UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Mr. Mitchell Yergert, Director
Division of Plant Industry
Colorado Department of Agriculture
305 Interlocken Parkway
Broomfield, Colorado 80021

MAY 19 2015

Subject: Special Local Needs Registration for pesticide uses for legal marijuana production in Colorado

Dear Mr. Yergert:

Thank you for your inquiry regarding the utilization of Special Local Need (SLN) registrations of pesticides under FIFRA section 24(c) for use on cannabis. As you are aware, EPA's regulations, 40 CFR 162.152(a)(4), state that any SLN registration must be in accord with the purposes of FIFRA, which authorizes the registration of a pesticide only on a finding that it will not lead to "unreasonable adverse effects on the environment." In order to facilitate this finding, EPA strongly encourages a State to pursue SLN authorizations only where a federally registered pesticide is approved for use(s) similar to the manner in which the SLN pesticide would be used. EPA expects that a showing of such similarity would provide the best support for making the necessary determinations. Given our understanding of how cannabis is cultivated and the intended way cannabis plant materials may be consumed by humans, we anticipate that a federally registered pesticide would be regarded as having similar use patterns if the federally registered pesticide is approved for use:

1. on food (in order to have a complete toxicity database to evaluate the potential toxicity of acute, short-term, intermediate, and chronic exposure);
2. on tobacco (in order to have a pyrolysis study to determine the breakdown products formed when the treated plant material is burned);
3. by the same type(s) of application methods (in order to assess the exposure of workers who mix, load, and apply the pesticides);
4. on crops with agronomic characteristics similar to cannabis (in order to adequately protect workers reentering areas following application of the pesticide); and
5. in the same kind of structure (e.g., greenhouses/shadehouses) or on the same kind of site (e.g., outdoor dryland site) as the proposed SLN use (in order to ensure that workers handling the pesticide are adequately protected when applying the pesticide – for example, ensuring that the adequate personal protective equipment is required – and that the environmental fate and effects of the SLN use are adequately understood and that any appropriate measures are in place to protect non-target organisms and water resources).

In addition, EPA encourages the State to consider pesticides for which the agency's aggregate and cumulative risk assessment indicate that some modest additional exposure would not approach a risk of concern, i.e., that there is "room in the human health risk cup."

If the State decides to pursue a SLN registration for use of a pesticide on cannabis, it could meet its responsibility for showing that a proposed SLN registration would be appropriate by identifying a federally registered pesticide with similar use(s) and relying on the agency's most recent risk assessments showing that the pesticide meets the no "unreasonable adverse effects on the environment" standard. In addition, please be certain that any submission contains the information described in 40 CFR part 162 and characterized at the following website: http://www.epa.gov/opprd001/24c/. Like other SLN registrations, the State would need to submit a full label that describes the use pattern and associated mitigation for protecting human health and the environment.

EPA agrees with the State's assessment that pesticides considered for an SLN use on cannabis should have an appropriate dataset for use in assessing the potential for use of the pesticide and for residues on treated plant material to cause human health and environmental risks. In the event that the State cannot identify a federally registered pesticide with use(s) similar to the proposed SLN use, EPA would expect the requesting State to take responsibility for providing information and analysis to support the SLN registration for cannabis. To aid the State in preparing these assessments, an overview of the human and ecological risk assessment methodologies used by the Office of Pesticide Programs (OPP) is presented in the attachment. OPP is available to provide further guidance or answer any questions as to how to ensure the safety of a use under an SLN on cannabis.

