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

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM

DATE: June 1, 2017

SUBJECT: **Florpyrauxifen-benzyl:** New Active Ingredient, First Food Use. Human Health Risk Assessment for the Establishment of Permanent Tolerances on Rice, Fish, and Shellfish and Registration for Uses on Rice and Freshwater Aquatic Weed Control.

PC Code: 030093
Decision No.: 509428

Petition No.: 5F8403
Assessment Type: Single Chemical/ Aggregate
MRID No.: NA
TXR No.: NA

DP Barcode: D429767
Registration No.: 62719-AOI, 62719-AOO, 62719-TNN, 62719-TNR
Regulatory Action: Section 3 Registration
Case No.: NA

CAS No.: 1390661-72-9

FROM: Barry O'Keefe, Senior Biologist and Risk Assessor B. O'Keefe
Whang Phang, PhD, Senior Toxicologist
Meheret Negussie, Chemist Meheret Negussie
Risk Assessment Branch III
Health Effects Division (7509P)

THRU: Barbara Madden, Acting Branch Chief
Risk Assessment Branch III
Health Effects Division (7509P)
and
Mike Metzger, RARC Reviewer
Elizabeth Mendez, RARC Reviewer
Risk Assessment Review Committee
Health Effects Division

TO: Karen Samek
Dan Kenny, Branch Chief
Herbicide Branch
Registration Division (7505P)

The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The Registration

Division (RD) of OPP has requested that HED evaluate hazard and exposure data and conduct dietary, occupational, residential and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from the proposed uses of the new herbicide active ingredient florpyrauxifen-benzyl.

Table of Contents

1.0 EXECUTIVE SUMMARY

Florpyrauxifen-benzyl (alternate names: XDE-848 BE, XDE-848 benzyl ester, and Rinskor™) (benzyl 4-amino-3-chloro-6-[4-chloro-2-fluoro-3-methoxylphenyl]-5-fluoropyridine-2-carboxylate) is a new arylpicolinate systemic herbicide, developed by Dow Agrosciences, LLC (DAS), in the same pyridine carboxylic acid family as aminocylopyrachlor, aminopyralid, clopyralid, and picloram.

Florpyrauxifen-benzyl controls grasses, broadleaf weeds, and sedges, and controls or suppresses most herbicide resistant biotype weeds in rice. Additionally, it is proposed for use for freshwater aquatic weed control in ponds, lakes, reservoirs, marshes, wetlands, bayous, drainage ditches, canals, and other aquatic use sites. Target plants for the aquatic uses (other than rice) include invasive species such as hydrilla (*Hydrilla verlicillata*), Eurasian watermilfoil (*Myriophyllum spicatum*), and crested floating heart (Nymphoides cristata). In addition to in-water application for control of aquatic weeds, a foliar use has been proposed for nuisance floating and emergent aquatic weed management. Tolerances on rice, freshwater fish, and shellfish (crustacean and mollusk) are being proposed to support these uses.

Proposed Use Profile

Florpyrauxifen-benzyl is proposed for use on rice as a new selective, systemic, post-emergence herbicide with broad spectrum activity on important grass, sedge, and broadleaf weed species in rice. There are four end-use products (EPs) relevant to this registration action. The EPs are proposed for a maximum of two foliar spray applications using ground or aerial equipment at a maximum single application rate of 0.027 lb ai/A/Application, with a maximum yearly rate of 0.0525 lb ai/A. The proposed pre-harvest interval (PHI) is 60 days. One end use product (GF-3301, EPA File Symbol 62719-AOO, U.S. only) can be applied directly to water or sprayed onto emergent foliage of aquatic plants with a maximum active ingredient water concentration of 50 ppb per application.

Hazard Characterization

The toxicology database for florpyrauxifen-benzyl is complete for risk assessment. One of the unique features for florpyrauxifen-benzyl is that with oral administration, the maximum absorption occurs at approximately 300 mg/kg, above which the blood level of the test material remains constant. Hence, 300 mg/kg is considered as the kinetically-derived maximum dose. No single or repeated dose study performed by any route of exposure produced an adverse effect following florpyrauxifen-benzyl exposure at or above the limit dose (1000 mg/kg/day) or kinetically derived maximum dose.

Florpyrauxifen-benzyl is not likely to be carcinogenic as there is no compound-related increase in tumor incidence found in rat and mouse carcinogenicity studies. The mutagenicity battery provides no evidence of genotoxic potential.

Based on the review of the available florpyrauxifen-benzyl toxicological studies, no toxicity endpoints or points of departure were selected for risk assessment. Hence, a

safety factor to protect children is not needed and the toxicity data indicate a qualitative risk assessment is appropriate for this pesticide.

Residue Chemistry & Tolerance Considerations

Based on the lack of toxicity, the USEPA would typically grant florpyrauxifen-benzyl an exemption from the requirement of tolerances. However, DAS has requested that tolerances/maximum residue limits (MRLs) be set for florpyrauxifen-benzyl for international trade purposes. As a result, the registrant has proposed tolerances for florpyrauxifen-benzyl based on the parent compound and its acid metabolite X11438848 (florpyrauxifen; 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoropyridine-2-carboxylic acid), as determined by the Residues of Concern Knowledgebase Subcommittee (ROCKS; D436519, I. Negrón-Encarnación, 11/15/2016). Rice straw is no longer considered to be a significant livestock feedstuff; therefore, no tolerance is required for rice straw. Data from rice processing studies indicate that residues of florpyrauxifen-benzyl were non-quantifiable, and therefore, residues do not concentrate in processed commodities (hulls, bran and flour).

Human Health Risk Assessment

HED has determined that a quantitative risk assessment is not needed at this time for dietary, residential, occupational, or aggregate exposure. A qualitative human health risk assessment has been conducted to support the proposed uses of florpyrauxifen-benzyl. No risks of concern have been identified since no adverse effects were observed in the submitted toxicological studies for florpyrauxifen-benzyl regardless of the route of exposure.

2.0 HED RECOMMENDATIONS

HED has examined the residue chemistry, toxicity, and exposure databases for florpyrauxifen-benzyl and concluded that, provided a revised Section B and F are submitted, there are no deficiencies that would preclude granting a Section 3 registration and establishing the recommended tolerances for residues of florpyrauxifen-benzyl on rice, fish and shellfish.

2.1 Data Deficiencies

No data have been provided to account for potential residues on irrigated crops resulting from applications to irrigation ditches and channels. To account for the lack of these data, the registrant proposed labeling language that reads “Do not use water from any treated site for food/feed crop irrigation, other than rice, at concentrations >1 ppb unless a 30-day pre-harvest interval can be observed and authorization is obtained from DAS, or unless concentrations are ≤1 ppb. For food/feed crops and in areas irrigated with GF-3301 at >1 ppb, consult DAS for site-specific risk evaluations before planting rotational crops or other plants unless a 90-day pre-planting interval is observed between end of irrigation with treated water and time of planting.” HED does not consider these proposed restrictions enforceable and these statements would not normally eliminate the need for magnitude of the residue data for irrigated crops in cases where tolerances are being established on the treated crop.

However, HED has determined that a quantitative risk assessment is not needed based on the lack of toxicity; therefore, the USEPA would typically grant florpyrauxifen-benzyl an exemption from the requirement of tolerances, precluding the need for irrigated crop residue data. Therefore, the registrant can either prohibit applications to water that will be applied to irrigated crops or revise the Section F and propose an exemption from the requirement of tolerances for the indirect or inadvertent residues of florpyrauxifen-benzyl on commodities resulting from treatment of water for irrigation.

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

An adequate analytical method which uses high-performance liquid chromatography with tandem mass spectrometry (HPLC/MS-MS) to quantitate residues of florpyrauxifen-benzyl and XDE- 848 Acid (X11438848) in various crops and livestock commodities is available for enforcement.

The method is based on the multiresidue analytical method, QuEChERS (EN 15662) sample preparation technique. Briefly, residues of florpyrauxifen-benzyl and X11438848 are extracted from samples with acetonitrile. After addition of $MgSO_4$, NaCl, and buffering citrate salts, the samples are shaken and centrifuged. For fatty samples only, extracts are stored for ≥4 hours in a freezer in order to precipitate the majority of fat from the sample. For oilseed rape (seeds) samples only, an additional clean-up step is carried out by transferring an aliquot into a tube containing C18 material and intensively shaking. For all matrices, an aliquot of the acetonitrile phase is evaporated to dryness before reconstitution in methanol/water (1:1) containing 0.1% formic acid. The final sample is analyzed for florpyrauxifen-benzyl and X11438848 by LC-MS/MS.

This multiresidue method is applicable for the quantitative determination of residues of florpyrauxifen-benzyl and X11438848 in agricultural commodities, represented by wheat grain (high starch content), lettuce (high water content), lemon (whole fruit) (high acid content) and oilseed rape (seeds) (high oil content) and in livestock commodities (poultry eggs and bovine fat, liver, meat, and whole milk). The method was validated over the concentration range of 0.01-0.1 ppm with a validated limit of quantification of 0.01 ppm for each analyte.

The ion transitions monitored for florpyrauxifen-benzyl are *m/z* 439→91 (quantitation) and *m/z* 441→65 (confirmation) and for X11438848 are *m/z* 349→268 (quantitation) and *m/z* 349→270 (confirmation).

For fish, residues of florpyrauxifen-benzyl and X11438848 were extracted from samples by homogenizing and shaking with acetonitrile/0.1 N HCl (90/10, v/v) (2x). After centrifuging and decanting the supernatant, an aliquot of the sample was diluted with an internal standard diluent solution and centrifuged at a high speed. The sample was analysed for florpyrauxifen-benzyl and X11438848 using LC-MS/MS. The method was

validated over the concentration range of 0.01-1.0 ppm with a validated limit of quantification of 0.01 ppm.

The ion transitions monitored for florpyrauxifen-benzyl are *m/z* 439→91 (quantitation) and *m/z* 441→91 (confirmation) and for X11438848 are *m/z* 349→268 (quantitation) and *m/z* 351→270 (confirmation).

FDA multiresidue methods (MRMs) were not submitted.

2.2.2 Recommended Tolerances

The petitioner, DAS, proposed the establishment of tolerances for residues of florpyrauxifen-benzyl, including its metabolites and degradates, in or on the agricultural commodities as shown in Table 2.2.2 below.

