

Inert Ingredient Approval Process

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Presentation Overview

- Pesticide Inert Ingredient Regulations
- Types of Inert Ingredients
- New Inert Ingredient Approval Process
 - Food Uses
 - Nonfood Uses
 - Polymers
- Presubmission and Contact Information



Pesticide Inert Ingredient Regulations

Inert Ingredients are regulated under both **FIFRA** and **FFDCA**:

FIFRA: The standard for registration of a pesticide product is that the **product** will not cause unreasonable adverse effects on the environment.

FFDCA: Under section 408 of the Federal Food, Drug and Cosmetic Act, EPA establishes tolerances or exemptions from the requirement of tolerances for pesticide chemicals (**including inert ingredients**) residues in or on food.



Pesticide Inert Ingredient Regulations

Section 408(b)(2)(C) of FFDCA requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to “ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue...”

Types of Inert Ingredients

- All inert ingredients used in pesticide products need to be approved by the Agency and are generally divided into the following categories:
 - **Food Use** – Food use inert ingredients require a tolerance/tolerance exemption and can be found in 40 CFR Part 180.
 - New/Amended Food Use
 - Safeners
 - Low Risk Polymers
 - **Nonfood Use** – Approved nonfood use inerts can be found on the “Inert Ingredients Permitted for Use in Non Food Use Pesticide Products”.

New Inert Ingredient Approval Process: Food Use





New Inert Ingredient Approval Process: Food Use-Overview

- What exemption citations are relevant?
- What needs to be submitted?
- What is the review process?

New Inert Ingredient Approval Process: Food Use

What Exemption Citations are relevant?

Tolerances/exemptions are established in the following sections of 40 CFR:

- **180.910** applied to growing crops or to raw agricultural commodities after harvest.
- **180.920** applied to growing crops only
- **180.930** applied to animals
- **180.940** antimicrobial formulations applied as food contact surface sanitizing solutions
- **180.950** permits unlimited use of minimal risk active and inert ingredients
- **180.960** low-risk polymer
- **180.XXXX** For specific inert ingredients where the use is significantly limited. (For examples see 180.1011 to 180.2020).



New Inert Ingredient Approval Process: Food Use

What needs to be submitted?

- **Petition Package**
 - Cover Letter/Transmittal Document**
 - Notice of Filing (NOF)**
 - Petition/Supporting Data**

New Inert Ingredient Approval Process: Food Use-Petition Package

Cover Letter:

- Subject line indicating Chemical name, CAS Reg. No., and Request for food-use exemption
- Summary of your request
 - CFR description
 - Proposed use
 - Purpose in formulation
 - Use limitation (if applicable)
- A list of data/information included in the package

New Inert Ingredient Approval Process: Food Use-Petition Package

Notice of Filing (NOF):

- The NOF is a summary of the petition
- The NOF is published in the *Federal Register*
 - This does not constitute approval of your chemical
 - Notifies the public of petition
 - 30 day public comment period
- The NOF template can be found at <http://www.epa.gov/opptsfrs/home/rules1.html>

New Inert Ingredient Approval Process: Food Use-Petition Package

NOF Content:

- The first paragraph:
 - Chemical name (9CI name)
 - CAS Reg. No.
 - CFR description
 - Purpose in the formulation (e.g., solvent, emulsifier, etc.)
 - Use limitations (e.g. % in formulation)
- Body of NOF
 - A summary of the petition (Toxicological profile, aggregate exposure, and safety determination).
 - All fields of the template must be addressed



New Inert Ingredient Approval Process: Food Use-Petition Package

Petition/Supporting Data:

- Proposed use/limitations of chemical
- Description of physical/chemical properties
- Discussion of toxicity
- Discussion of anticipated exposure (dietary and residential exposures) from the proposed use.
- Discussion of Aggregate Exposure
- Summary of submitted data and a rationale as to why based on the toxicity and expected exposure, the chemical is safe for human health and the environment.

