RESIDUE CHEMISTRY DATA REQUIREMENTS

40 CFR PART 158W

Topics

- Brief Statutory Framework
- Dietary Risk Assessment
- Uses Resulting in Dietary Exposure
- Direct Food Use, Indirect Food Use, and Nonfood Use Descriptions
- Use Site Index
- 158W Residue Chemistry Data Requirements
  - Provisions
  - Screening-Level Assessments
  - Data Requirement Sections

Statutes Allowing Authority to Require Residue Chemistry Data

Federal Insecticide, Fungicide & Rodenticide Act (FIFRA)

- Must prove no unreasonable adverse effect to humans via the dietary route
- **Submission: Data to support registration and risk assessment**

Federal Food, Drug, and Cosmetic Act (FFDCA)

- May need to set maximum residue levels, or tolerances, for pesticides used in or on foods or animal feed
- Must determine that tolerance is safe meaning that no harm will result from aggregate exposure to the pesticide residue
- **Submission: Petition for Tolerance/Exemption**
- **Submission: Data to support aggregate assessment**

Aggregate Assessment

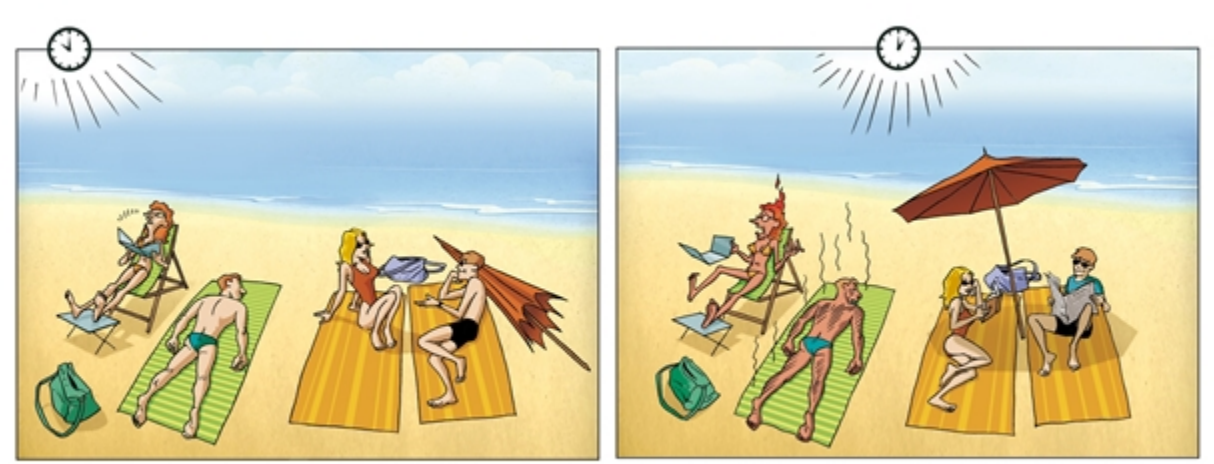
- FQPA defines "safe" as:

  "a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposure and all other exposure for which there is reliable information."

- Aggregate typically includes:
  - Food
  - Drinking water
  - Other non-occupational exposures (e.g., painting your house, carpet, pets, toys, treated lawns)

Human Health Risk Assessment

- When is a human health risk assessment conducted?
  - If there are adverse effects associated with the active (determined by toxicologist) and
  - If there is human exposure expected from the active's use pattern (determined by residue chemist or exposure assessor)



How Residue Chemistry Data are Used in Risk Assessment

Residue chemistry data are used:

- to estimate acute and chronic dietary risks (risk assessment), which contributes to aggregate risks
- to establish a tolerance, tolerance exemption, or to determine that neither of these steps are necessary

3 Routes of Exposure

1. **INHALATION**: Inhaling pesticides
2. **DERMAL**: Absorbing pesticides through skin
3. **ORAL**: Getting pesticides in the mouth or digestive tract