A compliance statement was not included as per the S. Knizner memo dated 5/27/09. A revised Section F is needed to state the following:

General (a). Tolerances are established for residues of florpyrauxifen-benzyl, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of florpyrauxifen-benzyl (phenylmethyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoro-2-pyridinecarboxylate) and its acid metabolite (4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoropyridine-2-carboxylic acid) calculated as the stoichiometric equivalent of florpyrauxifen-benzyl, in or on the commodity.

A revised Section F is needed to propose the tolerances as recommended in Table 2.2.2 below.

Table 2.2.2. Tolerance Summary for Florpyrauxifen-benzyl.

Commodity	Proposed Tolerance (ppm)	HED-Recommended Tolerance (ppm)	Comments (correct commodity definition)
Rice, grain, (dehulled)	0.01	None	
Rice, grain	0.2	0.30	Rice, grain
Fish, freshwater	2	2.0	Fish - freshwater finfish
Shellfish, crustacean	0.5	0.50	Fish - shellfish, crustacean
Shellfish, mollusc	9	20	Fish - shellfish, mollusc

2.2.3 Revisions to Petitioned-For Tolerances

HED's recommended tolerances differ from the registrant's proposed tolerances. The Agency is revising the commodity definitions for the requested tolerances (fish and shellfish) to reflect the correct commodity vocabulary currently used by the Agency. Additionally, the Agency is revising the significant figures for the tolerance levels based on current policy. Therefore, a revised Section F needs to be submitted.

The proposed tolerance for residues of florpyrauxifen-benzyl in/on rice, grain is 0.2 ppm. Based on the Organization for Economic Cooperation and Development (OECD) statistical calculation applied to the field trial (U.S.) residue data, a value of 0.30 ppm is recommended.

The recommended tolerances for residues of florpyrauxifen-benzyl in/on freshwater fish, shellfish crustacean and shellfish mollusc are 2.0, 0.50 and 20 ppm, respectively. The recommended tolerance for shellfish mollusc was revised based on the residue data provided, which included the 0-day data. It appears that the registrant did not consider the 0-day data. The OECD calculation procedures were not used to estimate these tolerances since only decline data were available.

2.2.4 International Harmonization

There are no Codex/Canadian maximum residue limits (MRLs) established on florpyrauxifen-benzyl; therefore, there are no harmonization issues.

2.3 Label Recommendations

The following restrictions listed on the proposed labels should be removed:

"Do not use water from any treated site for food/feed crop irrigation, other than rice, at concentrations >1 ppb unless a 30-day pre-harvest interval can be observed and authorization is obtained from DAS, or unless concentrations are ≤1 ppb. For food/feed crops and in areas irrigated with GF-3301 at >1 ppb, consult DAS for site-specific risk evaluations before planting rotational crops or other plants unless a 90-day pre-planting interval is observed between end of irrigation with treated water and time of planting."

"Do not use water for irrigation of greenhouse or nursery plants unless herbicide concentration is <1 ppb or authorization is received from Dow AgroSciences."
HED does not consider these proposed restrictions enforceable and these statements do not eliminate the need for magnitude of the residue data for irrigated crops.

HED recommends that the registrant either prohibit applications to water that will be applied to irrigated crops, greenhouse and nursery plants. Or revise the Section F and propose an exemption from the requirement of tolerances for the indirect or inadvertent residues of florpyrauxifen-benzyl on commodities resulting from treatment of water for irrigation.

3.0 INGREDIENT PROFILE

Florpyrauxifen-benzyl is a new arylpicolinate systemic herbicide. It is proposed for use on rice and for freshwater aquatic weed control in ponds, lakes, reservoirs, marshes, wetlands, bayous, drainage ditches, canals, and other aquatic use sites (which include both direct in-water applications and foliar applications to aquatic vegetation). It controls grasses, broadleaf weeds, and sedges and controls or suppresses most herbicide resistant

biotypes of these weeds in rice. Target plants for the aquatic uses (other than rice) include invasive species such as hydrilla (*Hydrilla verlicillata*), Eurasian watermilfoil (Myriophyllum spicatum or EWM), and crested floating heart (*Nymphoides cristata*).

3.1 Structure and Nomenclature

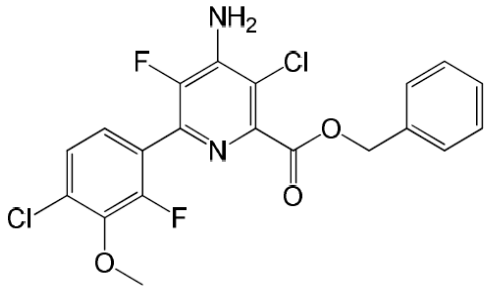
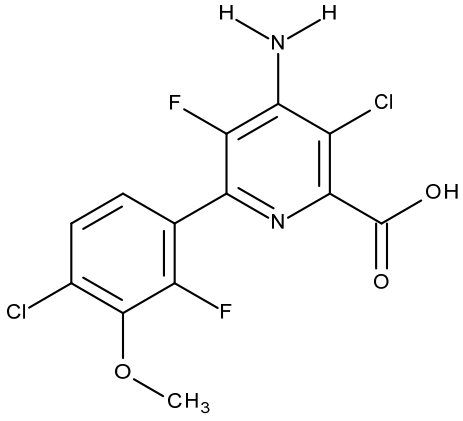
Table 3.1. Florpyrauxifen-benzyl Nomenclature.	
Compound	
Common name	florpyrauxifen-benzyl (XDE-848 BE, Florpyrauxifen-benzyl, and Rinskor™)
Identity	florpyrauxifen-benzyl (XDE- 848 Benzyl Ester) (benzyl-4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carboxylate)
Molecular Weight	439.2 g/mole
Chemical Formula	$C_{20}H_{14}Cl_2F_2N_2O_3$
CAS no.	1390661-72-9
Company experimental names	Florpyrauxifen-benzyl, XDE-848 BE, XR-848 BE, and Rinskor™
IUPAC name	benzyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoropyridine-2-carboxylate
CAS name	phenylmethyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoro-2-pyridinecarboxylate
End-use products (EPs)	GF-3206 (A.I. Florpyrauxifen-benzyl) EPA File Symbol 62719-AOI GF-3301 (A.I. Florpyrauxifen-benzyl) EPA File Symbol 62719- AOO GF-3480 (A.I. Florpyrauxifen-benzyl, cyhalofop-butyl) EPA File Symbol 62719-TNN GF-3565 (A.I. Florpyrauxifen-benzyl, penoxsulam) EPA File Symbol 62719-TNR
Compound (metabolite)	
Common name	Florpyrauxifen (also known as X11438848)
IUPAC name	4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoropyridine-2-carboxylic acid

Table 3.1. Florpyrauxifen-benzyl Nomenclature.	
CAS no.	943832-81-3

3.2 Physical/Chemical Characteristics

Florpyrauxifen-benzyl has a low water solubility (0.015 mg/L in water at 20°C) and has a low vapor pressure (3.2 x 10-5 Pa at 20°C) and therefore is not highly volatile. It has an octanol/water partition coefficient of 5.5.

Refer to Appendix C for physical/chemical properties.

3.3 Summary of Proposed Uses

Florpyrauxifen-benzyl is proposed for use on rice and aquatic vegetation. For the rice use, the application rate is in fluid ounces per acre, with the maximum single rate of 0.0272 lb ai/A. Two applications are allowed per year, with a maximum yearly rate of 0.0535 lb ai/A. Four products are proposed for use on rice. Applications can be done using aerial or ground equipment.

For the aquatic use, the concentration of the active ingredient in the volume of water must be calculated. There is only one product with aquatic uses (GF-3301). Three applications a year are proposed, with a maximum active ingredient water concentration of 50 ppb per application, for a total of 150 ppb per year.

The proposed florpyrauxifen-benzyl formulations are liquids. There are four end use products proposed for use in the U.S.: GF-3206 an emulsifiable concentrate (EC) formulation containing 25 g ai/L, 0.21 lb ai/gal; GF-3301 a suspension concentrate (SC) formulation containing 300 g ai/L 2.5 lb ai/gal (US only); GF-3480 a multiple active ingredient (MAI) EC formulation (containing cyhalofop) 20 g ai/L, 0.17 lb ai/gal; GF-3565 MAI EC formulation (containing penoxsulam) 12.5 g ai/L, 0.10 lb ai/gal.

For occupational handlers, the proposed personal protective (PPE) equipment is long-sleeved shirt and long pants, socks, and shoes. The proposed restricted entry interval (REI) is 12 hours. The proposed uses are summarized in Tables 3.3.1 and 3.3.2.

Table 3.3.1. Summary of Directions for Use of Florpyrauxifen-benzyl.						
Applic. Timing, Type, and Equip.	Formulation [EPA File Symbol]	Applic. Rate/Season g/ha (lb ai/A)	Max. No. Applic./ Year	Max. Applic. Rate/Year g/ha (lb ai/A)	PHI[a] (days)	Use Directions and Limitations
Rice in the states of Arkansas, Florida, Louisiana, Mississippi, Missouri, South Carolina, Tennessee and Texas						
Broadcast Foliar spray; Aerial or Ground	GF-3206 EC [62719-AOI]	30 (0.027)	2	60 (0.054)	60	GF-3206 can be applied to rice fields used for crayfish production. Except for crayfish, do not fish or commercially grow fish, shellfish or crustaceans on treated acres during the year of treatment. Use of an agriculturally approved methylated seed oil adjuvant at a rate of 0.5 pints per acre is required. RTI of 14 days or greater is recommended.
Broadcast Foliar spray; Aerial or Ground	GF-3301 SC [62719-AOO]	30 (0.027)	2	60 (0.054)	60	RTI of 14 days or greater is recommended. Except for crayfish, do not fish or commercially grow fish, shellfish or crustaceans on treated acres during the year of treatment.
Broadcast Foliar spray; Aerial or Ground	GF-3480 EC (MAI) [62719-TNN]	30 (0.027)	1	30 (0.027)	60	Do not fish or commercially grow fish, shellfish or crustaceans on treated acres during the year of treatment.
Broadcast Foliar spray; Aerial or Ground	GF-3565 OD (MAI) [62719-TNR]	24 (0.021)	1	24 (0.021)	60	Except for crayfish, do not fish or commercially grow fish, shellfish or crustaceans on treated acres during the year of treatment.