Sincerely,

Jack E. Housenger, Director
Office of Pesticide Programs

Attachment

cc: Mr. John Scott, Pesticides Section Chief, Colorado Department of Agriculture
Ms. Laura Quakenbush, Pesticide Registration Coordinator, Colorado Department of Agriculture
Mr. Eric Johansen, Washington State Department of Agriculture
Ms. Melanie Wood, Division Director, Pesticides Program, EPA Region 8
Ms. Jennifer Schuller, Pesticides Team Leader, EPA Region 8
Ms. Rebecca Perrin, Agriculture Advisor, EPA Region 8
Mr. Ed Kowalski, Division Director, Pesticides Program, EPA Region 10
Ms. Kelly McFadden, Section Chief, Pesticides Program, EPA Region 10

ATTACHMENT

The following sections describe how EPA assesses the risks to human health and the environment resulting from use of pesticides.

I. HUMAN HEALTH ASSESSMENT

OPP evaluates pesticide chemicals prior to registration, and reevaluates older pesticides already on the market, to ensure that they can be used without causing unreasonable adverse effects on the environment. OPP employs the National Research Council's four-step process for human health risk assessment: hazard assessment; exposure assessment; risk characterization; and risk assessment. Details are available at http://www.epa.gov/pesticides/factsheets/riskassess.htm

1. Hazard Assessment

In evaluating toxicity or hazard, OPP reviews toxicity data, typically from studies with laboratory animals, to identify any adverse effects on the test animals. Where available and appropriate, OPP will also take into account studies involving humans, including human epidemiological studies. An extensive battery of toxicological studies are required for full pesticide registration. Toxicology data requirements are described in 40 CFR §158 subpart F http://www.epa.gov/ocspp/pubs/frs/home/guidelin.htm. Toxicology data requirements for a food-use chemical are presented in Table 1.

Once a pesticide's potential hazards are identified, OPP determines a toxicological endpoint of concern for evaluating the risk posed by human exposure to the pesticide. Two critical parts of this evaluation involve identification of a quantitative dose level(s) from these studies to be used in assessing the pesticide's safety to humans, referred to as the Point of Departure (POD), and selection of appropriate uncertainty/safety factors for translating the results of toxicity studies in relatively small groups of animals or humans to the overall human population, including major identifiable subgroups of consumers.

A POD is the dose serving as the 'starting point' in extrapolating a risk to the human population. The POD can be a no observed adverse effect level (NOAEL), the lowest-observed adverse effect level (LOAEL) or an extrapolated benchmark dose (BMD). For details refer to http://www.epa.gov/raf/publications/pdfs/rfd-final.pdf.

For threshold effects, risk assessments are normally conducted using the Reference Dose (RfD) approach. The RfD is calculated by dividing the POD by the appropriate uncertainty/safety factors. OPP's safety/uncertainty factor practice with regard to pesticides was altered to a degree by the Food Quality Protection Act (FQPA). FQPA requires EPA to use an additional safety factor of 10X to protect infants and children, unless EPA determines, based on reliable data, that use of another safety factor would protect infants and children. For pesticides, a Population Adjusted Dose (PAD) is derived by dividing the RfD by the FQPA Safety Factor. For complete details, refer to http://www.epa.gov/pesticides/trac/science/determ.pdf. An example of the toxicity endpoint selection is presented in Table 2.

For compounds causing non-threshold effects, such as carcinogens, an RfD approach is not used. Instead, a cancer risk assessment is conducted which provides an estimate (expressed as a probability) of the excess cancer risk resulting from exposure to a pesticide chemical. http://www.epa.gov/raf/publications/pdfs/

As an unreasonable adverse effects finding is developed for any prospective SLN, EPA encourages you to use the assessment endpoints that have been identified by EPA for that chemical.

2. Dietary Exposure Assessment

Acute, chronic, and cancer dietary exposure and risk assessments are conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID). This software uses 2003-2008 food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). The Agency is in the process of transitioning from the 2003-2008 NHANES/WWEIA consumption data to the 2005-2010 NHANES/WWEIA consumption data. The DEEM model that incorporates the 2005-2010 consumption data can be downloaded from http://www.epa.gov/pesticides/science/deem/

Generally, it would not be expected that the requesting State would have the residue and consumption data needed to perform a quantitative assessment of oral exposure for a SLN on cannabis. In the absence of such data, however, the State could estimate potential dietary exposure by making reasonable assumptions about high end consumption and residue levels. In addition, the State's risk assessment should address, at least qualitatively, why the additional exposure from the use of SLN on cannabis would not result in exposure exceeding the remaining room in the "human health risk cup." We expect that such an assessment will be more straight-forward if the active ingredient being proposed for the SLN registration has ample room in the risk cup for the new use.

