge. If the chemical has a high K_{ow}, it may persist in the

environment, therefore, you should consider its potential to bioaccumulate. You may want to use FDA's *Environmental Assessment Technical Handbook* (Table of Contents as Attachment 1 (/food/ingredients-additives-gras-packaging/guidance-industry-preparing-claim-categorical-exclusion-or-environmental-assessment-submission-4)) that contains technical assistance documents as guidance for environmental fate testing (Sections 3.01-3.12). You also may want to consider using environmental fate test protocols based on scientifically validated methods issued by other organizations, *e.g.*, the Environmental Protection Agency (EPA; see 40 CFR part 796 for EPA's Chemical Fate Testing Guidelines, or EPA's Office of Pollution Prevention and Toxic Substances (OPPTS) Harmonized Test Guidelines: 835 - Fate, Transport and Transformation Test Guidelines (https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-835-fate-transport-and-transformation-test)) and the Organization for Economic Co-operation and Development (OECD; the OECD's Guidelines for the Testing of Chemicals (http://www.oecd.org/document/22/0,2340,en_2649_34377_1916054_1_1_1_1,00.htm) (http://www.fda.gov/about-fda/website-policies/website-disclaimer), Section 1--PHYSICAL-CHEMICAL PROPERTIES and Section 3--DEGRADATION AND ACCUMULATION are available on the Internet.)

We suggest that you use a table, such as the Sample Data Summary Table (Attachment 2 (/food/ingredients-additives-gras-packaging/guidance-industry-preparing-claim-categorical-exclusion-or-environmental-assessment-submission-5)), to summarize environmental fate data.

8. **Environmental effects of released substances:** FDA recommends that the EA compare the EEC of the substance and its degradation products to the relevant toxicity endpoints (*i.e.* LC_{50}. EC_{50}, NOEL) so that the potential for adverse environmental effects may be determined. The EA should report, or incorporate by reference, existing data relating to the environmental effects of the substance and its degradation products. The EA should report the toxicity of the substance or its degradation products to organisms that may be exposed in the environment, *e.g.*, vertebrates, invertebrates, plants, fungi, and bacteria. FDA recommends that you consider environmental testing if no effects data are available, or are available only for species not representative of those found in environments predicted to have significant concentrations of the substance or its degradation products. Chronic toxicity testing should be considered for compounds that persist in the environment and have the potential to bioaccumulate or are introduced continuously into the environment. You may want to use FDA's *Environmental Assessment Technical Handbook* (Table of Contents as Attachment 1) that contains protocols (Sections 4.01-4.12) that may be used for conducting environmental effects tests. You also may want to consider using environmental toxicity test protocols based on scientifically validated methods used by other organizations, *e.g.*, EPA (see 40 CFR part 797 for EPA's Environmental Effects Testing Guidelines, or EPA's OPPTS Harmonized Test Guidelines: 850 - Ecological Effects

Test Guidelines (https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-850-ecological-effects-test-guidelines)) and OECD (the OECD's Guidelines for the Testing of Chemicals (http://www.oecd.org/document/22/0,2340,en_2649_34377_1916054_1_1_1_1,00.html) (http://www.fda.gov/about-fda/website-policies/website-disclaimer), Section 1--PHYSICAL-CHEMICAL PROPERTIES and Section 3--DEGRADATION AND ACCUMULATION are available on the Internet).

We suggest that you use a table, such as the Sample Data Summary Table (Attachment 2), to summarize environmental effects data. FDA believes that adverse environmental effects may occur if a comparison of the EECs with the toxicity endpoints shows that an EEC exceeds the toxicity endpoint after taking appropriate safety factors into consideration.

The EA should discuss the potential effects of the substance on the efficient operation of POTWs or individual household disposal systems (primarily septic tanks). FDA recommends that you consider, as part of such a discussion, fate information provided under Format Item 7, and, if applicable, any testing undertaken to evaluate this issue, *e.g.*, studies on primary or secondary wastewater treatment processes.

If a significant percentage of the substance is expected to remain with sewage sludge and subsequently be applied to agricultural or forestry lands, FDA recommends that you discuss the potential effects of the substance on the physical/chemical properties of the soil (*e.g.*, soil structure, pore size, water holding capacity, water percolation, cation exchange capacity).

Existing laws and regulations may apply to introductions resulting from use and disposal of the substance. If this is the case, FDA recommends that the EA cite the specific laws or regulations and discuss how such laws or regulations will control the introduction of substances into the environment and prevent adverse environmental impacts. FDA recommends that such a discussion consider, based on the environmental fate and effects information provided under Format Items 7 and 8, whether the proposed use presents unique emissions circumstances that would threaten a violation of such laws and regulations.

If you think that there are uncertainties about the potential for, or significance of, environmental effects, we recommend that you consult CFSAN for specific guidance.

