

## OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

WASHINGTON, D.C. 20460

#### **MEMORANDUM**

**DATE:** June 17, 2024

SUBJECT: Imidacloprid. Updated Occupational Exposure Assessment for Seed Treatment Uses in

Support of Registration Review.

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**Exposure Assessment** 

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FROM: Jennifer R. Tyler, Chemist Junifer & Tyler

Risk Assessment Branch I (RAB1)
Health Effects Division (HED; 7509T)

THRU: Rosanna Louie-Juzwiak, Branch Supervisor Run Judyje

Risk Assessment Branch I (RAB1) Health Effects Division (HED; 7509T)

and

Matthew Zampariello, ExpoSAC Reviewer

Melantha Jackson, ExpoSAC Reviewer

Exposure Science Advisory Committee (ExpoSAC)/HED

TO: Matthew Khan, Chemical Review Manager

Dana Friedman, Branch Chief

Risk Management and Implementation Branch I (RMIB I)

Pesticide Re-evaluation Division (PRD; 7508M)

The conclusions conveyed in this assessment were developed in full compliance with *EPA Scientific Integrity Policy for Transparent and Objective Science*, and EPA Scientific Integrity Program's *Approaches for Expressing and Resolving Differing Scientific Opinions*. The full text of *EPA Scientific Integrity Policy for Transparent and Objective Science*, as updated and approved by the Scientific Integrity Committee and EPA Science Advisor can be found here: <u>EPA's Scientific Integrity Policy</u>. The full text of the EPA Scientific Integrity Program's *Approaches for Expressing and Resolving Differing Scientific Opinions* can be found here: <u>Approaches for Expressing and Resolving Differing Scientific Opinions</u> | US EPA.

#### Introduction

PRD has requested HED conduct an updated exposure and risk assessment for the registered seed treatment uses of the active ingredient (ai) imidacloprid (1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine). This memorandum, which supports the ongoing imidacloprid Registration Review, incorporates new and updated exposure data and policies for seed treatment scenarios (Policies 14.1 and 15.2, January 2022). This memorandum serves as an addendum to HED's 2017 Registration Review human health draft risk assessment (DRA; Memo, J. Tyler et al., D437947, 22-JUN-2017).

It is HED policy to use the best available data to assess exposure. Several sources of generic data were used in this assessment as surrogate data in the absence of chemical-specific data, including the Agricultural Handler Exposure Task Force (AHETF) database and ExpoSAC Policy 14 and 15 (SOPs for Seed Treatment). Some of these data are proprietary, and subject to the data protection provisions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

**Note:** This memorandum was reviewed by the Exposure Science Advisory Committee (ExpoSAC) on 31-AUG-2023.

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#### 1.0 Executive Summary

HED has conducted an updated occupational exposure assessment for the registered conventional seed treatment uses for imidacloprid. This streamlined memorandum, which supports the ongoing imidacloprid Registration Review, incorporates new and updated exposure data and policies for seed treatment scenarios (Policies 14.1 and 15.2, released January 2022¹). Therefore, the updated seed treatment assessment presented here supersedes those assessed in ORE assessment supporting the DRA (Memo, J. Tyler and C. Walls, D438434, 08-JUN-2017) and updated liquid on-farm seed treatment assessment (Memo, J. Tyler, D460918, 19-APR-2021).

For a detailed summary of the use and exposure profiles, hazard characterization and dose response, non-occupational spray drift, residential handler and post-application assessment, occupational handler (agricultural and non-seed treatment uses), and occupational post-application risk assessment, refer to the 2017 ORE assessment (Memo, J. Tyler and C. Walls, D438434, 08-JUN-2017) and revised residential and aggregate risk assessment (Memo, J. Tyler, D460920, 19-APR-2021), which are available under docket ID EPA-HQ-OPP-2008-0844 on <u>regulations.gov</u>. These sections are not impacted by this update which is solely intended to update the seed treatment uses.