[a] PHI = Pre-Harvest Interval

Restrictions: Applications are to be made in a minimum of 10 gallons per acre (GPA). Do not rotate treated land to crops other than rice for 3 months following application. Except for crayfish, do not fish or commercially grow fish, shellfish or crustaceans on treated acres during the year of treatment. Do not apply this product through any type of irrigation system. Do not use on wild rice.

Table 3.3.2. Summary of Directions for Use for GF-3301 of Florpyrauxifen-benzyl.					
Aquatics: Ponds, lakes, reservoirs, marshes, wetlands, bayous, drainage ditches, canals, and other aquatic sites (freshwater aquatic vegetation).					
In-Water Application - Three applications a year are proposed, with a maximum active ingredient water concentration of 50 ppb per application, for a total of 150 ppb per year.					
Percent Area of Waterbody Treated* %.	**Days of Irrigation Precaution in Treated Area**				**Use Directions and Limitations**
	5 - 10 ppb	**10 - 20 ppb**	**20 - 50 ppb**	**>50 ppb**	No restrictions on consumption of treated water for potable water use or by livestock, pets, or other animals. No restrictions on the use of treated water for recreational purposes, including swimming and fishing, or for irrigating established turf. Do not use water from any treated site for food/feed crop irrigation, other than rice, at concentrations >1 ppb unless a 30-day pre-harvest interval can be observed, or unless concentrations are ≤1 ppb. For food/feed crops and in areas irrigated with GF-3301 at >1 ppb, consult DAS for site-specific risk evaluations before planting rotational crops or other plants unless a 90-day pre-planting interval is observed between end of irrigation with treated water and time of planting.
2% or less	5 days	7 days	10 days	**	
3 – 10	10 days	21 days	28 days	**	
11 – 20	21 days	28 days	**	**	
>20	**	**	**	**	
Foliar Application (emergent foliage)-Maximum application rate 5.4 fl oz/A (0.105 lb ai/A).					
	Up to 1.4 fl oz/A (0.027 lb ai/A)		Up to 2.7 fl oz/A (0.0527 lb ai/A)		For post-emergence foliar applications, mix GF-3301 with a surfactant. Use only surfactants approved for aquatic use.
2% or less	3 days		3 days		
3 - 10	5 days		10 days		

Restrictions: Do not use water-containing GF-3301 for hydroponic farming. Do not use water for irrigation of greenhouse or nursery plants unless herbicide concentration is <1 ppb. Applications are to be made in a minimum of 15 GPA (air).

Conclusions: Pending submission of a revised label (as listed in Section 2.3), the labels are adequate to allow the evaluation of the field trial residue data relative to the proposed uses. A plant-back (PBI) of 3-months is proposed.

3.4 Anticipated Exposure Pathways

RD has requested that HED perform an assessment of human health risk to support the proposed uses of the new herbicide active ingredient florpyrauxifen-benzyl on rice and aquatic sites. Humans could potentially be exposed to florpyrauxifen-benzyl residues in food because florpyrauxifen-benzyl may be applied directly to growing crops. These applications can also result in florpyrauxifen-benzyl reaching surface and ground water, both of which can serve as sources of drinking water. In addition, because of the agricultural uses, applicators might be exposed while handling the pesticide prior to

application, mixing/loading the pesticide, and during application. Also, there is a potential for post-application exposure for workers re-entering treated fields. There are no proposed uses in residential settings and there are no anticipated residential exposures.

3.5 Consideration of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," (http://www.archives.gov/federal-register/executive-orders/pdf/12898.pdf). As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the USDA's NHANES/WWEIA, are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

4.0 HAZARD IDENTIFICATION/TOXICOLOGY

Florpyrauxifen-benzyl is a synthetic auxin (plant hormone) belonging to arylpicolinate class of herbicides. It asserts its effect via binding to auxin receptor, causing the affected plants to enter a state of uncontrollable growth and death. The mechanism of action with respect to mammalian toxicity is not available.

4.1 Toxicology Database

All the required toxicological studies are available except a subchronic inhalation toxicity study and an acute neurotoxicity study. These two studies were waived (TXR 0057486, HASPOC, 11/15/2016) because for the acute neurotoxicity study, no neurotoxicity was seen in a subchronic neurotoxicity or other studies in the florpyrauxifen-benzyl database and for the inhalation study, florpyrauxifen-benzyl has low acute inhalation toxicity and no potential for portal of entry effects. The available studies for assessing the health risk are the following:

- subchronic oral toxicity studies in rats, dogs, and mice,
- combined chronic/carcinogenicity study in rats,

- carcinogenicity study in mice,
- developmental toxicity studies in rats, rabbits,
- reproduction study in rats,
- acute and subchronic neurotoxicity studies in rats,
- battery of mutagenicity studies,
- metabolism study in rats, and
- immunotoxicity study in rats.

4.2 Absorption, Distribution, Metabolism, and Excretion (ADME)

The ADME data demonstrate that orally administered florpyrauxifen-benzyl was absorbed moderately at a low dose level (10 mg/kg) (36-42% of the administered dose). In contrast, at the high dose (300 mg/kg), the absorption was low relative to the increase in dose levels (8-9% of the administered dose) (Note: this pattern of absorption will be explored further in this section). The maximum plasma concentration was reached within 2 hours of dosing. The tissue distribution data indicated the administered compound was mostly found in the portal of entry (GI tract), the blood, excretory organ (urinary bladder, plasma, kidneys), and liver. The data also suggest little potential for bioaccumulation.

The absorbed compound undergoes hydrolysis resulting in a major metabolite (X11438848 or XDE-848 acid) which is present in the blood in substantially higher quantity than the parent compound (Appendix A, Metabolic Pathway). In contrast, the parent compound is essentially undetectable in the majority of blood samples but it is found in large quantities in feces indicating much of the administered dose is not absorbed. In the blood, X11438848 concentration was considered to reflect the concentration of total residue as the absorbed parent compound was mostly hydrolyzed to this major metabolite. The majority of the administered dose was eliminated within the first 24 hours post-dosing.

Overall, the kinetic data indicate only ≈40% of the administered dose is absorbed. The absorption reaches a plateau between 200 and 300 mg/kg as indicated in Figure 1, which has been graphed with the data from the 90-day oral toxicity in rats only. Figure 2 is graphed from a composite data set composed of 90-day, 6-month, and 12-month data on the blood concentrations X11438848. The data set is derived from studies employing the same strain of rats, experimental procedures, and similar dose levels. This figure clearly shows that blood concentration of X1143848 reached an inflection point for absorption at approximately 200 mg/kg/day and a definite maximum level for absorption at 300 mg/kg/day. Based on these data, the rat reproduction and the chronic/carcinogenicity toxicity studies employed 300 mg/kg/day as the highest dose. The 300 mg/kg/day is considered as the kinetically derived maximum dose (KMD).

Figure 1: Blood AUC_{24h} of the Metabolite X11438848 in Rats After 90-days of Exposure to XR-848 Benzyl Ester via the Diet

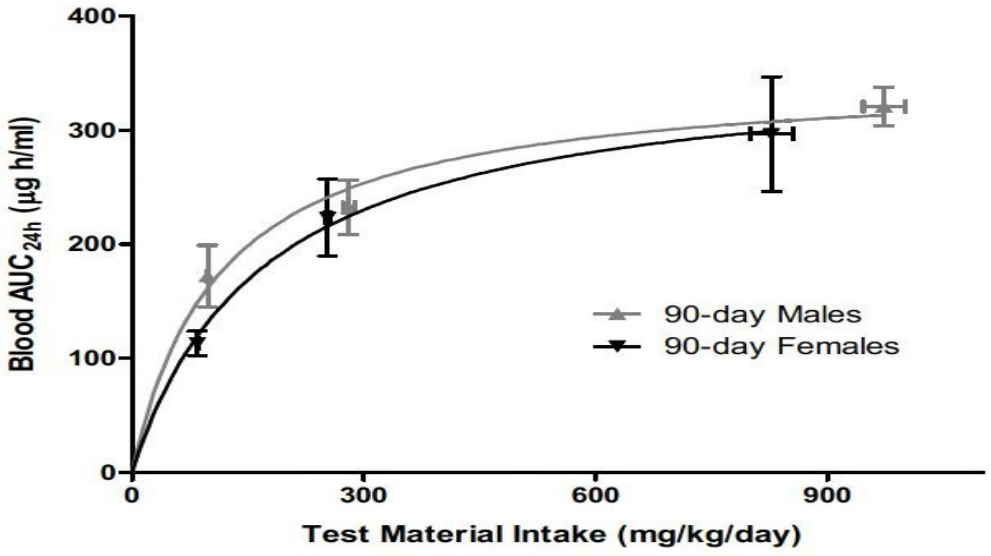
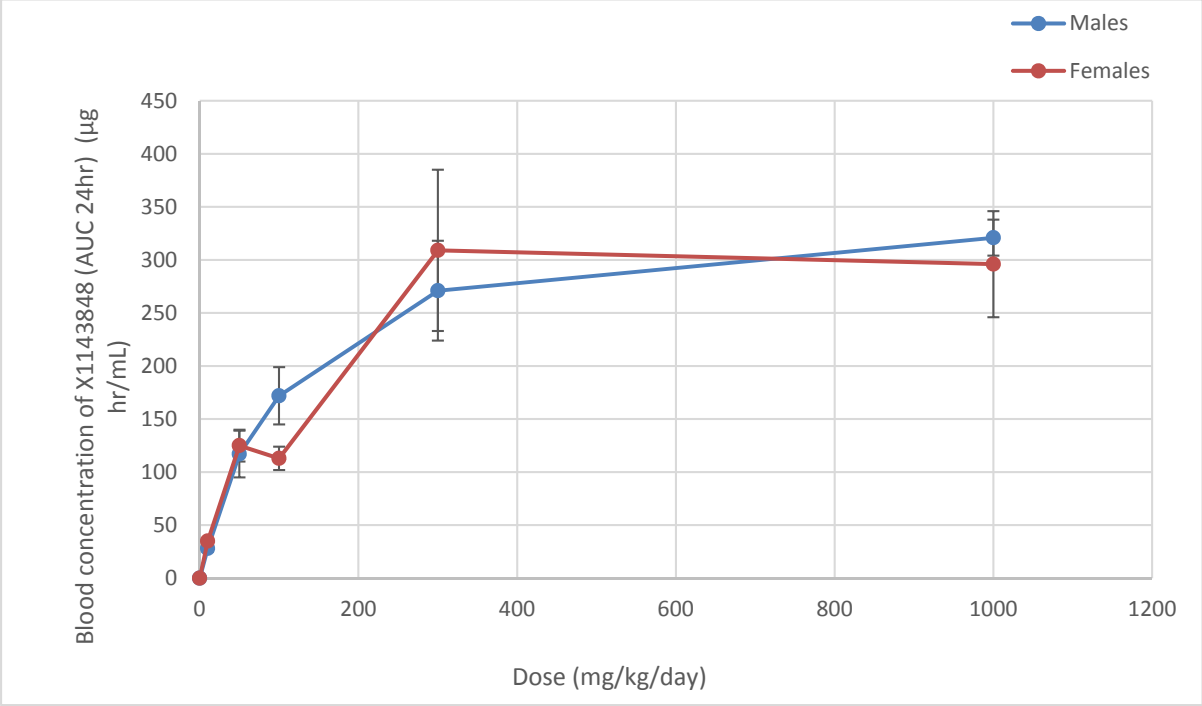


Figure 2. Blood concentrations of X11438848 from 90-day, 6-month and 12-month kinetics data (Composite data).