3. Occupational and Residential Exposure Assessment

Occupational and residential exposure data requirements are described in 40 CFR part 158 subpart H available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series875.htm

In general, the data needed for a human health risk assessment for an agricultural crop, outdoor residential use, and a greenhouse use are similar; however, the exposure scenarios assessed may differ. A typical exposure assessment is divided into two parts. The handler assessment addresses potential exposure from the individuals who mix, load, and apply a pesticide, and the post-application assessment addresses the potential exposure of individuals who enter into previously treated areas and engage in activities that bring them into contact with pesticide residues. An overview of the residential human health risk assessment methodology and corresponding data for the various residential handler and post-application scenarios can be found at http://www.epa.gov/pesticides/science/residential-exposure-sop.html.

Occupational handler scenarios are assessed for the dermal and inhalation exposure pathways. (http://www.epa.gov/pesticides/science/handler-exposure-data.html) OPP uses non-chemical specific unit exposures and information from the labels about application type, site, formulation, rates, and personal protective equipment (PPE) to define each scenario. The resulting risk estimates from the handler assessment inform the risk management decisions on whether additional PPE requirements or other mitigation measures are necessary. PPE requirements on the label also fall under the Worker Protection Standard (WPS) related to the acute toxicity of the end-use product.

The occupational post-application scenarios are assessed for the dermal exposure pathway. OPP uses non-chemical specific transfer coefficients to capture the potential dermal exposure from different crop and activity combinations (http://www.epa.gov/opp00001/science/post-app-exposure-data.html).

OPP also uses chemical-specific data to inform the potential pesticide residue that is available on a foliar surface after an application; these data are referred to as dislodgeable foliar residue (DFR) and turf transferable residue (TTR) studies. When these data are not available, OPP currently uses default assumptions of 25% for DFR and 1% and 0.2% for TTR for the liquid and granular formulations, respectively. The post-application risk estimates determine how many days after treatment an individual may safely reenter the treated area for routine post-application activities. The more protective Restricted Entry Interval value is typically required on the labels. In addition, specifically for greenhouse uses, the WPS provides information on proper ventilation requirements to protect workers from post-application inhalation exposure.

If the pesticide proposed for a SLN use has no federally registered indoor uses, the State should specifically address whether handlers applying the pesticide indoors or others who would contact the pesticide treated plants would be adequately protected without additional PPE, and if not, what additional PPE would be needed to prevent unacceptable exposures from the anticipated application and post-application scenarios.

4. Risk Characterization and Risk Assessment

(i) <u>Dietary Exposure Risk Assessment</u>

The State's risk assessment should provide a general characterization of risk for the general population and should take into account both potential acute and chronic exposures.

(ii) <u>Occupational Exposure Risk Assessment</u>

- <u>Occupational Handlers</u>

In this section, the State's risk assessment should identify the occupational handler exposure scenarios based on the proposed use (list representative scenarios only). Briefly describe the data sources used such as an existing EPA risk assessment or, if a new assessment is being conducted, PHED, biomonitoring studies, or chemical specific data. Summarize the risks assessed. If there are no risks at baseline PPE, simply state the lowest Margin of Exposures (MOEs). If there are scenarios with risks of concern at baseline and additional personal protective equipment (PPE) will be needed to

achieve MOEs greater than the level of concern (LOC), summarize the MOEs at different PPE levels. The summary can be in tabular or paragraph form. As noted earlier, we encourage the State to use existing risk assessments to prepare this information.

