UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
Office of Chemical Safety and Pollution Prevention
Office of Pesticide Programs
Registration Division
Chemistry, Inerts, and Toxicology
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May 2023

General Guidance for Requesting the Approval of a New Nonfood Use Inert Ingredient[1] or Amending a Currently Approved Nonfood Use Inert Ingredient under PRIA 5

The general process for submitting a nonfood use request to the Environmental Protection Agency, herein referred to as the EPA or the Agency, under PRIA 5 is provided below.

The following topics are outlined in this guidance document:

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Pre-submission Consultation

If there are any questions that cannot be answered via email or if this is the first time the submitter is preparing an inert ingredient petition, the Agency recommends that a submitter request a pre-submission meeting with the Inert Ingredients Team prior to submitting your request. This is an informal discussion to determine if the submitter has enough information to proceed with the review process. The submitter will need to provide a brief summary of the

[1] For low-risk polymer nonfood submissions, please see the document titled "General Guidance for Requesting the Establishment of a Tolerance Exemption for a Low Risk Polymer or Nonfood Use Approval of a Low Risk Polymer under PRIA 5."

information they have regarding the inert ingredient, including use information, limitations, and toxicity and environmental fate data as well as their list of questions at least two weeks in advance of the meeting. This meeting will help determine if additional information is needed to make a safety finding regarding the chemical before submitting a formal application to the Agency. Pre-submission meetings can be requested at InertsBranch@epa.gov.

Applicable PRIA 5 Fees

Inert ingredient approvals are a covered application under PRIA 5. See the PRIA 5 Fee Category Table (https://www.epa.gov/pria-fees/pria-fee-category-table-inert-ingredients) for descriptions of the inert ingredient categories, their PRIA 5 fees and corresponding decision review times.

The nonfood use inert ingredient PRIA 5 codes covered in this document are I004, I005, I006, and I007. Additional information regarding PRIA 5 (e.g., fee waivers, exemptions, reductions, and refunds and Q and A's) can be found at https://www.epa.gov/pria-fees.

Submission Contents

The submission package should include a transmittal document, EPA Form 8570-1, an informative summary of the submission, and a complete copy of all data used to support your request. See "Data Formatting" section of this document for data formatting requirements.

1. **Transmittal document** (often submitted as a cover letter) should include:
    a. Identity and contact information of the Submitter/Applicant and Agent (if applicable). If an agent is representing the applicant, then a letter from the company granting permission to act on their behalf needs to accompany the submission.
    b. Transmittal Date
    c. Subject line that reads one of the following.
        i. "Request for approval of a new nonfood use inert ingredient: PRIA 5 category I004" [Insert your inert ingredient chemical name and CAS Reg. No.] or
        ii. "Request to amend a currently approved nonfood inert ingredient with new use pattern (new data): PRIA 5 category I005" [Insert your inert ingredient chemical name and CAS Reg. No.] or
        iii. "Request to amend a currently approved nonfood inert ingredient with new use pattern (no new data): PRIA 5 category I006" [Insert your inert ingredient chemical name and CAS Reg. No.] or
        iv. "Request to approve a substantially similar nonfood use inert ingredient with similar use pattern: PRIA 5 category I007" [Insert your inert ingredient chemical name and CAS Reg. No.]
    d. Brief summary of your request including the regulatory action being requested (e.g. proposed use, purpose in formulation, any limits in formulation, other known uses, etc.)
    e. A list of the data/information you are attaching to your package in support of your request

2. **EPA Form 8570-1** can be found at https://www.epa.gov/sites/default/files/2013-07/documents/8570-1.pdf . For instructions on how to complete this form for an inert ingredient please see Appendix A.

3. **Submission Summary:** Your submission should contain a summary of your request; a summary of the data, information, and arguments submitted or cited in support of the submission; and a justification for why the submitted data is appropriate and sufficient to make a safety finding.

    a. Summary of the request
        i. Name, chemical identity, and composition of the inert ingredient.
        ii. Indicate the proposed purpose in formulation and a full description of the use pattern. Include any proposed limitations.
        iii. Current uses of the chemical including any existing tolerance or tolerance exemptions for the chemical, as well as non-pesticidal uses.
    b. Summary of the data: It is not acceptable to just provide results from literature searches, studies, modeled data, etc. without summarizing the information. Please give clear explanations as to:
        i. Relevancy of each submitted study: This should include a rationale of how the submitted data supports the request and a discussion on the adequacy of the data.
        ii. Study description, results and conclusions, including information about the chemical tested (purity, CAS Reg, No), number and strain of animals used (if an animal study), doses, length of treatment, parameters measured, interpretation of results and NOAELs, LOAELs, if selected.
        iii. A discussion of any data gaps and a justification as to why this information is not needed to make a safety finding for your chemical.
    c. Summarize how, based on the toxicity, expected exposure, and environmental fate properties of the chemical; the proposed use of the chemical would be considered safe for human health and the environment.
    d. Key Studies- Identify the key studies used to support your submission. A pre-submission meeting or conference call, as noted above, may be helpful in identifying the key studies you will be using to support your request.