The kinetics data from the 2-generation reproduction and developmental toxicity studies in rats demonstrated that the major metabolite, X11438848, was found in milk and blood of dams, pups and fetuses. The concentrations were less in the milk, and in the blood of

pups and fetuses, when compared to the concentrations in the blood of the maternal animals. Blood levels of X11438848 in pups ranged from approximately 6% to 17% of those in dams on PND 4. Milk levels of X11438848 were approximately 50% of blood levels for dams. Fetal blood concentration of X11438848 was approximate 56% of the dam blood concentration. **The data indicated that fetuses were exposed to florpyrauxifen-benzyl *in utero*, and the pups were exposed during the *in utero* and postnatal life stages.**

4.2.1 Dermal Absorption

No dermal penetration study on technical grade is available. However, a 28-day dermal toxicity study in rats demonstrated no adverse effects at the limit dose (1000 mg/kg/day). In addition, the kinetics data from this dermal toxicity study indicated less than 1% of the applied dose was found in the blood.

4.3 Toxicological Effects

The submitted animal toxicity studies on florpyrauxifen-benzyl demonstrate low toxicity in the required guideline studies. In subchronic oral toxicity studies in rats, mice and dogs, florpyrauxifen-benzyl did not produce adverse effects at doses at or above the limit dose (1000 mg/kg/day). Similarly, developmental toxicity studies in rats and rabbits did not demonstrate adverse effects in maternal test animals or fetuses up to the limit dose. In the 2-generation reproduction study in rats, no adverse parental, reproductive, or offspring effects were found at the kinetically derived maximum dose (KMD) (300 mg/kg/day) as described above.

The combined chronic/carcinogenicity in rats conducted at the kinetically derived maximum dose (300 mg/kg/day) showed no adverse effect, and no compound-related increase in tumor incidence was found.

A carcinogenicity study in mice was conducted at the limit dose and found no adverse effect or any evidence of carcinogenic potential. There is no evidence of mutagenicity in *in vivo* or *in vitro* assays. Florpyrauxifen-benzyl has a low acute toxicity (Toxicity Category IV) by the oral, dermal, and inhalation exposure routes, but it has a weak dermal sensitization potential.

In summary, given the absence of adverse toxicity at the limit dose or the KMD, no toxicity endpoints and points of departure for various exposure scenarios can be established. It follows that a quantitative risk assessment is not needed for florpyrauxifen-benzyl.

The executive summaries for the florpyrauxifen-benzyl toxicological studies are not included as part of this risk assessment, but are available in the HED florpyrauxifen-benzyl toxicology chapter (W. Phang, D436327, 10/27/2016).

4.4 FQPA Safety Factor

Since no adverse toxicity is found in any of the available toxicological studies, and no toxicity endpoints and points of departure are established for risk assessment, FQPA safety factor is not applicable.

4.4.1 Residual Uncertainty in the Exposure Database

There are no residual uncertainties in the florpyrauxifen-benzyl exposure database.

4.5 Cancer Classification and Risk Assessment Recommendation

Florpyrauxifen-benzyl is not likely to be carcinogenic to human as there is no compound-related increase in tumor incidence found in rat and mouse carcinogenicity studies, which have been tested up to the limit dose or kinetically derived maximum dose. The mutagenicity battery provides no evidence of genotoxic potential.

5.0 DIETARY EXPOSURE AND RISKS

5.1 Metabolite/Degradate Residue Profile

Note: Structures of parent and its metabolites are shown in Appendix B.

5.1.1 Summary of Plant and Animal Metabolism Studies

The nature of the residue in rice is adequately understood based on an acceptable study conducted on rice. The study was conducted using three different scenarios: water-injected scenario (W), foliar-flooded scenario (F), and dry-seeded scenario (D). Florpyrauxifen-benzyl, X11438848 (florpyrauxifen or XDE-848 acid), and X11966341 were major components of the residue.

The primary pathway involved cleavage of the benzyl ester to give X11438848 (XDE-848 acid) metabolite and benzyl alcohol (theoretical hydrolysis product). The XDE-848 acid was then further modified by demethylation to give X11966341 (XDE-848 hydroxy acid). No metabolites were observed that would suggest cleavage of the bond between the phenyl and pyridine rings.

The nature of the residue in rotational crops is adequately understood based on an acceptable confined rotational crop study conducted on wheat (small grain), lettuce or mustard (leafy vegetable), and radish (root vegetable). The metabolism in confined rotational crops was similar to that in primary plants, with similar metabolites.

The nature of the residue in ruminants and poultry is adequately understood based on acceptable studies conducted on lactating goats and laying hens. Additionally, a bluegill sunfish metabolism study was submitted. The metabolism studies indicate degradation pathways similar to the plant and rat metabolism pathways.

5.1.2 Summary of Environmental Degradation

The mean K_{OC} for florpyrauxifen benzyl is 32,280 ml/g_{OC} (hardly mobile). The relatively high K_{OC} displayed by this test substance suggests that it is more likely to partition with soils and sediments, especially if they are organic carbon-rich. The vapor pressure and Henry's Law constant for florpyrauxifen benzyl are indicative of a test substance with relatively low potential to volatilize (3.2×10^{-5} Pa and 9.2×10^{-6} atm-m^3/mole at 20°C, respectively). The water solubility of florpyrauxifen benzyl is relatively low, compared to the application rates in the field of up to 0.150 mg/L for the in water aquatics uses (solubility in water is 0.015 mg/L at 20°C). It appears that the formulation improves the chemical's solubility in water.

Florpyrauxifen-benzyl degradation is dependent on the environmental conditions, and it degrades from rapidly to slowly in different environments; further, it yields several degradates. Major degradates differ when the test substance is exposed to light, compared to soil/sediment metabolism studies. Levels of unextracted radioactivity were high in most of the metabolism studies. In the field, it appears that a combination of routes of dissipation takes place. The majority of the mass of parent is expected to reach paddy water/soil, while a smaller amount is expected to reach adjacent surface water by drift. Parent reaching paddy water/soil is expected to partition into the soil and in the paddy environment and degrade rather quickly [$t_{½}$ = 12-31 days in aerobic soil (flooded system), and 15-46 days in anaerobic soil environments; if the test substance is applied to dry soils, the half-lives will range from 8.9-67.2 days]. The following degradates are expected to form in the aquatic environments (based on the aerobic flooded and anaerobic soil metabolism studies): XDE-848 acid (73.5% maximum, with a half-life of 14 days under aerobic conditions); XDE-848 benzyl hydroxy (15.9% maximum, with a half-life of 87 days); and XDE-848 hydroxy acid (68.9% maximum, with a half-life of 127-729 days). Parent reaching water bodies by drift or applied directly to water (aquatics use) is expected to degrade rather quickly ($t_{½}$ = 4.0-6.2 days in aerobic aquatic, and 2.1-2.4 days in anaerobic aquatic environments), forming the following degradates: XDE-848 acid (46.9% maximum, with a half-life of 6.3-18 days under aerobic aquatic metabolism conditions); XDE-848 benzyl hydroxy (43.1% maximum, with a half-life of 6-14 days); and XDE-848 hydroxy acid (104.4% maximum, with a half-life of 53-121 days aerobic aquatic conditions, while it was the terminal degradate under anaerobic aquatic metabolism conditions).

5.1.3 Comparison of Metabolic Pathways

The metabolic pathway in rice is well understood based on characterization and identification of the residues. The metabolism in confined rotational crops was similar to that in primary plants, with similar metabolites. Parent, florpyrauxifen-benzyl, X11438848, and X11966341 are the major residues. The majority of the metabolites in plants are also rat metabolites.

The nature of the residue in ruminants, poultry, and fish is adequately understood based on acceptable studies conducted on lactating goats, laying hens, and bluegill sunfish

metabolism studies. The metabolism studies indicate degradation pathways similar to the plant and rat metabolism pathways.

On the basis of the metabolites identified, the major metabolic pathway in plants, rotational crops, and livestock includes cleavage of the benzyl ester to give X11438848 metabolite and benzyl alcohol (theoretical hydrolysis product). The X11438848 acid was then further modified by loss of the methyl group to give X11966341. No metabolites were observed that would suggest cleavage of the bond between the phenyl and pyridine rings.

5.1.4 Residues of Concern Summary and Rationale

As shown in Table 5.1.4 below, the Agency recommends parent florpyrauxifen-benzyl and its acid metabolite (X11438848) only as the residue of concern to be included in the tolerance expression (ROCKS; D436519, I. Negrón-Encarnación, 11/15/2016). Since there are no toxicological endpoints, a quantitative risk assessment will not be conducted; therefore, the Agency is not identifying residues of concern for risk assessment. Based on the currently proposed uses, the Agency does not have any hazard concern for metabolites and/or degradates of florpyrauxifen-benzyl that may be found in drinking water, plants, and livestock. The Agency assumes that environmental metabolites and degradates that may be found in food and drinking water would have a similar mammalian hazard profile as compared to the parent compound and can therefore be excluded from a quantitative dietary risk assessment.

Table 5.1.4. Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression.

Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop	Not applicable[1]	florpyrauxifen-benzyl + X11438848 (4-Amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carboxylic acid), expressed as florpyrauxifen-benzyl
	Rotational Crop	Not applicable[1]	florpyrauxifen-benzyl + X11438848 (4-Amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carboxylic acid), expressed as florpyrauxifen-benzyl
Livestock	Ruminant	Not applicable[1]	florpyrauxifen-benzyl + X11438848 (4-Amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carboxylic acid), expressed as florpyrauxifen-benzyl
	Poultry	Not applicable[1]	florpyrauxifen-benzyl + X11438848 (4-Amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carboxylic acid), expressed as florpyrauxifen-benzyl
Fish (including shellfish)		Not applicable[1]	florpyrauxifen-benzyl + X11438848 (4-Amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carboxylic acid), expressed as florpyrauxifen-benzyl
Drinking Water		Not applicable	

[1] No hazard has been identified in the toxicological studies conducted on florpyrauxifen-benzyl, therefore no quantitative risk assessment is required.

Rationale

Residues of Concern for Tolerance Enforcement: Parent florpyrauxifen-benzyl and X11438848 were the predominant residues observed in primary crops, rotational crops, fish and livestock. Based on this, HED recommends parent florpyrauxifen-benzyl and X11438848 as the residues of concern for tolerance enforcement. It is important to note that the tolerance on rice grain is being established for trade purposes only.

Residues of Concern for Risk Assessment: Residues of concern in plants, livestock, fish, and water were not selected for risk assessment purposes based on the absence of adverse effects at the highest doses tested in all of the required toxicity studies for florpyrauxifen-benzyl, and the structural similarity of most degradates/metabolites with the parent compound. Those that retain all the rings of the parent compound are expected to have the same or lesser toxicity. Based on this, no quantitative assessment is necessary for parent or degradates/metabolites at this time.

5.2 Food Residue Profile

Adequate residue data are available to support the proposed tolerances for the herbicide florpyrauxifen-benzyl in/on rice commodities and fish. Residues are quantifiable in fish treated in accordance with the proposed aquatic use label. Residues are quantifiable in rice treated in accordance with the proposed label (foliar uses). Rice straw is no longer considered to be a significant livestock feedstuff; therefore, no tolerance is required for rice straw. Processing studies were conducted on rice; residues of florpyrauxifen-benzyl were non-quantifiable. The data indicate that residues of florpyrauxifen-benzyl do not concentrate in processed commodities (hulls, bran and flour). Based on no transfer of residues (<0.001), tolerances are not needed in livestock commodities (i.e., no finite residues of florpyrauxifen-benzyl and/or its metabolites are expected (the proposed uses fall under 40 CFR §180.6(a)(3)).

5.3 Water Residue Profile

As noted in section 5.1.4, there are no residues of toxicological concern expected in drinking water from the use of florpyrauxifen-benzyl. Thus, no drinking water exposure assessments are needed for HED to conclude with reasonable certainty that drinking water exposures to florpyrauxifen-benzyl do not pose a significant human health risk.

5.4 Dietary Risk Assessment

There is potential for exposure to florpyrauxifen-benzyl via food and drinking water based on the proposed uses. However, no adverse effects were observed in the submitted toxicological studies for florpyrauxifen-benzyl regardless of the route of exposure. Thus, no dietary exposure assessments are needed for HED to conclude with reasonable certainty that dietary exposures to florpyrauxifen-benzyl do not pose a significant human health risk.

6.0 RESIDENTIAL EXPOSURE AND RISKS

DAS has not currently requested any residential uses for florpyrauxifen-benzyl. However, HED would typically still need to conduct an assessment for swimmers in treated waters. However, given that there are no toxicity endpoints or points of departure, such an assessment was not conducted.

7.0 AGGREGATE EXPOSURE AND RISKS

No adverse effects were observed in the submitted toxicological studies for florpyrauxifen-benzyl regardless of the route of exposure. Therefore, a quantitative aggregate exposure assessment was not conducted. HED concludes with reasonable certainty that aggregate exposures to florpyrauxifen-benzyl do not pose a significant human health risk.

8.0 CUMULATIVE EXPOSURE AND RISKS

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to florpyrauxifen-benzyl and any other substances and florpyrauxifen-benzyl does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that florpyrauxifen-benzyl has a common mechanism of toxicity with other substances. In 2016, EPA's Office of Pesticide Programs released a guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework). This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. This framework supplements the existing guidance documents for establishing common mechanism groups (CMGs)[1] and conducting cumulative risk assessments (CRA)[2]. During Registration Review, the agency will utilize this framework to determine if the available toxicological data for florpyrauxifen-benzyl suggests a candidate CMG may be established with other pesticides. If a CMG is established, a screening-level toxicology and exposure analysis may be conducted to provide an initial screen for multiple pesticide exposure.

9.0 OCCUPATIONAL EXPOSURE AND RISKS

Florpyrauxifen-benzyl is being proposed for registration as liquid formulations for occupational use on rice and aquatic areas. It may be applied using aerial, ground, and handheld equipment. No adverse effects were observed in the submitted toxicological

[1] *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999)

[2] *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (USEPA, 2002)

studies for florpyrauxifen-benzyl regardless of the route of exposure; therefore, a quantitative occupational exposure assessment was not conducted. Thus, no occupational exposure assessments are needed for HED to conclude with reasonable certainty that occupational exposures to florpyrauxifen-benzyl do not pose a significant human health risk.

References

I. Negrón-Encarnación, 11/15/2016, D436519, "Florpyrauxifen-benzyl. Report of the Residues of Concern Knowledgebase Subcommittee (ROCKS)."

M. Negussie, 11/15/16, D436516, "Florpyrauxifen-benzyl. First Food Use Petition for the Establishment of Permanent Tolerances and Registration for Use on Rice, Fish and Shellfish. Summary of Analytical Chemistry and Residue Data."

J. Melendez, 11/01/2016, D429727, "Drinking Water Assessment for the New Chemical Florpyrauxifen-benzyl (XDE-848 Benzyl Ester, Rinskor™), in Support of the Health Effects Division's Human Health Risk Assessment."

W. Phang, 10/27/2016, D436327, "Rinskor Toxicology Chapter"

U. Habiba, 11/15/2016, TXR# 0057486, XDE-848 benzyl ester: Summary of the Hazard and Science Policy Council (HASPOC) meetings of Aug 4, 2016: Recommendations on the Need for Acute Neurotoxicity and Subchronic Inhalation Toxicity Studies.

APPENDIX A. TOXICOLOGY PROFILE

A.1 Toxicology Data Requirements

The requirements (40 CFR §158.500) for food and non-food uses for florpyrauxifen-benzyl are in Table A.1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Table A.1. Summary of Toxicology Data Requirements

Study		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Primary Eye Irritation	yes	yes
870.2500	Primary Dermal Irritation	yes	yes
870.2600	Dermal Sensitization	yes	yes
870.3050	28-Day Oral (rodent)	no	yes
870.3100	Oral Subchronic (rodent)	yes	yes
870.3150	Oral Subchronic (nonrodent)	yes	yes
870.3200	21-Day Dermal	yes	yes
870.3250	90-Day Dermal	CR[a]	-
870.3465	90-Day Inhalation (28-Day Inhalation)	yes	waived[b]
870.3700a	Developmental Toxicity (rodent)	yes	yes
870.3700b	Developmental Toxicity (nonrodent)	yes	yes
870.3800	Reproduction	yes	yes
870.4100b	Chronic Toxicity (nonrodent-dog)	no	yes
870.4200b	Carcinogenicity (mouse)	yes	yes
870.4300	Chronic Toxicity/Oncogenicity (rodent-rat)	yes	yes
870.5100	Mutagenicity—Gene Mutation - bacterial	yes	yes
870.5300	Mutagenicity—Gene Mutation - mammalian	yes	yes
870.5xxx	Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5xxx	Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100a	Acute Delayed Neurotoxicity (hen)	no	-
870.6100b	90-Day Neurotoxicity (hen)	no	-
870.6200a	Acute Neurotoxicity Screening Battery (rat)	yes	waived[b]
870.6200b	90-Day Neurotoxicity Screening Battery (rat)	yes	yes
870.6300	Develop. Neurotoxicity	CR[a]	-
870.7485	General Metabolism	yes	yes
870.7600	Dermal Penetration	CR[a]	yes
870.7800	Immunotoxicity	yes	yes

[a]: CR = conditionally required.
[b]: TXR 0057486, HASPOC 11/15/16

A.2 Toxicity Profiles

Table A.2.1. Summary of acute toxicity data for XDE-Benzyl Ester (Technical ai)			
Type of Study	**MRID**	**Results**	**Toxicity Category**
Acute oral LD_{50}-rat	49677703	LD_{50} >5000 mg/kg	IV
Acute dermal LD_{50}-rat	49677704	LD_{50} >5000 mg/kg body weight	IV
Acute inhalation LC_{50} (4 h)-rat	49677705	LC_{50} >5.23 mg/L	IV
Skin irritation-rabbit	49677707	Not a skin irritant	IV
Eye irritation-rabbit	49677706	Slightly irritating	III
Skin sensitisation-mouse (local lymph node assay)	49677708	EC_3 at 19.1% of the applied concentration:	weak dermal sensitization potential