- Occupational Post-Application

In this section, identify the occupational post application exposure scenarios based on the proposed use in a general manner. Briefly describe the data sources used such as an existing EPA risk assessment or, if a new assessment is being conducted, biomonitoring studies or chemical-specific data. Indicate whether or not dislodgeable foliar residue (DFR) studies are available. Indicate whether or not the most recent transfer coefficients were used to determine post-application exposure and risk. Summarize the scenarios with risks of concern, and provide a summary of the MOEs. Data can be in tabular or text form.

- Inhalation Exposure Assessment

It is OPP's policy to assess risk following short-term exposure to pesticide residues in tobacco products as the chronic health effects from tobacco use are well documented. OPP uses data from a pyrolysis study (Test Guideline 860.1000) and a magnitude of residue study (Test Guideline 860.1500) for this assessment. This assessment assumes: (1) 100% of the inhaled residue is absorbed; (2) the average U.S. smoker smokes 15 cigarettes per day (Pierce, J. P., *et al.* (1989), Tobacco use in 1986 – Methods and Basic Tabulations from Adult Use of Tobacco Survey, U.S. Dept. of Health and Human Services Publication Number OM90-2004, Office on Smoking and Health, Rockville, Maryland); (3) 1 gram of tobacco per cigarette; and (4) male/female body weight of 70/60 Kg. The POD established for short-term exposure is used to derive a MOE for expressing risk via this exposure scenario. If there is no federally registered tobacco use of the proposed SLN pesticide, the State's risk assessment should assess the potential acute risk from inhaling residues from smoking treated plant material; the assessment should use the above assumptions or justify the use of different assumptions.

II. ECOLOGICAL EFFECTS AND ENVIRONMENTAL FATE

In general, the types of data used to support an ecological risk assessment for a SLN pesticide registration should be comparable to the ecological effects and environmental fate data required for a Section 3 pesticide registration (see 40 CFR part158, subpart G and subpart N). Note the data requirements for outdoor terrestrial uses and greenhouse/indoor uses are substantially different in regards to the number and types of studies required for registration. Outdoor terrestrial uses are also subject to the data requirements for pollinators (see Guidance for Assessing Pesticide Risks to Bees). Tables 3 and 4 provide an overview of the data requirements for ecological effects and environmental fate respectively. An overview of the ecological risk assessment framework and supporting documentation can be found at: http://www.epa.gov/oppefed1/ecorisk_ders/.

The ecological risk assessment should consist of a problem formulation, an analysis characterizing the exposure and effects of the chemical stressor and a risk characterization.

1. Problem Formulation

Problem formulation provides the foundation for the ecological risk assessment. It is an iterative process for generating hypotheses concerning whether ecological effects could occur from human activities. The problem formulation articulates the purpose and objectives of the risk assessment and defines the problem and regulatory action. The quality of the assessment depends on rigorous development of the following products of problem formulation: 1) assessment endpoints that reflect management goals and the ecosystem they represent; 2) conceptual model(s) that represents predicted key relationships between stressor(s) and assessment endpoint(s); and 3) a plan for analyzing the risk.

2. Analysis of Exposure and Effects

For a pesticide risk assessment, the exposure characterization describes the potential or actual contact of a pesticide with a plant, animal, or media. The objective is to describe exposure in terms of intensity, space, and time and to describe the exposure pathway(s). A complete picture of how, when, and where exposure occurs or has occurred is developed by evaluating sources and releases of the pesticide, distribution of the pesticide in the environment, and extent and pattern of contact with the pesticide.

For greenhouse/indoor uses there are several factors the State will need to consider. First there is a difference between a greenhouse and a shadehouse. A greenhouse is defined as "operations that produce agricultural plants indoors in an area that is enclosed with nonporous covering and that is large enough to allow a person to enter." Shadehouses are defined as "a roof made of fencing or fabric to provide shade on plants (no walls)." Growing operations in a shadehouses are typically considered an outdoor terrestrial use.