Routes of Dietary Exposure

- Drinking Water
- Food
  - Indirect exposure
  - Direct exposure

Residue Chemist will investigate these routes of exposure

Examples of Uses Resulting in Dietary Exposure

Food

<u>Direct Food</u>

*Fruit & Veggie Rinses/Fumigation

*Fogging poultry houses when animals are present

<u>Indirect Food</u>

*Food Contact Sanitizers in various use sites

*Impregnated Cutting Boards

*Food packaging adhesives

Drinking Water

*Anything that may go down the drain (e.g., detergent)

*Industrial discharges

Direct Food Use

A use is generally considered to be a direct food use if an antimicrobial pesticide is intended to be directly applied to food (defined for purposes of the Federal Food, Drug, and Cosmetic Act at 21 U.S.C. § 201(f)) or applied to a material or article for the purpose of treating food. Use patterns that fall into this category include, but are not limited to: fruit and vegetable rinses, fogging of poultry areas, and egg washing treatments. These types of uses are generally subject to a FFDCA clearance.

Indirect Food Use

A use is generally considered to be an indirect food use if the use involves application of the antimicrobial pesticide in or on a material or article that comes into contact with food and may result in residues in or on food, but the use is not intended for pesticidal treatment of food. As a result of food contact with a surface and/or material that has been treated and/or impregnated with an antimicrobial pesticide, there is a potential for residues in or on food.

Indirect Food Use *(continued)*

Although a pesticide does not have directions for direct application to food or to a material or article for treatment of food, exposure to an antimicrobial pesticide may still occur resulting in residues in or on food.

Use patterns that fall into this category include, but not limited to:

- sanitization of food-contact dishes utensils
- food processing equipment and countertops
- disinfection of food-use areas and,
- impregnation of cutting boards, conveyor belts or food containers and/or packaging for a pesticidal purpose other than treating food.

These types of uses may be subject to a FFDCA clearance.

Uses that Could Result in Dietary Exposure

These uses include:

- Paper/Paperboard/Pulp
- Adhesives
- Coatings
- Plastics
- Polymers
- Cleaning Products/Detergents (non-laundry)
- Materials Preservatives
- Wood Products

