than that of the raw agricultural commodity.

17. Required when residues at the tolerance level may result in risk of concern. These data may include washing, cooking, processing, or degradation studies as well as market basket surveys for a more precise residue determination.

18. The proposed tolerance must reflect the maximum residue likely to occur in crops, in meat, milk, poultry, or eggs.

19. Required when a residue analytical method is required.

§ 158.2050 Biochemical pesticides human health assessment data requirements table.

(a) *General.* (1) Sections 158.100 through 158.130 describe how to use this table to determine the biochemical human health assessment data requirements for a particular biochemical pesticide product.

(2) The data in this section are not required for straight chain lepidopteran pheromones when applied up to a maximum use rate of 150 grams active ingredient/acre/year.

(b) *Use patterns.* (1) Food use patterns, in general, include products classified under the following general uses: terrestrial food crop use; terrestrial feed crop use; aquatic food crop use; greenhouse food crop use.

(2) Nonfood use patterns include products classified under the general use patterns of terrestrial nonfood crop use; aquatic nonfood residential use; aquatic nonfood outdoor use; aquatic nonfood industrial use; greenhouse nonfood crop use; forestry use; residential outdoor use; residential indoor use; indoor food use; indoor nonfood use; indoor medical use.

(c) *Key.* R=Required; CR=Conditionally required; NR=Not required; MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of the active ingredient; Residue of concern=the active ingredient and its metabolites, degradates, and impurities of toxicological concern; All=All of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (e) of this section, and apply to the individual tests in the following table:

(d) *Table.* The following table shows the data requirements for biochemical pesticides human health assessment. The test notes are shown in paragraph (e) of this section.

TABLE—BIOCHEMICAL PESTICIDES HUMAN HEALTH ASSESSMENT DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Patterns		Test Substance		Test Notes
		Food	Nonfood	MP	EP	
Tier I						
Acute Testing						
870.1100	Acute oral toxicity - rat	R	R	TGAI and MP	TGAI and EP	1
870.1200	Acute dermal toxicity	R	R	TGAI and MP	TGAI and EP	1, 2
870.1300	Acute inhalation toxicity - rat	R	R	TGAI and MP	TGAI and EP	3
870.2400	Primary eye irritation - rabbit	R	R	TGAI and MP	TGAI and EP	2
870.2500	Primary dermal irritation	R	R	TGAI and MP	TGAI and EP	1, 2
870.2600	Dermal sensitization	R	R	TGAI and MP	TGAI and EP	2, 4
none	Hypersensitivity incidents	R	R	All	All	5
Subchronic Testing						
870.3100	90-day oral (one species)	R	CR	TGAI	TGAI	6

TABLE—BIOCHEMICAL PESTICIDES HUMAN HEALTH ASSESSMENT DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Use Patterns		Test Substance		Test Notes
		Food	Nonfood	MP	EP	
870.3250	90-day dermal - rat	CR	CR	TGAI	TGAI	7
870.3465	90-day inhalation - rat	CR	CR	TGAI	TGAI	8
Developmental Toxicity						
870.3700	Prenatal developmental - rat preferably	R	CR	TGAI	TGAI	9
Mutagenicity Testing						
870.5100	Bacterial reverse mutation test	R	CR	TGAI	TGAI	10
870.5300 870.5375	*In vitro* mammalian cell assay	R	CR	TGAI	TGAI	10, 11
Tier II						
Mutagenicity Testing (*In vivo* cytogenetics)						
870.5385 870.5895	*In vivo* Mammalian Cytogenetics	CR	CR	TGAI	TGAI	13
Developmental Toxicity						
870.3700	Prenatal developmental	CR	CR	TGAI	TGAI	9
Special Tests						
880.3550	Immunotoxicity	CR	CR	TGAI	TGAI	12, 13
Applicator/User Exposure						
875.1100	Dermal outdoor exposure	CR	CR	TGAI	TGAI	15
875.1200	Dermal indoor exposure	CR	CR	TGAI	TGAI	15
875.1300	Inhalation outdoor exposure	CR	CR	TGAI	TGAI	15
875.1400	Inhalation indoor exposure	CR	CR	TGAI	TGAI	15
875.1500	Biological monitoring	CR	CR	TGAI	TGAI	15
Tier III						
Chronic Testing/Special Testing						
880.3800	Immune response	CR	CR	TGAI	TGAI	14
870.3800	Reproduction and fertility effects	CR	CR	TGAI	TGAI	16
870.4100	Chronic oral - rodent and nonrodent	CR	CR	TGAI	TGAI	17
870.4200	Carcinogenicity - two species - rat and mouse preferred	CR	CR	TGAI	TGAI	18
870.5380	Mammalian spermatogonial chromosome aberration test	CR	CR	TGAI	TGAI	19
Special Testing						
870.7200	Companion animal safety	CR	CR	NR	TGAI or EP	20