The other factor to consider in the risk assessment for greenhouse/indoor use is the potential for "Down the Drain" release to publically owned treatment works or in some cases direct discharge to the environment. The "Down the Drain" assessment accounts for the normal use of a pesticide in a greenhouse, not the illegal disposal of a pesticide.

An ecological effects characterization describes how toxic a pesticide is to different organisms and/or to other ecological entities (e.g., community), what effects it produces, how the effects relate to the assessment endpoints, and how these effects change with varying levels of pesticide exposure. This characterization is based on a stressor-response profile that describes how toxic a pesticide is to various plants and animals, the cause-and-effect relationships, how fast the organism(s) recovers, relationships between the assessment endpoints and measures of effect, and the uncertainties and assumptions associated with the analysis. The stressor-response profile is the final product of the ecological effects characterization.

3. Risk Characterization

The risk characterization integrates the analyses from the exposure characterization and ecological effects characterization; describes the uncertainties, assumptions, and strengths and limitations of the analyses; and synthesizes the overall conclusion about risk that is used by risk managers in making risk management decisions.

Risk characterization has two major components: risk estimation and risk description. Risk estimation compares exposure and effects data, considers integrated exposure and effects data in context of Levels of Concern (LOCs), and states the potential for risk. The risk description interprets risks based on assessment endpoints. In interpreting the risk, the risk assessor evaluates the lines of evidence supporting or refuting risk estimates in terms of the following factors: adequacy and quality of data; degree and type of uncertainty; and the relationship of evidence to risk assessment questions.

As noted above for the human health risk assessment, EPA encourages the State to consider and use EPA's existing ecological risk assessments, where appropriate, to assess the environmental fate and ecological effects of any proposed SLN on cannabis.

Table 1. Toxicology Data Requirements

The requirements (40 CFR 158.340) for a typical food-use chemical are listed below:

Study Type		Requirement
870.1100	Acute Oral Toxicity	yes
870.1200	Acute Dermal Toxicity	yes
870.1300	Acute Inhalation Toxicity	yes
870.2400	Primary Eye Irritation	yes
870.2500	Primary Dermal Irritation	yes
870.2600	Dermal Sensitization	yes
870.3100	Oral Subchronic (rodent)	yes
870.3150	Oral Subchronic (nonrodent)	yes
870.3200	21-Day Dermal	yes
870.3250	90-Day Dermal	No
870.3465	90-Day Inhalation	**CR**
870.3700a	Developmental Toxicity (rodent)	yes
870.3700b	Developmental Toxicity (nonrodent)	yes
870.3800	Reproduction toxicity	yes
870.4100a	Chronic Toxicity (rodent)	yes
870.4100b	Chronic Toxicity (nonrodent)	yes
870.4200a	Carcinogenicity (rat)	yes
870.4200b	Carcinogenicity (mouse)	yes
870.4300	Combined chronic toxicity/carcinogenicity	yes
870.5100	Mutagenicity—Gene Mutation - bacterial	yes
870.5300	Mutagenicity—Gene Mutation - mammalian	yes
870.5xxx	Mutagenicity—Structural Chromosomal Aberrations	yes
870.5xxx	Mutagenicity—Other Genotoxic Effects	yes
870.6100a	Acute Delayed Neurotoxicity (hen)	no
870.6100b	90-Day Neurotoxicity (hen)	no
870.6200a	Acute Neurotoxicity Screening Battery (rat)	yes
870.6200b	90-Day Neurotoxicity Screening Battery (rat)	yes
870.6300	Develop. Neurotoxicity	**CR**
870.7485	General Metabolism	yes
870.7600	Dermal Penetration	yes
870.7800	Immunotoxicity	yes

CR= Conditionally Required. See footnotes in Part 158 Table.