Nonfood Use

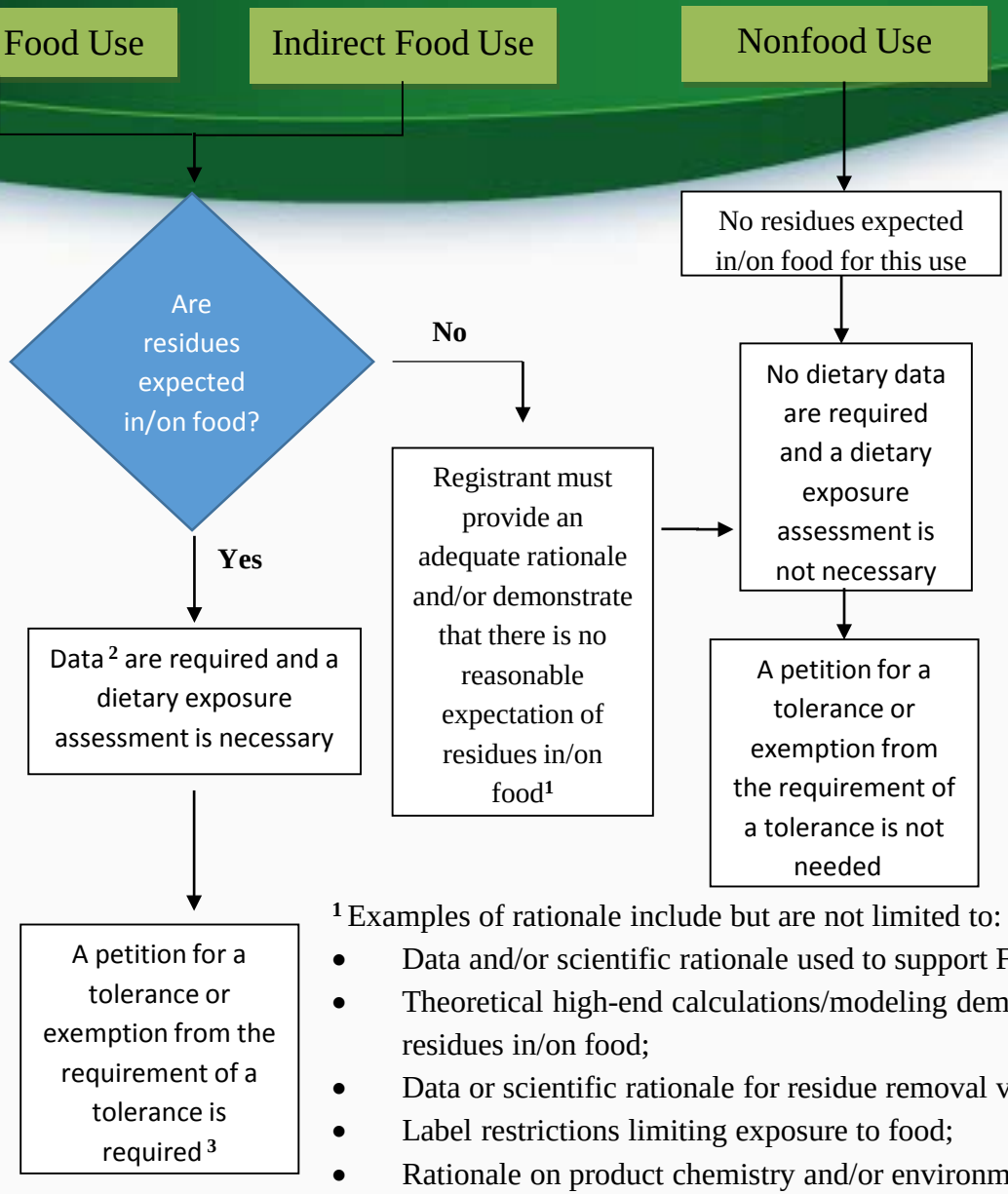
A use is generally considered to be a nonfood use when there are no residues expected in or on food, for example because the antimicrobial pesticide is not expected to come into contact (directly or indirectly) with food as a result of its intended use.

Use patterns that fall into this category include, but are not limited to:

- fuel tanks
- human footwear
- or nonfood areas of eating establishments. (e.g., kitchen floor cleaner)

These types of uses are not subject to a FFDCA clearance.

Food Use Description Flow Chart



[1] Examples of rationale include but are not limited to:

- Data and/or scientific rationale used to support FDA food additive regulation or FCN;
- Theoretical high-end calculations/modeling demonstrating that there is no reasonable expectation of residues in/on food;
- Data or scientific rationale for residue removal via a potable water rinse;
- Label restrictions limiting exposure to food;
- Rationale on product chemistry and/or environmental fate characteristics (i.e., volatility, solubility); or
- Residue data

[2] In this context, the word "data" refers to any data to satisfy 40 CFR Part 158W data requirements (e.g., residue chemistry and toxicity data)

[3] Uses from strictly residential products do not require a tolerance or tolerance exemption.