New Inert Ingredient Approval Process: Food Use-Petition Package

Acceptable Sources of Data:

- Actual data on the subject chemical
- Publically available, peer-reviewed literature and/or assessments (e.g. OECD, IUCLID, ATSDR, WHO, EPA HPV, journals, etc.)
- Analog/Structure activity relationship (SAR) data (rationale for bridging to the subject chemical must be included)
- Modeled data
- See useful websites provided in package

New Inert Ingredient Approval Process: Food Use-Petition Package

Supporting Data:

- IIAB must have sufficient data to make a safety finding regarding the chemical as mandated by FIFRA.
- Data/information typically used by IIAB for decision-making:
 - Physical/chemical properties (including chemical structure)
 - Toxicity data (from animal studies)
 - Environmental fate data (e.g. persistence, bioaccumulation)
 - Ecotoxicity data (acute toxicity)



New Inert Ingredient Approval Process: Food Use-Petition Package

Physical/Chemical Properties:

- Molecular Weight
- Melting Point
- Boiling Point
- Density
- Vapor Pressure
- Partition Coefficient (*usually the Log P or Kow*)
- Water Solubility
- Henry's Law Constant



New Inert Ingredient Approval Process: Food Use-Petition Package

Types of Toxicology Data:

- Acute
- Subchronic
- Chronic
- Developmental
- Reproduction
- Neurotoxicity
- Carcinogenicity
- Immunotoxicity
- Metabolism

New Inert Ingredient Approval Process: Food Use-Petition Package

Types of Environmental Fate/Ecotoxicity Data:

- Environmental Fate: degradation/persistence and bioaccumulation data
- Ecotoxicity: aquatic, terrestrial, and phytotoxicity
- The following models may be useful:

- EPI Suite

<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

- ECOSAR

<http://www.epa.gov/oppt/newchemicals/tools/21ecosar.htm>

New Inert Ingredient Approval Process: Food Use-Review Process

What is the Review Process?

- Front End Processing
- Petition is screened by IIAB for completeness, major deficiencies addressed
- NOF published in the Federal Register
- Data reviewed
- Decision document prepared and peer reviewed
- Final Rule Written and sent to Office of General Counsel (OGC) for concurrence
- Rule sent to Federal Register staff for encoding
- Division Director signature
- Final Rule published in Federal Register
- After the Final Rule (FR) is published, the chemical is permitted for use as an inert ingredient in pesticide product as outlined in FR



New Inert Ingredient Approval Process: Food Uses

Safeners

- Follow the Petition Process
- A tolerance is usually established for safeners
- Generally require a full data set similar to those for active ingredients (see 40 CFR Part 158)

New Inert Ingredient Approval Process: Nonfood Use





New Inert Ingredient Approval Process: Nonfood Use

- What are the proposed use patterns and/or limitations?
- What needs to be submitted?
- What is the review process?



New Inert Ingredient Approval Process: Nonfood Use

What are the proposed use patterns and/or limitations?

- IIAB receives requests for a variety of approvals for new nonfood use inert ingredients.
- Some examples:
 - wood preservatives
 - antifouling treatments
 - application to ornamental plants
 - uses in pet products
 - etc.



New Inert Ingredient Approval Process: Nonfood Use-Submission Package

What needs to be submitted?

- Cover letter/transmittal document
- Submission/Supporting data

(Non-rulemaking- Notice of Filing and Final Rule are not required)



New Inert Ingredient Approval Process: Nonfood Use-Submission Package

Cover Letter:

- Subject line indicating chemical name, CAS Reg. No., and Request for Nonfood Use Inert Ingredient
- Summary of your request
 - Proposed Use
 - Purpose in Formulation
 - Use Limitation (if applicable)
- A list of data/information included in the package

New Inert Ingredient Approval Process: Nonfood Use-Submission Package

Supporting data:

- IIAB must have sufficient data to make a safety finding regarding the chemical as mandated by FIFRA.
- Data/information typically used by IIAB for decision making is the same as that used for food use petitions.
 - Physical/chemical properties
 - Toxicity data
 - Environmental fate data
 - Ecotoxicity data

New Inert Ingredient Approval Process: Nonfood Use-Submission Package

Supporting data:

- Proposed use/limitations of chemical
- Description of physical/chemical properties
- Discussion of toxicity
- Discussion of anticipated exposure from the proposed use. (**Dietary exposures not required**)
- Summary of submitted data and a rationale as to why based on the toxicity and expected exposure, the chemical is safe for human health and the environment.