Table A.2.2. Subchronic, Chronic and Other Toxicity Studies on XDE-848 Benzyl Ester.			
Guideline No.	**Study Type**	**MRID No. (Year)/ Classification /Doses**	**Results**
Subchronic Toxicity Studies			
Non-guideline	Palatability-rat (F344) & mice	49677866 0, 250, 500 or 1000 mg/kg/day	No effect was seen at highest dose tested (HDT) Only 3 animals/sex/dose
870.3050	28-Day feeding study –rats (F344)	49677845 (2012) Acceptable/guideline 0, 250, 500, or 1000 mg/kg/day	NOAEL = 1000 mg/kg/day (HDT)
	28-Day Oral -mice	49677846 (2012) Acceptable/guideline 0, 250, 500 or 1000 mg/kg/day	NOAEL = 1000 mg/kg/day (HDT)
	28-Day oral -dogs	49677867 (2013) Unacceptable/non-guideline 15,000 ppm (286 to 718 mg/kg/day) for females only. 30000 ppm (≈ 657 to 1344 mg/kg/day for males and ≈345.6 to 1283 mg/kg/day for females)	NOAEL = 1344/1283 (M/F) (HDT) (**This study did not have a control group)**. 1500 ppm group employed only 2 female dogs, while 30,000 ppm employed 2 dogs/sex)
870.3100	90-day feeding study –rats (F344)	49677848 (2013) Acceptable/guideline 0, 100, 300, or 1000 mg/kg/day	NOAEL = 1000 mg/kg/day (HDT)
870.3100	90-day feeding study –mice	49677847 (2015) Acceptable/guideline 0, 100, 300 and 1000 mg/kg/day	NOAEL = 1000 mg/kg/day (HDT)
870.3150	90-day oral toxicity in dogs (dietary)	49677849 (2014) Acceptable/guideline 0; 3000; 10000 and 30000 ppm (M: 0, 106, 366, & 1008 mg/kg/day; F: 0, 115, 329, & 1216 mg/kg/day)	NOAEL = 1008/1216; M/F) (HDT)
870.3200	28-Day Dermal in Rats	49677850 (2015) Acceptable/guideline 0, 1000 mg/kg/day	NOAEL = 1000 mg/kg/day (HDT) The kinetics data showed a small percentage of the applied dose was absorbed (<1%).
870.3465	28-Day inhalation toxicity	Waived (TXR 0057486, HASPOC 08/04/2016)	
Developmental and Reproductive Toxicity Studies			

Table A.2.2. Subchronic, Chronic and Other Toxicity Studies on XDE-848 Benzyl Ester.			
Guideline No.	**Study Type**	**MRID No. (Year)/ Classification /Doses**	**Results**
870.3700a	Prenatal Developmental Toxicity Study in Rats (dietary) Probe (range finding) study	49677854 (2015) Acceptable/guideline 0, 14000 ppm (0, 975 m/kg/day) (limit test) 49677868 (2012) 0, 6750, & 13,500 ppm (0, 445, 898 mg/kg/day)	Maternal and developmental NOAEL = 975 mg/kg/day (HDT) *Kinetics data indicated fetuses were exposed to the test compound in-utero.* No effect was seen at 898 mg/kg/day
870.3700b	Prenatal Developmental Toxicity Study in Rabbits (dietary) Probe (range-finding) study	49677853 (2014) Acceptable/guideline 0 and 27000 ppm (0, 1042 mg/kg/day) (limit test) 49677869 (2014) 0, 8000, 14000, 20000, & 27000 ppm (0, 304, 353, 752, & 116 mg/kg/day)	Maternal and developmental NOAEL =1042 mg/kg/day (HDT) *Kinetics data indicated fetuses were exposed to the test compound in-utero.* No maternal or developmental effects were seen.
870.3800	2- Generation Reproduction - rats (diet) Probe (range-finding) study	49677855 (2015) Acceptable/guideline 0, 10, 50, & 300 mg/kg/day *(300 mg/kg/day is the kinetically derived maximum dose)* 49677852 (2013) 0, 100, 300, 1000 mg/kg/day	Parental, reproductive, and offspring NOAEL = 300 mg/kg/day (HDT) *Kinetics data indicated pups were exposed to the test compound in-utero.* No parental, reproductive, and offspring effects were seen at any dose levels.
Chronic toxicity studies			
870.4100 & 870.4200	Combined Chronic/Carcino-genicity (2-yrs)-rat	49677857 (2015) Acceptable/guideline 0, 10, 50, 300 mg/kg/day *(300 mg/kg/day is the kinetically derived maximum dose)*	No adverse effect was seen at the highest dose tested (HDT) NOAEL = 300 (HDT) No increase in compound-related tumor incidence was found.
870.4200b	Carcinogenicity study-mice (78 weeks)	49677856 (2015) Acceptable/guideline Males 0,5,0, 200,1000 mg/kg/day Females: 0,5,0, 200,1000 mg/kg/day	No adverse effect was seen at the highest dose levels tested (1000 and 800 mg/kg/day for males and females respectively); NOAEL = 1000/800 mg/kg/day (M/F) (HDT). No increase in compound-related tumor incidence was found.
Genotoxicity studies			
870.5100	Bacterial Reverse Mutation Test (*S. typhimurium* and *E. coli)*	49677859 (2012) Acceptable/guideline 51.2 to 5000 µg/plate +/- S9	Negative
870.5300	*In Vitro* Mammalian Cell Gene Mutation Test (CHO/HGPRT)	49677860 (2012) Acceptable/guideline <u>Initial Assay:</u> 0, 2.3, 4.7, 9.4, 18.8, 37.5, and 75 µg/ml +/- S9 (solubility limit) <u>Confirmatory Assay:</u> 2.5 to 60 µg/ml in - S9; 5.0 to 80 µg/ml in the + S9	Negative

Table A.2.2. Subchronic, Chronic and Other Toxicity Studies on XDE-848 Benzyl Ester.			
Guideline No.	**Study Type**	**MRID No. (Year)/ Classification /Doses**	**Results**
870.5375	*In Vitro* Mammalian Chromosome Aberration Test (rat lymphocytes)	49677862 (2012) Acceptable/guideline 4 hr treatment: 0, 1.2, 2.3, 4.7, 9.4, 18.8, 37.5, 75.0 µg/ml +/- S9; 24 hr treatment: 0, 0.6, 1.2, 2.3, 4.7, 9.4, 18.8, 37.5, 75.0 µg/ml - S9. (solubility limit)	Negative
870.5395	(Other Genotoxic Effects) *In vivo* Mouse bone marrow micronucleus *(dietary administration))*	49677846 (2012) Acceptable/guideline 0, 250, 500 or 1000 mg/kg/day via diet for 28 days *(Integrated in the 28-day oral toxicity study in mice)*	Negative
Neurotoxicity Studies			
870.6200a	Acute Neurotoxicity-rats (gavage)	Waived(TXR 0057486, HASPOC 08/04/2016) .	
870.6200b	90-Day Dietary Neurotoxicity Study – rats	49677848 (2013) Acceptable/non-guideline 0, 100, 300, & 1000 mg/kg/day *(Integrated into the 90-day oral toxicity study in rats)*	NOAEL=1000 mg/kg/day (HTD)
Metabolism Studies			

870.7485	Metabolism Study – Rat ADME	49677864 (2014) Acceptable/guideline 10 mg/kg (low dose), single dose of 300 mg/kg (high dose) (gavage) With repeated dosing at 10 mg/kg/day	Orally administered ^{14}C-XDE-848 Benzyl ester was absorbed rapidly without any apparent lag time. The absorption occurred within 12 hours post dosing, accounting for ≈ 91% of the absorbed radioactivity for the low dose males and females; 73% and 59% for high dose males and females, respectively. In the low dose group, the percent absorption was as high as 42% and 41% of the administered dose in males and females, respectively. The percent absorption in the high dose group was approximately 6% of the administered dose in males and 9% in females. The percent absorption for the high dose group is substantially less that than that for the low group by at least 3 folds; the data appear to suggest there is a saturation of absorption at 300 mg/kg. The peak plasma concentration was reached at approximately 2 hours post-dosing in both males and females irrespective of dose levels. Less than 0.02% of the orally administered ^{14}C-XDE-848 Benzyl ester remained in the tissues after 168 hours (7 days) post-dosing in all of the groups suggesting negligible bioaccumulation. A portion (≈ 42% in low dose and ≈ 8% in high dose) of the administered ^{14}C-XDE-848 Benzyl ester-derived radioactivity was rapidly excreted in urine without any difference between the sexes. The majority of the urinary elimination (51-92%) occurred within the first 12 hours post-dosing. Most of the remaining oral dose (51-101%) was eliminated in feces, with the majority of the fecal elimination (88-97%) occurring within the first 24 hours post-dosing. It should be noted that in a separate study with bile duct cannulation, there was approximately 6.6% of the administered dose seen in the bile (MRID 49677873). Therefore, majority of the radioactivity in the feces represents unabsorbed parental compound. The results from the metabolite analysis indicated that XDE-848-Benzyl ester under goes mainly o-demethylation at 3-methoxyphenyl moiety, hydrolysis at the benzyl ester moiety, and subsequent glucuronidation at the hydroxyl and carboxylic acid moieties leading to the various metabolites. **In the urine,** no detectable amount of parent XDE-848-Benzyl ester was found, and X11438848 was most abundant metabolite in the urine, accounting for ~6

Table A.2.2. Subchronic, Chronic and Other Toxicity Studies on XDE-848 Benzyl Ester.			
Guideline No.	**Study Type**	**MRID No. (Year)/ Classification /Doses**	**Results**
			% to ~39 % of the administered dose. In the **feces**, parent XDE-848-Benzyl ester was most abundant, accounting for ~35 % to ~92 % of the dose. Two additional metabolites were observed in the feces, accounting for > 5% of the dose. The metabolite X11438848 was also found in the feces in substantially less amount relative to the urine, accounting for ~3 % to ~6 % of the administered dose. X12300837 also had been identifies and accounted for ~2% to ~11 % of the administered dose. The remaining metabolites observed in the radiochemical profiles of rat fecal samples accounted for < 5% of the administered dose.
	Tissue distribution study in rats	49677865 (2014) Acceptable/non-guideline 10 & 300 mg/kg	Under the conditions of this study, total radioactivity recovery cross all groups was ≈ 94% of administered dose. The radioactivity concentration at C_{max} was highest in the GI tract (ranging from 70% to 90% of administered dose), followed by urinary bladder, plasma, kidney and liver in males and females. Th data indicated that, with oral dosing, the test material primarily found in the portal of entry and excretory tissues. The radioactivity in the majority of the other tissues (other than portal of entry and excretory) were similar to, or lower than, that of systemic blood indicating low potential for accumulation. There were no major sex differences in the distribution for XDE-848 Benzyl ester.
	Bile duct cannulation study in rats	49677873 (2014) Acceptable/non-guideline This study only provides qualitative information at best because it employed only 2 rats/sex at 100 mg/kg.	Over 48-hours post doing for **males**, approximately 13% of the dose was eliminated in the urine and 6.6% of the dose was found in the bile. For **females** approximately 9.1% of the dose was excreted in the urine and approximately 0.5% of the dose was found in the bile. However, not all test animals produced bile at all intervals. One female did not produce bile from 0-24 hours, while another female also produced no bile at 12-24 hour period. As a result, no bile sample was collected from 12-24 hour period for female rats. One male did not produce bile at 8-12 hours post-dosing period. Approximately 10% and 20% of the dose was recovered within 48 hours post-dosing for females and males, respectively.