Table 2. Summary of Points of Departure and Toxicity Endpoints Used in Human Risk Assessment

Summary of Toxicological Doses and Endpoints for [Chemical] for Use in Dietary and Non-Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty/FQPA Safety Factors**	**RfD, PAD, Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary (General Population, including Infants and Children)	NOAEL= [ ] mg/kg/day	UF_A= [ ]x UF_H=[ ]x FQPA SF= [ ]x	Acute RfD = [ ] mg/kg/day aPAD =[ ] mg/kg/day	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Acute Dietary (Females 13-49 years of age)	NOAEL = [ ] mg/kg/day	UF_A= [ ]x UF_H=[ ]x FQPA SF= [ ]x	Acute RfD = [ ] mg/kg/day	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Chronic Dietary (All Populations)	NOAEL= [ ] mg/kg/day	UF_A= [ ]x UF_H=[ ]x FQPA SF= [ ]x	Chronic RfD = [ ] mg/kg/day cPAD = [ ] mg/kg/day	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Incidental Oral Short-Term (1-30 days)	NOAEL= [ ] mg/kg/day	UF_A= [ ]x UF_H=[ ]x	Residential LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Incidental Oral Intermediate-Term (1-6 months)	NOAEL= [ ] mg/kg/day	UF_A= [ ]x UF_H=[ ]x FQPA SF= [ ]x	Residential LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Dermal Short-Term (1-30 days)	NOAEL= [ ] mg/kg/day	UF_A= [ ]x UF_H=[ ]x FQPA SF= [ ]x	Residential LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Dermal Intermediate-Term (1-6 months)	NOAEL= [ ] mg/kg/day	UF_A= [ ]x UF_H=[ ]x FQPA SF= [ ]x	Residential LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Inhalation Short-Term (1-30 days)	NOAEL= [ ] mg/kg/day	UF_A= [ ]x UF_H=[ ]x FQPA SF= [ ]x	Residential LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Inhalation Intermediate-Term (1-6 months)	NOAEL= [ ] mg/kg/day	UF_A= [ ]x UF_H=[ ]x FQPA SF= [ ]x	Residential LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]

Summary of Toxicological Doses and Endpoints for [Chemical] for Use in Dietary and Non-Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty/FQPA Safety Factors**	**RfD, PAD, Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Cancer (oral, dermal, inhalation)	Classification: This should be consistent with section 4.5.3 and the CARC document.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key data (i.e., lack of a critical study). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

Summary of Toxicological Doses and Endpoints for [*Chemical*] for Use in Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Dermal Short-Term (1-30 days)	NOAEL= [ ] mg/kg/day	UF_A=10x UF_H=10x	Occupational LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Dermal Intermediate-Term (1-6 months)	NOAEL= [ ] mg/kg/day	UF_A=10x UF_H=10x	Occupational LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Inhalation Short-Term (1-30 days)	NOAEL= [ ] mg/kg/day	UF_A=10x UF_H=10x	Occupational LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Inhalation Intermediate-term (1-6 months)	NOAEL= [ ] mg/kg/day	UF_A=10x UF_H=10x	Occupational LOC for MOE = [ ]	[insert study name] LOAEL = [ ] mg/kg/day based on [ ]
Cancer (oral, dermal, inhalation)	Classification: This should be consistent with section 4.5.3 and the CARC document.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment. UF_{DB} = to account for the absence of key data (i.e., lack of a critical study). MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

Table 3. Ecotoxicology Studies[1]