4. **Data**: Information/data typically used by the Agency to make a decision for a new nonfood use inert ingredient include physical/chemical properties, toxicity data from animal studies, metabolism data, ecotoxicity, exposure studies, and environmental fate and effects data. Please see the "Data Formatting" section of this document for information on how to arrange your submission. Any data right claims should be clearly stated in the petition summary.
    a. **Physical/chemical properties** (e.g., Series 830 Group B type data)-Make sure to include a statement indicating whether or not the material is a nano material. If it is a particulate, give the particle size.
    b. **Toxicity Data**: Toxicological information should be addressed for all of the following.
        i. Acute toxicity: the acute oral toxicity study must be submitted. Data from surrogates or from alternative methods to animal testing may be submitted to

address dermal, inhalation, eye/skin irritation and skin sensitization.

1. Oral
2. Dermal
3. Inhalation
4. Skin irritation
5. Eye irritation
6. Skin sensitization

ii. Chronic/repeat dose toxicity data: At least one animal repeated dose toxicity study must be submitted

iii. Reproduction/Developmental: if no data are available on the chemical of interest, data from surrogate chemicals or predictive Quantitative Structure Activity Relationship (QSAR) models may be submitted.

iv. Mutagenicity: *in vivo* or *in vitro* data may be submitted

v. Carcinogenicity- if data is not included, the submitter should provide the results of a predictive QSAR model (e.g., the OncoLogic™ Model, OECD QSAR Toolbox, or

equivalent predictive models) and/or provide a scientific explanation why it would not be carcinogenetic

vi. Neurotoxicity

vii. Endocrine disruption

viii. Immunotoxicity

c. **Human/animal metabolism**-

i. Is the chemical absorbed by the body?

ii. How much of the chemical is excreted and how is it excreted (e.g. urine, feces)?

iii. Will it bioaccumulate?

iv. Are the degradates/metabolites of the chemical more toxic than the parent chemical? If no metabolism information is available, registrants are asked to provide potential metabolic/degradation products based on currently available scientific information.

d. **Exposure**- Identify all anticipated exposure pathway/s (e.g., residential and occupational) for both pesticidal and non-pesticidal uses of the chemical.

i. Residential-dermal, inhalation, and incidental oral from residential uses such as personal care products, home use, handler exposure and post application exposure, pet use, etc. Approximate or high-end value of the percentage in non-pesticidal formulations

ii. Occupational-what is the anticipated exposure to workers mixing, loading, and applying the inert to the treatment area? Make sure to also include a discussion of post-application exposure.

e. **Environmental Fate and Effects**-(e.g., Series 835 Group A & B type information) if there is no data on the chemical provide the Estimation Program Interface model (EPISuite)[2] model data for the chemical.

i. Biodegradation/Persistence in the environment

ii. Expected fate of the chemical-may use the physical/chemical properties or fugacity models to describe the anticipated fate

[2] https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface

f. **Ecotoxicity**- Please provide a rationale for why ecotoxicity is not expected to be of concern. Submit all available studies. If no data are available, the results of the EPI Suite or the Ecological Structural Activity Relationship model (ECOSAR)[3] should be provided.
   i. Aquatic
   ii. Avian
   iii. Invertebrate

Sources of Data

Sources of information that may be submitted to the Agency include, but are not limited to, OCSPP guideline studies[4]; publicly available literature and data, including peer-reviewed assessments and journals (e.g. WHO, OECD SIDS, IUCLID, EPA HPV, IRSI, etc.); modeled data[5]; and analog/surrogate data.

If sufficient data does not exist on the submitted chemical and analog/surrogate data (e.g. Structural Activity Relationship (SAR) data) are being submitted, please include a scientific discussion as to why the surrogate data are relevant/adequate for read across/bridging to the subject chemical. A comparison table of physicochemical properties, molecular weight, chemical structure, similarity scores, and available toxicity information should be provided, together with a rationale as to why it is appropriate to bridge data between the chemicals. If sufficient explanation and rationale is not provided, then the application will be rejected, and the data will not be considered for review.

Unacceptable sources of data include:

1. MSDS sheets: A MSDS is only useful if the product contains 100% of the chemical in question and it clearly states this on the MSDS. In addition, in order for the toxicity data to be used by the Agency in the risk assessment process it must come from an acceptable accessible source and the source must be cited on the MSDS and a copy of the study must also be provided.
2.
3. Unpublished studies that are submitted without the full study report.

Data Formatting

1. **PR Notice 2011-3[6]:** there are standard data format requirements for all study data submitted to the Agency under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and Certain Provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA). These requirements are outlined in (PR) Notice 2011-3. Submitted data packages that do not conform to these requirements may be rejected by the Agency's Document Processing Desk and returned to you for revision.

[3] https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model
[4] OCSPP Harmonized Test Guidelines: http://www.epa.gov/ocspp/pubs/frs/home/guidelin.htm
[5] Models: http://www.epa.gov/pesticides/science/models_pg.htm
[6] https://www.epa.gov/pesticide-registration/prn-2011-3-standard-format-data-submitted-under-fifra-and-certain-provisions

2. **Submission Layout:** The EPA Pesticide Registration Manual[7] provides additional information about the format of the submission. We encourage you to use these formatting guidelines for your inert ingredient submission.