Table A.2.2. Subchronic, Chronic and Other Toxicity Studies on XDE-848 Benzyl Ester.			
Guideline No.	**Study Type**	**MRID No. (Year)/ Classification /Doses**	**Results**
Non-guideline	ADME study –dog (a probe study)	49677872 (2013) Unacceptable/non-guideline 100 mg/kg (Single dose by gavage) The study used only 2 dogs/sex.	Male and female animals excreted XDE-848 benzyl ester primarily in the feces (about 60% to 80% of the dose). Males and females excreted approximately 7 to 12% and 0.4 to 5%, respectively, of the radioactivity in the urine. Radioprofiling of select urine and feces samples indicated that XDE-848 benzyl ester is metabolized primarily to a single metabolite that was identified as XDE-848 acid (X11438848). In plasma, the concentration of total radioactivity was insufficient for metabolite profiling analysis.
Non-guideline	Probe ADME in rats, mice, & rabbits (F344, Crl:CD1, & NZW)	49677871 (2012) Unacceptable/non-guideline 100 mg/kg (gavage) (Only 1 or 2 animals/sex/study)	The orally absorbed dose was rapidly excreted in urine. Total urinary elimination accounted for 11-15% of the dose in rats, 37-48% of the dose in mice and 67% in rabbits. Fecal elimination accounted for 59-77% in rats, 39-46% in mice and 25% in rabbits. No parent XDE-848 benzyl ester was detected in the urine, blood or liver samples. In the urine profiles, the most abundant urinary metabolite in all species was positively identified as XDE-848 acid (X11438848)
Immunotoxicity Study			
870.7800	90-Day Immunotoxicity Study in rats (diet) (primary humoral response to SRBC)	49677848 (2013) Acceptable/guideline 0, 100, 300, or 1000 mg/kg/day *(Integrated in the 90-day oral toxicity study in rats)*	NOAEL = 1000 mg/kg/day (limit dose) No treatment-related effect on the primary antibody response to SRBCs in male and female rats.

APPENDIX B. METABOLISM INFORMATION

TableB1. Tabular Summary of Metabolites and Degradates.

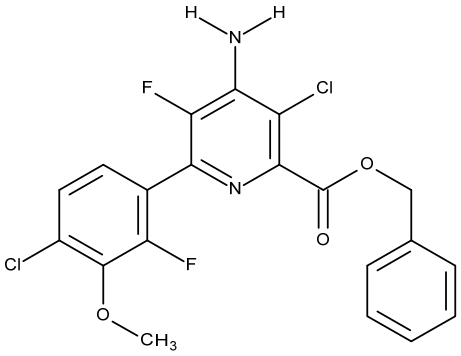
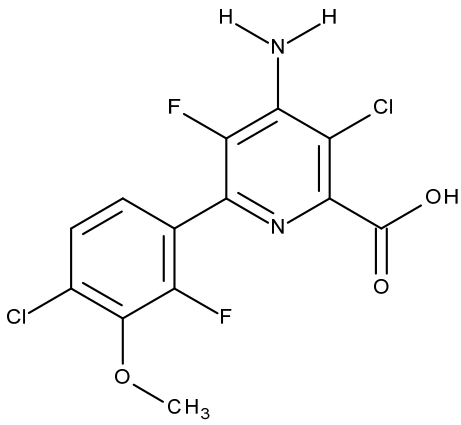
Table B1. Tabular Summary of Metabolites and Degradates from Metabolism Studies.			
Chemical Name (other names in parentheses) and Structure	Matrix	Percent TRR (PPM)	
		Matrices - Major Residue (≥10% TRR)	Matrices - Minor Residue (<10% TRR)
 IUPAC: Benzyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carboxylate XDE-benzyl ester (X11959130)	Mature Rice Straw (W)	10.1 (0.011)-PH 13.0 (0.014)-BE	8.3 (0.006)-PY
	Mature Rice Hulls (W)		7.0 (0.002)
	Mature Rice Straw (F)	17.4 (0.175)-PH 19.1 (0.199)-PY 38.8 (0.781)-BE	
	Mature Rice Hulls (F)	14.2 (0.056)-PH 15.7 (0.049)-PY 19.2 (0.016)-BE	
	Mature Rice Grain (F)		6.0 (0.002)-PH 3.9 (0.001)-PY
	Mature Rice Straw (D)	20.3 (0.223)-PH 23.0 (0.390)-PY 20.5 (0.098)-BE	
	Wheat Hay (271-PBI)		3.5 (0.001)-PY
	Fillet (bluegill fish)	27.8 (0.331)	
 IUPAC: 4-Amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carboxylic acid X11438848, XDE-848 acid	Mature Rice Straw (W)	47.8 (0.054)-PH 41.9 (0.029)-PY	
	Mature Rice Hulls (W)	38.6 (0.014)	
	Mature Rice Straw (F)	38.8 (0.781)-BE	4.3 (0.043)-PH 5.4 (0.056)-PY
	Mature Rice Hulls (F)		3.4 (0.013)-PH 3.8 (0.012)-PY
	Mature Rice Grain (F)		4.0 (0.001)-PH
	Mature Rice Straw (D)		4.5 (0.050)-PH 6.0 (0.101)-PY
	Liver (Goat)		6.9 (0.001)-PH 6.0 (0.001)-PY
	Kidney	27.9 (0.004)-PH 44.7 (0.01)-PY	
	Wheat Straw (30-PBI)		4.1 (0.001)-PY
	Wheat Hay (90-PBI)		2.7 (0.001)-PH 3.0 (0.001)-PY
	Wheat Hay (271-PBI)	17 (0.004)-PY	

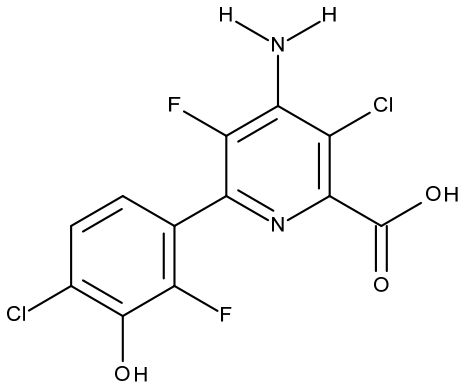
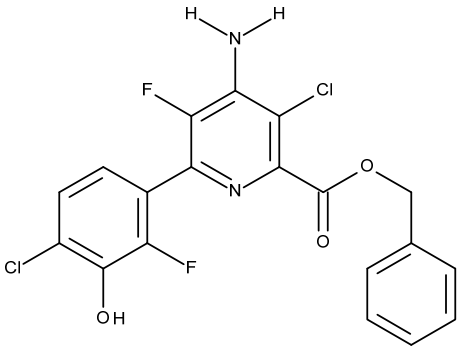
Table B1. Tabular Summary of Metabolites and Degradates from Metabolism Studies.			
Chemical Name (other names in parentheses) and Structure	Matrix	Percent TRR (PPM)	
		Matrices - Major Residue (≥10% TRR)	Matrices - Minor Residue (<10% TRR)
	Wheat Straw (271-PBI)		4.5 (0.001)-PY
	Fillet (bluegill fish)	52.6 (0.626)	
 IUPAC: 4-Amino-3-chloro-6-(4-chloro-2-fluoro-3-hydroxy-phenyl)-5-fluoro-pyridine-2-carboxylic acid X11966341 Hydroxy acid (XDE-848 hydroxy acid, XR-848 hydroxy acid)	Mature Rice Straw (W)		2.4 (0.003)-PH
	Mature Rice Hulls (F)		1.6 (0.006)-PH 1.7 (0.005)-PY
	Mature Rice Grain (F)		3.2 (0.001)-PH 2.1 (0.001)-PY
	Mature Rice Straw (D)	11.1 (0.123)-PH 14.0 (0.238)-PY	
	Liver (Goat)	20.8 (0.002)-PH 20.8 (0.003)-PY	
	Kidney	24.9 (0.003)-PH 24 (0.005)-PY	
	Wheat Hay (30-PBI)	11.8 (0.002)-PH 10.4 (0.001)-PY	
	Wheat Straw (30-PBI)	22.6 (0.006)-PH 17.7 (0.006)-PY	
	Wheat Hay (90-PBI)	12.5 (0.002)-PH 10.9 (0.003)-PY	
	Wheat Straw (90-PBI)	24.6 (0.008)-PH 14.2 (0.007)-PY	
	Wheat Hay (271-PBI)	25.4 (0.007)-PH	
	Wheat Straw (271-PBI)	11.2 (0.004)-PY	
 IUPAC: Benzyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-hydroxy-phenyl)-5-fluoro-pyridine-2-carboxylate X12300837 Benzyl hydroxy (XDE-848 Hydroxy BE)	Mature Rice Straw (F)		2.6 (0.026)-PH 1.4 (0.028)-BE
	Mature Rice Hulls (F)		1.3 (0.005)-PH

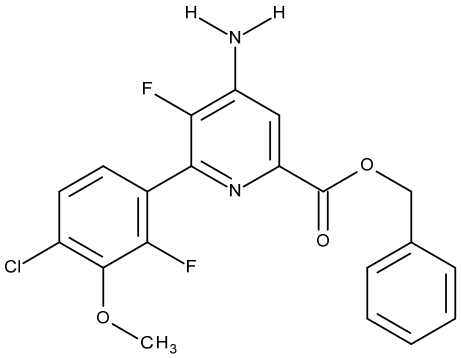
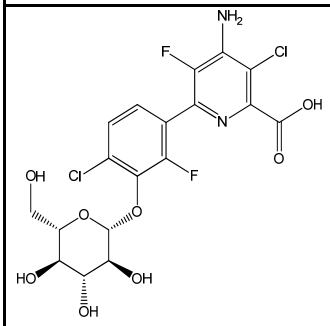
Table B1. Tabular Summary of Metabolites and Degradates from Metabolism Studies.			
Chemical Name (other names in parentheses) and Structure	Matrix	Percent TRR (PPM)	
		Matrices - Major Residue (≥10% TRR)	Matrices - Minor Residue (<10% TRR)
 IUPAC: Benzyl 4-amino-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carboxylate X12131932 Des-chloro XDE-848 Benzyl Ester (De-Chloro-BE)	Mature Rice Straw (F)		4.0 (0.04)-PH 3.8 (0.04)-PY 2.8 (0.055)-BE
	Mature Rice Hulls (F)		5.8 (0.023)-PH 4.2 (0.013)-PY
	Mature Rice Grain (F)		2.6 (0.001)-PH
	Mature Rice Straw (D)		5.5 (0.061)-PH 4.4 (0.074)-PY 4.4 (0.021)-BE
 4-amino-3-chloro-6-(4-chloro-2- fluoro-3-((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)- tetrahydro-2H-	Mature Rice Straw (F)		2.6 (0.027)-PH 2.2 (0.023)-PY
	Mature Rice Straw (D)		2.9 (0.032)-PH 9.2 (0.157)-PY
	Wheat Hay (30-PBI)	44.3 (0.007)-PH 50.5 (0.006)-PY	
	Wheat Straw (30-PBI)	19.6 (0.005)-PH 15.8 (0.005)-PY	
	Wheat Hay (90-PBI)	18.6 (0.002)-PH 14.2 (0.004)-PY	
	Wheat Straw (90-PBI)	17.3 (0.006)-PH 13.3 (0.006)-PY	
	Wheat Hay (271-PBI)		4.5 (0.001)-PY