Guideline	Study Type	Comments
850.2100	Avian acute oral	Data required for a passerine species and either a waterfowl or upland game species
850.2200	Avian sub-acute dietary	Data required for a waterfowl and upland game species
850.2300	Avian reproduction study	Data required for a waterfowl and upland game species
850.1075	Acute freshwater fish	Data required for a cold water species and a warm water species
850.1075	Acute estuarine/marine fish	
850.1010	Acute freshwater invertebrates	
850.1025 850.1035 850.1045 850.1055	Acute toxicity to estuarine/marine invertebrates	Data required for one mollusk and one invertebrate
850.1300	Chronic freshwater invertebrate	
850.1350	Chronic estuarine/marine invertebrate	Conditionally required depending on exposure and toxicity (see CFR 158 for more details)
850.1400 or 850.1500	Chronic freshwater fish	
850.1400 or 850.1500	Chronic estuarine/marine fish	Conditionally required depending on exposure and toxicity (see CFR 158 for more details)
850.1735	Acute sediment toxicity to freshwater benthic organisms	Conditionally required depending on the physical properties of the chemical and toxicity to non-benthic organisms (see CFR 158 for more details)
850.1740	Acute sediment toxicity to estuarine/marine benthic organisms	Conditionally required if chemical is applied directly to estuarine/marine water bodies or expected to enter them in significant amounts. Also depends depending on the physical properties of the chemical and toxicity to non-benthic organisms (see CFR 158 for more details)
Non-guideline	Chronic sediment toxicity	Conditionally required depending on the physical properties of the chemical and toxicity to non-benthic organisms (see CFR 158 for more details)
850.3020	Acute contact toxicity to honeybee	
OECD 213	Acute oral toxicity to adult honeybee	Pollinator Guidance Document requirement (not in CFR 158)
Non-guideline	Subchronic 10-day toxicity to adult honeybees	Pollinator Guidance Document requirement (not in CFR 158)

[1] With the exception of non-guideline data requirements, the studies listed in this table were compiled from tables in the CFR "Terrestrial and aquatic nontarget organisms data requirements table" in 40 CFR §158.630 and "Nontarget plant protection data requirements table" in 40 CFR §158.660. Please see the CFR for the full tables, all applicable footnotes, and several additional studies which are not typically required but may be required in specific instances.

Guideline	Study Type	Comments
Non-guideline	Acute and chronic larval honeybee toxicity	Pollinator Guidance Document requirement (not in CFR 158)
Non-guideline	Pesticide residues in pollen and nectar	Conditionally required if honeybee concerns are identified from the laboratory tests. Pollinator Guidance Document requirement (not in CFR 158)
850.3040	Field testing for pollinators	Conditionally required if honeybee concerns are identified from the laboratory tests.
850.4100	Seedling emergence	
850.4150	Vegetative vigor	
850.4400	Vascular aquatic plant testing	
850.4500	Non-vascular aquatic plant testing	Testing is required for one freshwater algal species, freshwater diatom, and estuarine/marine diatom
850.4550	Cyanobacteria toxicity	
870.1100	Acute mammalian oral toxicity	
870.3800	Two-generation rat reproduction study	

Table 4. Environmental Fate Studies[2]

Guideline	Study Type	Comments
835.2120	Hydrolysis	
835.2240	Photodegradation in water	
835.2410	Photodegradation in soil	
835.2370	Photodegradation in air	Conditionally required for terrestrial and greenhouse use patterns depending on Henry's law constant and other chemical factors. (See CFR 158 for more details.)
835.4100	Aerobic soil metabolism	
835.4200	Anaerobic soil metabolism	
835.4300	Aerobic aquatic metabolism	
835.4400	Anaerobic aquatic metabolism	
835.1230 835.1240	Leaching and adsorption / desorption	
835.1410	Volatility – laboratory	Conditionally required. (See CFR 158 for more details.)
835.8100	Volatility - field	Conditionally required. (See CFR 158 for more details.)
835.6100	Terrestrial field dissipation	
835.6200	Aquatic field dissipation	Conditionally required. (See CFR 158 for more details.)
835.7100	Ground water monitoring	Conditionally required. (See CFR 158 for more details.)

[2] The studies listed in this table were compiled from the "Environmental fate data requirements table" in 40 CFR §158.1300. Please see the CFR for the full table, all applicable footnotes, and several additional studies which are not typically required but may be required in specific instances.