Use Site Index (USI)

APPENDIX B - ANTIMICROBIAL PESTICIDE PRODUCT USE SITES ACCORDING TO USE PATTERNS

Contents

12 General Use Patterns

- Agricultural Premises & Equipment
- Food Handling/Storage Establishments, Premises and Equipment
- Commercial, Institutional and Industrial Premises and Equipment
- Residential and Public Access Premises
- Medical Premises and Equipment
- Human Drinking Water Systems
- Materials Preservatives
- Industrial Processes and Water Systems
- Antifouling Coatings and Ballast Water Treatments
- Wood Preservatives
- Swimming Pools and Spas
- Aquatic Areas

FIFRA 158W: Residue Chemistry Data Requirements

TABLE—ANTIMICROBIAL RESIDUE CHEMISTRY DATA REQUIREMENTS

Guideline No.	Data requirement	Uses				Test substance	Test note No.
		Agricultural premise	Indirect food	Direct food	Aquatic		
Supporting Information							
860.1100	Chemical identity	R	R	R	R	TGAI	
860.1200	Directions for use	R	R	R	R		
860.1550	Proposed tolerance/tolerance exemption.	R	R	R	R		1
860.1560	Reasonable grounds in support of petition.	R	R	R	R		1
860.1650	Submittal of analytical reference standards.	R	R	R	R	PAI/ROC	2
Food-Contact Surfaces or Impregnated Materials							
860.1460	Food-handling	CR	CR	CR	CR	TEP	3
None	Nature of residue on surfaces	CR	CR	CR	CR	PAIRA or TGAI.	4
None	Migration studies	CR	CR	CR	CR	TEP	5
860.1340	Residue analytical method for data collection.	CR	CR	CR	CR	ROC	6
860.1380	Storage stability	R	R	R	R	TEP or ROC	7
Higher tiered							
860.1300	Nature of the residue in plants	CR	CR	CR	CR	PAIRA	8
860.1300	Nature of the residue in livestock	CR	CR	CR	CR	PAIRA	9
860.1340	Residue analytical methods for tolerance/tolerance exemption enforcement.	CR	CR	CR	CR	ROC	10
860.1360	Multiresidue method testing	CR	CR	CR	CR	ROC	11
860.1400	Potable water	CR	CR	CR	CR	TEP	12
860.1400	Fish	CR	CR	CR	CR	TEP	13
860.1400	Irrigated crops	CR	CR	CR	CR	TEP	14
860.1480	Meat/milk/poultry/eggs	CR	CR	CR	CR	TGAI or ROC.	15
860.1500	Crop field trials	CR	CR	CR	CR	TEP	16
860.1520	Processed food or feed	CR	CR	CR	CR	TEP	17
None	Anticipated residues	CR	CR	CR	CR	ROC	18

General Provisions §158.2290(b)(1)

Residue chemistry data are required for antimicrobial end-use products with uses that may result in residues in or on food

General Provisions §158.2290(c)

Residue chemistry data are not required under paragraph (b) of this section if:

- No adverse effects (no toxicity endpoints) are associated with dietary exposure to the active ingredient

-OR-

- If theoretical (high-end) dietary exposure estimates combined with the applicable toxicity endpoint result in acute and chronic dietary risks below the Agency's level of concern

Residue Chemistry Data Requirements

Broken down into three separate sections:

1. Supporting Information (Test notes 1 and 2)
2. Food-Contact Surfaces or Impregnated Materials (Test notes 3 – 7)
3. Higher Tiered (Test notes 8– 18)

Supporting Information

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860.1550 ..	Proposed tolerance/tolerance exemption.	R	R	R	R	.....	1
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860.1650 ..	Submittal of analytical reference standards.	R	R	R	R	PAI/ROC	2

1. A petition proposing a tolerance is required under section 408 of FFDCA for food/feed uses unless the use is covered by an existing tolerance. If the use is covered under section 409 of FFDCA, this must be identified and a copy of the FDA petition should be submitted.
2. A reference standard is required for any use requiring a numerical tolerance or exemption.