9. **Use of resources and energy:** FDA recommends that the EA state whether the petitioned substance is intended to compete with and replace another food component already in use such that there is essentially no effect on the use of natural resources and energy. If so, the EA should contain a brief justification for this conclusion and identify the substance(s) being replaced. Otherwise, FDA recommends that the EA specify the natural resources, including land use, minerals, and energy, required to produce, transport, use, and/or dispose of wastes generated from production, use, and/or disposal of the petitioned substance. If the substance is derived from a plant or animal, the EA must specifically state

whether extraordinary circumstances exist, such as when the action may adversely affect a species or the critical habitat of a species determined under the Endangered Species Act or the Convention on International Trade in Endangered Species of Wild Fauna and Flora to be endangered or threatened, or wild fauna or flora that are entitled to special protection under some other Federal law (21 *CFR* 25.21(b)).

10. **Mitigation measures:** The EA must describe mitigation measures, which are not included in the proposed action or alternatives, for the purpose of avoiding or mitigating potential adverse environmental impacts associated with the proposed action (40 *CFR* 1502.14(f) and 1502.16(h); 21 *CFR* 25.40(a)). The EA must include the environmental impacts of the proposed action (21 *CFR* 25.40(a)). Thus if, based upon a review of adequate and complete data and information, no adverse environmental effects have been identified, you need to state that in the EA.
11. **Alternatives to the proposed action:** If potential adverse environmental impacts have been identified for the proposed action, the EA must 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 the petitioner could undertake) (40 *CFR* 1502.14 and 1502.16). The EA must describe any reasonable course of action that offers less environmental risk or that is environmentally preferable to the proposed action (21 *CFR* 25.40(a)). The EA should discuss the environmental benefits and risks of the proposed action and of each alternative.
12. **List of preparers:** The EA should list the name, job title, and qualifications (*e.g.*, educational background or professional discipline) for each person preparing the EA. The EA must identify any persons or agencies consulted (21 *CFR* 25.40(a)).
13. **Certification:** FDA recommends that the EA 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 of the knowledge of (insert company name)."

    _____

    (Date)

    _____

    (Signature of responsible official)

    _____

    (Name and title of responsible official, printed)
14. **References:** The EA should provide complete citations for all material referenced in the EA either in footnotes within the EA or as endnotes under this format item.
15. **Attachments:** The EA should provide a list of any materials that are attached to the EA. Confidential materials must not be attached to the EA, but must be provided in a separate section of the petition, as provided in 21 *CFR* 25.51(a).

Notes

(1) The term "Locations of use" refers to the sites of use of the manufactured substance, not the locations where the substance itself is produced or manufactured. If the suggested descriptions of use and disposal sites provided in subsections 4.c. and 4.d. are not applicable for the substance, FDA recommends that you provide the appropriate descriptions. (Return to text)

(2) After reviewing hundreds of EAs, the agency found that FDA-regulated articles produced in compliance with applicable emission and occupational safety requirements do not affect the environment significantly. Therefore, as provided in 21 *CFR* 25.40(a), the EA must focus on relevant environmental issues relating to the use and disposal from the use of FDA-regulated articles. (Return to text)

(3) The total flow of wastewater to POTWs in the United States is 32,175 million gallons per day (1.22×10^{11} liters per day). Table C-3, Appendix C, *1996 Clean Water Needs Survey*, U.S. Environmental Protection Agency. (Return to text)

(4) The volume of biosolids from POTWs was projected to be 7.1 million tons, or about 6.4 W 10^9 kg, for the year 2000 (*Biosolids Generation, Use, and Disposal in the United States*. EPA 530-R99-009; September 1999, p. 30). (Return to text)

(5) The proportion of biosolids from POTWs projected to be land applied or composted was estimated to be 55.5% for the year 2000. (*Biosolids Generation, Use, and Disposal in the United States*. EPA 530-R99-009; September 1999, p. 35). (Return to text)

(6) The EEC is the expected concentration of a substance that organisms would be exposed to in the environment after consideration of fate parameters. The EEC usually is lower than the EIC. (Return to text)

(7) If the degradation products of the substance are persistent in the environment, the EA should identify these products and provide any availble fate data. (Return to text)

(8) If a depletion mechanism is being used to claim a reduction in the expected introduction and/or environmental concentrations, FDA recommends that you provide an analysis of the depletion mechanism (*e.g.*, according to a standard test method, analysis of expected exposure time in the environment, test protocols and test data). (Return to text)

The above guidance document supercedes the previous version dated September 2003.

Submit Comments

Submit comments on this guidance document electronically via docket ID: FDA-2013-S-0610 (https://www.regulations.gov/docket/FDA-2013-S-0610) - Specific Electronic Submissions Intended For FDA's Dockets Management Staff (i.e., Citizen Petitions, Draft Proposed Guidance Documents, Variances, and other administrative record submissions)

If unable to submit comments online, please mail written comments to:

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