(e) *Test notes.* The following test notes are applicable to the data requirements for biochemical pesticides human health assessment as referenced in the last column of the table in paragraph (d) of this section.

1. Required unless the test material is a gas or highly volatile (vapor pressure $>10^{-4}$torr (mm/Hg)).

2. Required unless the test material is corrosive to skin or has pH <2 or >11.5.

3. Required when the pesticide, under conditions of use, would result in respirable material (e.g., gas, volatile substance or aerosol/particulate), unless it is a straight chain lepidopteran pheromone.

4. Required if repeated contact with human skin is likely to occur under conditions of use.

5. Hypersensitivity incidents must be reported as adverse effects data.

6. Required for non-food uses that are likely to result in repeated oral exposure to humans.

7. Required to support uses involving purposeful application to the human skin or which would result in comparable prolonged human exposure to the product (e.g., insect repellents) and if any of the following criteria are met:

i. Data from a 90–day oral study are not required.

ii. The active ingredient is known or expected to be metabolized differently by the dermal route of exposure than by the oral route and the metabolite is of toxicological concern.

iii. The use pattern is such that the dermal route would be the primary route of exposure.

8. Required if there is a likelihood of significant levels of repeated inhalation exposure to the pesticide as a gas, vapor, or aerosol.

9. Required if the use of the product under widespread and commonly recognized practice may reasonably be expected to result in significant exposure to female humans (e.g., occupational exposure or repeated application of insect repellents directly to the skin). Tier II data is required on a different test species from Tier I data when developmental effects are observed in the first study and information on species-to-species extrapolation is needed.

10. Required to support nonfood uses if either:

i. The use is likely to result in significant human exposure; or

ii. The active ingredient (or its metabolites) is structurally related to a known mutagen or belongs to any chemical class of compounds containing a known mutagen. Additional mutagenicity tests that may have been performed plus a complete reference list must also be submitted. Subsequent testing may be required based on the available evidence.

11. Choice of assay using either:

i. Mouse lymphoma L5178Y cells, thymidine kinase (tk) gene locus, maximizing assay conditions for small colony expression or detection;

ii. Chinese hamster ovary (CHO) or Chinese hamster lung fibroblast (V79) cells, hypoxanthine-guanine phosphoribosyl transferase (hgprt) gene locus, accompanied by an appropriate *in vitro* test for clastogenicity; or

iii. CHO cells strains AS52, xanthine-guanine phosphoribosyl transferase (xprt) gene locus.

12. Required if there are effects on hematology, clinical chemistry, lymphoid organ weights, and histopathology are observed in the 90–day studies.

13. The micronucleus rodent bone marrow assay is preferred; however, rodent bone marrow assays using metaphase analysis (aberrations) are acceptable.

14. Required if adverse effects are observed in the Tier II immunotoxicity study. The protocol for evaluating adverse effects to the immune response should be developed after evaluating the effects noted in the immunotoxicity study.

15. These data are required when the data used for the human health assessment indicates that the biochemical may pose a potential hazard to the applicator/user.