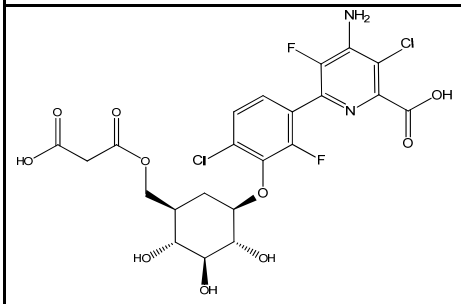
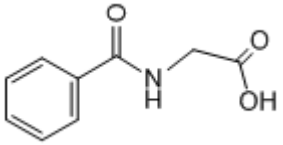
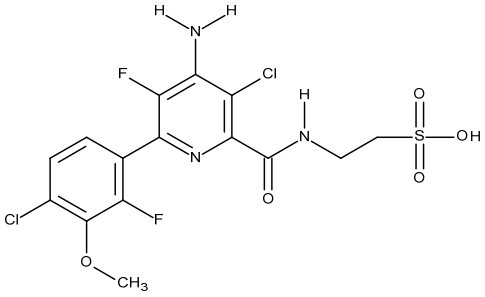
Table B1. Tabular Summary of Metabolites and Degradates from Metabolism Studies.			
Chemical Name (other names in parentheses) and Structure	Matrix	Percent TRR (PPM)	
		Matrices - Major Residue (≥10% TRR)	Matrices - Minor Residue (<10% TRR)
pyran-2- yoxyl)phenyl)-5-fluoropicolinic acid X12431091 Glucose conjugate of XR-848 Hydroxy Acid (X11966341)	Wheat Straw (271-PBI)		9.9 (0.003)-PY
 4-amino-6-(3-{[6-O-(carboxyacetyl)hexopyranosyl]oxy}- 4-chloro-2-fluorophenyl)-3-chloro-5- fluoropyridine-2-carboxylic acid X12431475 (glucose-malonic acid conjugate of X11966341)	Mature Rice Straw (D)		0.5 (0.005)-PH 0.8 (0.013)-PY
	Wheat Hay (30-PBI)		6.5 (0.001)-PH 4.2 (0.001)-PY
	Wheat Straw (30-PBI)		3.5 (0.001)-PH 2.9 (0.001)-PY
	Wheat Hay (90-PBI)		4.8 (0.001)-PH 4.2 (0.001)-PY
	Wheat Straw (90-PBI)		3.8 (0.001)-PH 3.1 (0.001)-PY
	Wheat Straw (271-PBI)		2.3 (0.001)-PY
(2S,3S,4S,5S)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2- yl-4-amino-3-chloro-6-(4-chloro-2-fluoro- 3-methoxypheyl)-5-fluoropicolinate X12427971	Mature Rice Straw (D)		2.3 (0.026)-PH 2.5 (0.042)-PY
 (2-oxo-2-phenylethyl)carbamic acid X194907 (conjugate of benzoic acid)	Liver (Goat)	13.8 (0.003)-BE	
	Kidney	99.7 (0.02)-BE	

Table B1. Tabular Summary of Metabolites and Degradates from Metabolism Studies.			
Chemical Name (other names in parentheses) and Structure	Matrix	Percent TRR (PPM) Matrices - Major Residue (≥10% TRR)	Matrices - Minor Residue (<10% TRR)
 **IUPAC:** 2-[[4-Amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxy-phenyl)-5-fluoro-pyridine-2-carbonyl]amino]ethanesulfonic acid Taurine conjugate of XDE-848 acid (Taurine conjugate of X11433848)	Fillet (bluegill fish)		6.2 (0.074)

Appendix C. Physical/Chemical Properties

Table C.1. Physicochemical Properties of Florpyrauxifen-benzyl.		
Parameter	Value	Reference (MRID or Source)
Physical State	Powder (as manufactured) @ 21.3°C	49677702
Relative Density Bulk Density	Relative density 1.39 Bulk Density 0.202 g/mL at 23.4°C Tap Density 0.320 g/mL at 23.4°C	49677702
Vapor Pressure	4.6×10^{-5} Pa (3.5×10^{-7} mmHg) at 25°C 3.2×10^{-5} Pa (2.4×10^{-7} mmHg) at 20°C Classified as 'Non-volatile under field conditions.' (1)(3)	49677702
Henry's Law Constant	9.2×10^{-6} atm-m^3/mole at 20°C 1.3×10^{-5} atm-m^3/mole, using VP at 25°C and S at 20°C	Estimated from water solubility and vapor pressure
Water Solubility	Purified Water: 0.015 mg/L at 20°C pH 5 buffer solution: 0.014 mg/L pH 7 buffer solution: 0.011 mg/L pH 9 buffer solution: 0.012 mg/L	49677702
Solubility in Organic Solvents	All at 20°C: methanol 13 g/L acetone 210 g/L xylene 14 g/L 1,2-dichloroethane 95 g/L ethyl acetate 120 g/L n-heptane 0.053 g/L n-octanol 4.9 g/L	49677702
Octanol – water partition coefficient (K_{OW})	pH 5 ($\log_{10}$ Pow = 5.4 ± 0.1) at 20°C pH 7 ($\log_{10}$ Pow = 5.5 ± 0.04) at 20°C pH 9 ($\log_{10}$ Pow = 5.5 ± 0.1) at 20°C	49677702
Dissociation Constant	Does not dissociate in the environmental pH range (pH 4 to 10)	49677702
pH	6.58 at 23.4 °C (1% dilution in water)	49677702
UV/Visible light absorption	Neutral: λ max at 212, 245 nm Acidic: λ max at 212, 245 nm Alkaline: λ max at 217, 241 nm	49677702

* PAI = Pure Active Ingredient. TGAI = Technical Grade Active Ingredient.

Appendix D. Residue Summary Table

Table D.1. Summary of Residue Data from Crop Field Trials with Florpyrauxifen-benzyl.									
Commodity	Total Applic. Rate, g ai/ha (lb ai/A)	PHI (days)	Residue Levels (ppm) (XDE-848 BE + XDE-848 acid (reported as XDE-848 BE equivalents)						
			N	Min.	Max.	HAFT*	Median (STMdR)	Mean (STMR)	Std. Dev.
Rice (proposed use = 0.053 lb ai/A total application rate, 60-day PHI)									
Whole grain	100 (0.090) (GF-3162)	60	24	ND	ND	ND	ND	ND	NA
Whole grain	400 (0.357) (GF-3187) [a]	60	24	ND	0.0257	0.0195	ND	0.0032	0.0062
Straw	100 (0.090) (GF-3162)	60	24	ND	0.574	0.538	0.0173	0.0713	0.148
Straw	400 (0.357) (GF-3187) [a]	60	24	ND	1.139	0.864	0.0604	0.2179	0.333

Table D.2. Summary of Residue Data from Crop Field Trials with Florpyrauxifen-benzyl.									
Commodity	Total Applic. Rate, g a.i./ha (lb ai/A)	PHI (days)	Residue Levels (ppm) (XDE-848 BE + XDE-848 acid (reported as XDE-848 BE equivalents)						
			N	Min.	Max.	HAFT*	Median (STMdR)	Mean (STMR)	Std. Dev.
Rice (proposed use = 0.053 lb ai/A total application rate, 60-day PHI)									
Whole grain	80 (0.07) (GF-3206)	58-64	24	ND	0.0926	0.0764	0.0764	0.0102	0.0246
Whole grain	150 (0.134) (GF-3187) [a]	58-64	24	ND	0.0178	(0.0089)	(0.0089)	ND	0.0036
Whole grain	80 (0.07) (GF-3301)	58-64	24	ND	0.2470	0.2146	0.2146	0.0330	0.0765
Straw	80 (0.07) (GF-3206)	58-64	24	ND	0.9776	0.9013	0.0443	0.1444	0.2534
Straw	150 (0.134 (GF-3187) [a]	58-64	24	ND	0.2150	0.1619	0.0325	0.0468	0.0503
Straw	80 (0.07) (GF-3301)	58-64	24	ND	1.9524	1.7989	0.2691	0.4784	0.6249

N = Number of Field Trials

* HAFT = Highest Average Field Trial.

[a] This use pattern is not intended for the US label.

APPENDIX E: INTERNATIONAL RESIDUE LIMITS

Florpyrauxifen-benzyl (PC Code 030093)

Summary of US and International Tolerances and Maximum Residue Limits			
Residue Definition:			
US	Canada	Mexico[2]	Codex
40 CFR 180.XXX: sum of florpyrauxifen-benzyl (phenylmethyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoro-2-pyridinecarboxylate) and its acid metabolite (4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-5-fluoropyridine-2-carboxylic acid) calculated as the stoichiometric equivalent of florpyrauxifen-benzyl	None		None

Commodity[1]	*Tolerance (ppm) /Maximum Residue Limit (mg/kg)*			
	US	Canada	Mexico[2]	Codex
Rice, grain	0.30			
Fish - freshwater finfish	2.0			
Fish - shellfish, crustacean	0.50			
Fish - shellfish, mollusc	20			
Completed: M. Negussie; 10/10/16				

[1] Includes only commodities of interest for this action. Tolerance values should be the HED recommendations and not those proposed by the applicant.

[2] Mexico adopts US tolerances and/or Codex MRLs for its export purposes.