3. **Study profile templates:** These templates describe the layout and scope of information that should be contained within a study profile and can serve as a guide for the preparation of study documents. While these templates are not required, they can be used by the Agency to efficiently develop its own review of the study. The templates can be found at https://www.epa.gov/pesticide-registration/study-profile-templates

4. **Submission of Data**:
    a. Independent/Company studies that have not been peer reviewed or previously reviewed by the Agency will need to be submitted in their entirety.
    b. MRID #s of previously submitted studies cited in support of your submission.
    c. A copy of and complete bibliography of all studies/documents cited and other supporting material.
    d. If the chemical has already been reviewed by EPA (e.g., chemical is also registered as an active ingredient, or it has another tolerance/tolerance exemption as an inert ingredient) then the company should provide a copy of the EPA assessment that summarized the data.

[7] https://www.epa.gov/pesticide-registration/pesticide-registration-manual

Inert Ingredient Review Process

The Agency screens all PRIA submissions during a 21 Day Screen for adequacy/completeness upon receipt. Submission packages not deemed acceptable are returned to the applicant to correct the deficiency. The PRIA 5 decision review times are listed in the PRIA Fee Category table (https://www.epa.gov/pria-fees/pria-fee-category-table-inert-ingredients). Once a more in-depth review of the chemical is underway, deficiencies may arise, and additional information may be requested.

In addition to the 21 Day Screen under PRIA 5, the Agency also conducts a preliminary technical screen of the application to determine if the application and the data and information submitted with the application are accurate and complete; and the application, data and information are consistent with the request; and the application, data and information are such that subject to full review could result in the granting of the application.

This screening is conducted no later than 45 days after the start of the decision review period for actions with decision review time periods equal to or less than six months and no later than 90 days after the start of the decision review period for actions with decision review time periods greater than six months. If the application fails the technical screen, and the deficiencies cannot be corrected by the applicant within 10 business days after receipt of the Agency's notification of the failure, the Agency will reject the application.

After the review and risk assessment are completed, a decision will be made regarding the safety of the inert ingredient in question. A letter outlining the decision will be emailed to the submitter. After the issuance of the letter granting the use of the chemical, the inert ingredient will be permitted for use in pesticide formulations under the appropriate use pattern.

How to Submit a Nonfood Request

All inert ingredient submissions are received and processed by our Document Processing Desk through the EPA CDX portal. To submit your application please see https://cdx.epa.gov/CDX/Login.

Applicants must submit fee payments at the time of application, and EPA will reject any application that does not contain evidence that the fee has been paid. The applicant must attach documentation that the fee has been paid with the application package.

Questions and Additional Information

Questions regarding an inert ingredient submission or requests to set up a pre-submission meeting should be directed to InertsBranch@epa.gov.

Additional information on pesticide inert ingredients (e.g., FAQs, InertFinder, FIFRA 25 (b) inert ingredients) can be found on our website https://www.epa.gov/pesticide-registration/inert-ingredients-overview-and-guidance

APPENDIX A

PAPERWORK REDUCTION ACT NOTICE and INSTRUCTIONS

PAPERWORK REDUCTION ACT NOTICE: Public reporting burden for this collection of information is estimated to average 0.85 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to **Director, Collection Strategies Division (2822T) U.S. Environmental Protection Agency,1200 Pennsylvania Ave., NW, Washington, DC 20460.**

INSTRUCTIONS: This form is to be used for all **inert ingredient** submission, (this form is also used for new registrations, amendment, resubmission, to applications for notifications, final printed labeling, reregistration, etc). In order to process an application, the following material must accompany the application:

1. Transmittal Document;
2. Notice of Filing (Food Use Only);
3. Three copies of any data submitted;

Submission of Data -Data submitted in support of this application must be submitted in accordance with PR Notice 2011-3

Block A -Check "Other"

Section I- This section must be completed, as applicable, for all inert ingredient submissions.

1. Company /Product Number - Insert your company number, if one has been assigned by EPA. This number may have been assigned to you as a basic registrant, a distributor, or as an establishment. Product Number- Leave Blank.

2. EPA Product Manager –Leave the first box blank and enter "8" under PM number

3. Proposed Classification –Check "None".

4. Company/Product (Name) – Enter the company name only.

5. Name and Address of Applicant -Enter the name and address of the company or person requesting the inert ingredient approval. If you are acting on behalf of another party, you must submit authorization from that party to act on their behalf. If applicable, the name and complete mailing address of such an agent must accompany this application.

6. **Expedited Review** -Leave Blank

Section II- Check "Other".

In the Explanation section write "Inert Ingredient" and provide a brief explanation of the regulatory action you are requesting. The Explanation Section should also be used for any additional information regarding Sections I and II.

SECTION III – Leave Blank

SECTION IV (Contact Point) -This section must be completed for all submissions.

1-5. Self-explanatory
6. EPA Use Only