16. Required if there is evidence of:

i. Endocrinological effects from the subchronic toxicity studies.

ii. Developmental effects in the prenatal developmental toxicity study(s), or

iii. Genotoxicity to mammals based on results from the mutagenicity tests.

The use of a combined study that utilizes the two-generation reproduction study in rodents (guideline 870.3800) as a basic protocol for the addition of other endpoints or functional assessments in the immature animal is encouraged.

17. Required if the potential for adverse chronic effects is indicated based on any of the following:

i. The subchronic effect level established in the following Tier I studies: 90–day oral toxicity study, 90–day dermal toxicity study, or 90–day inhalation toxicity study.

ii. The pesticide use pattern (e.g., rate, frequency, and site of application).

iii. The frequency and level of repeated human exposure that is expected.

18. Required if the product meets either of the following criteria:

i. The active ingredient (or any of its metabolites, degradation products, or impurities) produce(s) in Tier I subchronic studies a morphologic effect (e.g., hyperplasia or metaplasia) in any organ that potentially could lead to neoplastic change.

ii. Adverse cellular effects suggesting carcinogenic potential are observed in Tier II immunotoxicity and Tier III immune response study or in Tier II mammalian mutagenicity assays.

In addition, a 90–day range finding study in both rats and mice is required to determine the dose levels if carcinogenicity studies are required. If the mouse carcinogenicity study is not required, the 90–day mouse subchronic study is likewise not required.

19. Required if results from lower tiered mutation or reproductive studies indicate there is potential for chromosomal aberration to occur.

20. May be required if the product's use will result in exposure to domestic animals through, but not limited to, direct application or consumption of treated feed.

§ 158.2060 Biochemical pesticides nontarget organisms and environmental fate data requirements table.

(a) *General.* (1) Sections 158.100 through 158.130 describe how to use this table to determine the terrestrial and aquatic nontarget organisms and fate data requirements for a particular biochemical pesticide product. Notes that apply to an individual test including specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section. In general, for all outdoor end-use products including turf, the following studies are required: one avian acute oral, one avian dietary, one acute freshwater fish, one acute freshwater invertebrate study, plant toxicity testing, and a honeybee acute contact study.

(2) The data in this section are not required for arthropod pheromones when applied at up to a maximum use rate of 150 grams active ingredient/acre/year except when the product is expected to be available to avian species (*i.e.*, granular formulation).

(b) *Use patterns.* The terrestrial use pattern includes products classified under the general use patterns of terrestrial food crop, terrestrial feed crop, and terrestrial nonfood/nonfeed crop. The greenhouse use pattern includes products classified under the general use patterns of greenhouse food crop and greenhouse nonfood crop. The indoor use pattern includes products classified under the general use patterns of indoor food and nonfood use. The remaining terrestrial uses include: forestry and residential outdoor use. Data are also required for the general use patterns of aquatic food and nonfood crop use.

(c) *Key.* R=Required; CR=Conditionally required; NR=Not required; MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of the active ingredient; Residue of concern=the active ingredient and its metabolites, degradates, and impurities of toxicological concern; All=All of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (e) of this section, and apply to the individual tests in the following table:

(d) *Table.* The following table shows the data requirements for biochemical pesticides nontarget organisms and environmental fate. The test notes are shown in paragraph (e) of this section.

TABLE—BIOCHEMICAL PESTICIDES NONTARGET ORGANISMS AND ENVIRONMENTAL FATE DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Patterns					Test Substance	Test Notes
		Terrestrial	Aquatic	Greenhouse	Forestry, Residential Outdoor	Indoor		
		Food/Feed/Nonfood	Food/Nonfood	Food/Nonfood		Food/Nonfood		
Tier I								
Avian Testing								
850.2100	Avian acute oral toxicity	R	R	CR	R	CR	TGAI, EP	1, 2, 3, 4
850.2200	Avian dietary toxicity	R	R	CR	R	CR	TGAI, EP	1, 2, 3, 4
Aquatic Organism Testing								
850.1075	Fish acute toxicity, freshwater	R	R	CR	R	CR	TGAI, EP	2, 3, 4, 5