Food-Contact Surfaces or Impregnated Materials

Guideline No.	Data requirement	Uses				Test substance	Test note No.
		Agricultural premise	Indirect food	Direct food	Aquatic		
Food-Contact Surfaces or Impregnated Materials							
860.1460 ..	Food-handling	CR	CR	CR	CR	TEP	3
None	Nature of residue on surfaces	CR	CR	CR	CR	PAIRA or TGAI.	4
None	Migration studies	CR	CR	CR	CR	TEP	5
860.1340 ..	Residue analytical method for data collection.	CR	CR	CR	CR	ROC	6
860.1380 ..	Storage stability	R	R	R	R	TEP or ROC	7

3. Data are required unless information, including but not limited to, theoretical high-end estimates, radio labeled laboratory data, or NoR on surfaces data show that residues will not occur in food or feed.
4. If theoretical risk estimates described in (3) above exceed our LoC, then a nature of residue on surfaces study is required.
5. Based on (4) above, if residues of concern are identified, a migration study (protocol must be approved) is required.
6. If a migration study is required, a residue analytical method and supporting storage stability data (test note 7) are required.

Migration Studies

- This data requirement is composed of two study types:
  - Residue Reduction migration study
  - Food Transfer migration study
- The residue reduction migration study may be a potable water rinse (PWR) study, a leaching study and/or a volatility study.
- Nature of the residue on surfaces data may be needed if chemical fate properties not well understood.

High-End, Screening-Level Estimates

- Data requirements based on whether a screening-level assessment indicates that dietary risks are above or below the Agency's level of concern. When dietary risk estimates are above the level of concern (or LoC), data requirements are triggered.
- For re-evaluation assessments, the Agency uses this tiered assessment approach to determine the acute and/or chronic dietary risks and the associated residue chemistry data requirements.
- This approach starts with performing the conservative Residential Tier 1A or Commercial Tier 1A assessment (using the residential or commercial food-contact sanitizer model) for products with food-contact surface uses in order to generate high-end, screening-level dietary risk estimates.

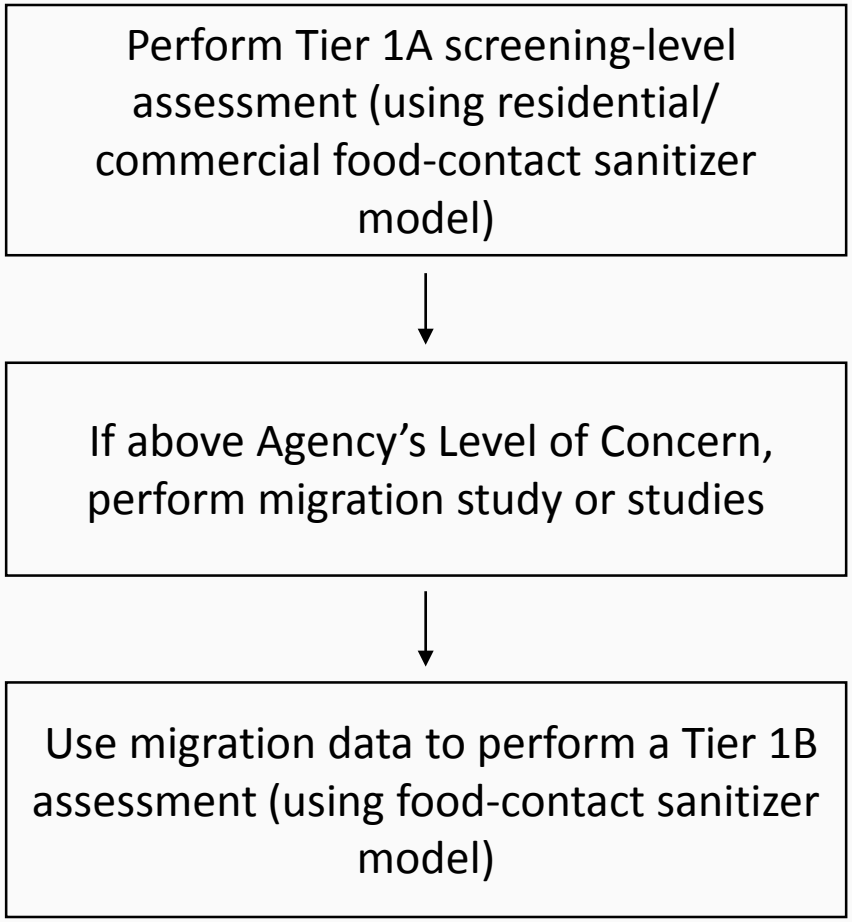
Assumptions used to Generate Tier 1A Screening-Level (High-End) Estimates