New Inert Ingredient Approval Process: Nonfood Use

What is the review process?

- Front End Processing
- Submission screened by IIAB for completeness, major deficiencies addressed
- Data reviewed
- Decision document prepared and peer reviewed
- Final decision document signatures
- Notification of decision is sent by mail to requestor
- If approval is granted, decision is in effect from date the letter is issued.
- Approved chemicals will be added to the list of “Inert Ingredients Permitted for Use in Non Food Use Pesticide Products” periodically.

New Inert Ingredient Approval Process: Low Risk Polymer





New Inert Ingredient Approval Process: Low Risk Polymer-Overview

- What is the basis for exemption?
- What are the criteria?
- What needs to be submitted?
- What is the petition process?
- Websites



New Inert Ingredient Approval Process: Low Risk Polymer

Basis for Low Risk Polymer Exemption:

- Rule making process established under 40 CFR 180.960
- Size of polymer (>1000 number average molecular weight)
 - Generally, too large to be absorbed through GI tract
 - Generally, too large to be absorbed through intact human skin
- Specific criteria needs to be met in order to qualify as a Low Risk Polymer (LRP)

New Inert Ingredient Approval Process: Low Risk Polymer-Criteria

- **Specific criteria need to be met in order to qualify as a Low Risk Polymer (LRP)**
 - Definition of polymer given in 40 CFR 723.250(b)
 - All criteria for a LRP under 40 CFR 723.250(d) and is not specifically excluded
 - One of the criteria under 40 CFR 723.250(e)

New Inert Ingredient Approval Process: Low Risk Polymer-Criteria

Definition of a polymer given in **40 CFR 723.250(b)**:

“...a chemical substance consisting of molecules characterized by the sequence of one or more types of monomer units and comprising a simple weight majority of molecules containing at least 3 monomer units which are covalently bound to at least one other monomer unit or other reactant and which consists of less than a simple weight majority of molecules of the same molecular weight. Such molecules must be distributed over a range of molecular weights wherein differences in the molecular weight are primarily attributable to differences in the number of monomer units. In the context of this definition, sequence means that the monomer units under consideration are covalently bound to one another and form a continuous string within the molecule, uninterrupted by units other than monomer units...”

New Inert Ingredient Approval Process: Low Risk Polymer-Criteria

Under 40 CFR 723.250(d):

- The polymer is not cationic nor is it reasonably anticipated to become cationic in a natural environment.
- The polymer does contain as an integral part of its composition at least two of the atomic elements carbon, hydrogen, nitrogen, oxygen, silicon, and sulfur.
- The polymer does not contain as an integral part of its composition, except impurities, any element other than those listed in 40 CFR 723.250(d)(2)(ii):
 - The elements carbon, hydrogen, nitrogen, oxygen, silicon, and sulfur.
 - Sodium, magnesium, aluminum, potassium, calcium, chloride, bromine, and iodine as the monatomic counter ions
 - Fluorine, chlorine, bromine, and iodine covalently bond to carbon
 - Less than 0.20 weight % of any combination of the atomic elements lithium, boron, phosphorus, titanium, manganese, iron, nickel, copper, zinc, tin, and zirconium

New Inert Ingredient Approval Process: Low Risk Polymer-Criteria

Under **40 CFR 723.250(d)**:

- Will not substantially degrade, decompose, or depolymerize.
- The polymer is manufactured or imported from monomers and/or reactants that are included on the TSCA Chemical Substance Inventory or manufactured under an applicable TSCA section 5 exemption.
- The polymer is not a water absorbing polymer (with a number average molecular weight (Mn) $\geq 10,000$ daltons).