Exposure assumptions:

- That 1 mg/cm2 of product remains on the treated food-contact surface
- That all food comes into contact with a treated surface (there is 100 percent likelihood of food-to-surface contact)
- That 100 percent of the residues are transferred from the surface to the food item

If the Tier 1A assessment yields dietary risks of concern, residue reduction and/or food transfer migration study data are generated.

A Tier 1B assessment is then performed using the migration data to reduce the 100 percent surface-to-food transfer value, thus providing a more realistic estimate of dietary exposure and risk.



Applicant Determination of Required Data

- Applicant use of tiered assessment process when requesting a new indirect food use through a PRIA action.
- Allows applicants to determine if residue chemistry migration studies are needed (based on acute and/or chronic dietary risks below the level of concern) before submitting an application.

Guidance for Applicants (w/ New AI or New Use)

To use screening-level assessments to determine if a product with an indirect food use on surfaces has acute and chronic dietary risks below the Agency's level of concern:

- Identify the dietary points of departure (PoDs) expressed as an aPAD/cPAD or aRfD/ cRfD
- Use the Agency's Registration Review Final Work Plan or most recent risk assessment on the active ingredient.
- Enter the dietary PoDs along with the necessary product-specific information into the appropriate screening-level model.

Applicant-Generated Assessments

- Dietary risks that are below the Agency's level of concern (exposure estimates less than 100% of the aPAD and/or cPAD using the appropriate inputs and model) indicate that residue chemistry migration studies should not need to be generated/submitted for the product.
- The Agency anticipates that many products will not require residue chemistry data after the screening level assessment is performed.

Applicant-Generated Assessments

- If Tier 1A assessment dietary risks exceed the Agency's level of concern and the fate properties of the active ingredient are well-understood, a migration study is needed.
- For products expected to have reduced surface residues, the residue reduction migration study should be conducted first. PWR study only for products with directions for the indirect food-use being assessed.
- Use residue reduction migration study results to perform a Tier 1B assessment to refine risk estimates.
- If refined dietary risks are below the Agency's level of concern, the residue reduction migration study should be submitted to the Agency with the new food-use application.

Applicant-Generated Assessments

- If refined dietary risks are still above the level of concern, or if a residue reduction migration study is not applicable, a food transfer migration study should be submitted with the new food-use application.
- Since testing guidance for the residue reduction and food transfer migration studies are under development, registrants should submit protocols for Agency review before the initiation of testing.

Applicant-Generated Assessments

- The agency has other, similar screening-level models available to estimate dietary exposure from antimicrobial uses of adhesives, food contact paper and dish washing detergents.

- See *Dietary Exposure and Risk Assessment Standard Operating Procedures* document

Higher Tiered

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860.1520 ..	Processed food or feed	CR	CR	CR	CR	TEP	17
None	Anticipated residues	CR	CR	CR	CR	ROC	18

- Test notes 8 – 9: If plants or animals can be exposed to an antimicrobial pesticide, Nature of the Residue (NoR) studies are required.
- Test notes 10 -11: If a numerical tolerance is required, residue analytical methods and multi-residue methods are required.
- Test notes 12-18: If an antimicrobial pesticide can be applied to potable water, fish, irrigated crops, meat, milk, poultry, eggs, food crops raw agricultural commodities (RACs); can concentrate in processed food/feed; or tolerance-level dietary exposure and risk estimates exceed our level of concern, residue data are required.

Questions?

Contact: OPP_AD_Ombudsman@epa.gov

This concludes our presentation on residue chemistry data requirements. Thank you for your interest!