New Inert Ingredient Approval Process: Low Risk Polymer-Criteria

The polymer must also meet one of the following exemption criteria specified in **40 CFR 723.250(e)**:

- **Option 1.** The polymer's number average molecular weight is greater than 1,000 and less than 10,000 daltons. The polymer contains less than 10% oligomeric material below MW 500 and less than 25% oligomeric material below MW 1,000
 - Does not contain any reactive functional groups.
 - If so, must also meet the exemption criteria in §723.250(e)
- **Option 2.** The polymer's number average MW is greater than or equal to 10,000 daltons. The polymer contains less than 2% oligomeric material below MW 500 and less than 5% oligomeric material below MW 1,000.
- **Option 3.** Polyesters Polymer-
 - as defined in paragraph §723.250(b)
 - manufactured solely from one or more of the reactants in Table 1 §723.250



New Inert Ingredient Approval Process: Low Risk Polymer- Petition Package

What do I need to submit?

■ Cover Letter:

- Subject line indicating chemical name, number average molecular weight (Mn), CAS Reg. No., and Request for Nonfood Use Inert Ingredient
- Purpose in formulation
- Summary of your request (i.e. that your polymer conforms to the definition of a LRP)
- A list of data/information included in the Petition Package

New Inert Ingredient Approval Process: Low Risk Polymer- Petition Package

■ Notice of Filing (NOF)

- Polymer name, CAS Reg. No., and number average molecular weight (Mn)
- Body of NOF
 - A summary of the petition
 - All fields of the template must be addressed
 - Concurrence with definition of LRP
 - Explicit statements that your polymer meets all of the LRP criteria
- Submit
 - Paper copy
 - Electronic copy



New Inert Ingredient Approval Process: Low Risk Polymer- Petition Package

■ Petition/Submission

- Must clearly state why the polymer conforms to the definition of a polymer.
- Must clearly state how the chemical meets all of the criteria under § 723.250(d) and §723.250(e)
- Any supporting data (e.g. biodegradation study)
- Chromatogram-
 - Give oligomeric content for MW <1000 and <500
 - Method used to obtain Mn and oligomeric content (e.g. GPC)
- Representative structure

New Inert Ingredient Approval Process: Low Risk Polymer-Petition Process

Petition Process:

- **Petition is screened for completeness**
 - Generally petition takes 4-6 months after being placed on the work plan
 - May vary depending on branch workload
- **NOF is published in Federal Register**
 - Does not imply that the Agency has made a determination regarding chemical
 - 30 day public comment period
- **Chemical Review**
 - Additional information may be necessary once a review is underway
 - Conducted by IIAB with expert Agency consultation if necessary
- **A final rule is published in the Federal Register**
 - Once the final rule is published the chemical is legally permitted in all food use and nonfood use pesticide products in accordance with good agricultural or manufacturing practices.
 - An exemption will be subsequently published under 40 CFR 180.960

New Inert Ingredient Approval Process: Low Risk Polymer-Useful Websites

- Electronic Code of Federal Regulations (e-CFR) 40 CFR 180.960
<http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=7de7678a1d2301654d66d266403f1d7a&rgn=div8&view=text&node=40:23.0.1.1.28.4.19.8&idno=40>
- e-CFR 40 CFR 723.250
<http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=a2398df59b188d7623468e2f0958d19e&rgn=div8&view=text&node=40:30.0.1.1.11.2.1.3&idno=40>
- Polymer Exemption guidance Manual
<http://www.epa.gov/oppt/newchems/pubs/polyguid.pdf>

Assistance from IIAB

- Presubmission consultation with IIAB is recommended prior to formal submission
 - Informal meeting or conference call
 - Company presents
 - Brief summaries of available information on the chemical
 - Description of requested exemption/use pattern
 - IIAB will provide general thoughts about potential data gaps and any known risk issues
 - This consultation assists company in developing a submission that is complete and successful

Assistance from IIAB

- Documents available from IIAB to aid with submission process
 - Inert Ingredient FAQ
 - General Guidance for Petitioning the Agency for the Establishment of a New/Amended Inert Ingredient Tolerance or Tolerance Exemption
 - General Guidance for Requesting a New Nonfood Use Inert Ingredient
 - General Guidance to Petitioners on Low Risk Polymer Submissions
 - Helpful Websites for Submitters

Contact information

- Please send all questions/comments/requests to inerts.branch@epa.gov
- If further assistance is needed please contact PV Shah, Branch Chief at shah.pv@epa.gov or (703)308-1846
- Presenters:
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