<u>Seed Treatment Use Profile</u>: Imidacloprid is an insecticide in the neonicotinoid class of chemicals. It is registered for seed treatment of several crops. Imidacloprid end use products registered for seed treatment are manufactured as dust (D) and flowable concentrate (FIC) formulations. Based on the registered labels, commercial worker activities are expected for both the D and FIC formulations; however, on-farm seed treatment work activities are only expected for FIC formulation on barley, canola, corn, cotton, millet, sorghum, and wheat. Application rates range from 0.000623 to 0.005 lb ai/lb seed. Both product labels direct mixers, loaders, applicators and other handlers to wear baseline attire (i.e., long sleeved shirts, long pants, and shoes and socks) as well as personal protective equipment (PPE) including chemical-resistant gloves made of waterproof material.

<u>Exposure Profile</u>: Based on the registered seed treatment uses of imidacloprid, it is expected that short- (1 to 30 days) and intermediate-term (1 to 6 months) dermal and inhalation occupational handler exposures will occur. Chronic exposure is not expected for the registered use patterns.

Hazard Characterization: Imidacloprid is classified as Toxicity Category II for acute oral toxicity and Category IV for acute dermal and acute inhalation toxicity and for skin and eye irritation potential. Imidacloprid is not a dermal sensitizer. The point of departure (POD) for short- and intermediate-term dermal and inhalation exposures, is the No Observed Adverse Effect Level (NOAEL) of 8 mg/kg/day, based on an increased incidence of tremors/trembling observed in the 90-day dog study (MRID 42256328) at the Lowest Observed Adverse Effect Level (LOAEL) of 22 mg/kg/day. The results of a dermal absorption study (MRID 50411201) supports a 4.8% dermal absorption factor (DAF). Toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure. Imidacloprid is characterized as "not likely to be carcinogenic to humans" and a quantitative cancer risk assessment was not conducted.

<sup>1</sup> Available online: Occupational Pesticide Exposure - Seed Treatment | US EPA

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100X for short- and intermediate-term risks.

The Agency's level of concern (LOC) for non-cancer risks (i.e., LOC for Margins of Exposure (MOEs)) is defined by uncertainty factors. The Agency applies a 10X factor to account for inter-species extrapolation and a 10X factor to account for intra-species variation. HED has concluded that the FQPA safety factor for imidacloprid can be reduced to 1X since the toxicology database for imidacloprid is adequate for risk assessment; the observed neurotoxic, fetal and offspring effects are well characterized and protected for; and the exposure assessments are sufficient and unlikely to underestimate exposure. The total uncertainty factor that is applied to occupational risk assessments is

Occupational Exposure and Risk: The occupational handler dermal and inhalation exposure and risk estimates were re-assessed for commercial and on farm seed treatment uses based on updated exposure data and policies. Since short- and intermediate-term PODs are the same, the results of the short-term risk assessment are protective of any intermediate-term exposures. For the registered commercial seed treatment uses, the occupational handler exposure and risk estimates indicate that the combined (dermal and inhalation) MOEs are not of concern to HED (i.e., MOE  $\geq$  LOC of 100) with baseline attire (long-sleeved shirts, long pants, shoes, and socks) and label-required PPE of chemical resistant gloves for most exposure scenarios, with the exception of the following:

- *Treating:* Safflower. Exposure estimate is not of concern with the addition of double-layered clothing. Combined risk is driven by the dermal route of exposure.
- *Packaging:* Safflower. Exposure estimate is not of concern with the of addition of PF-10 respirator. Combined risk is driven by the inhalation route of exposure.
- Loading/Planting: Navy beans. Exposure estimate is not of concern with the addition of PF-10 respirator. Combined risk is driven by the inhalation route of exposure.
- Cleaning: Canola, carrot, corn (field, pop, and sweet), cotton, crambe, flax, millet, mustard seed, safflower, sorghum, and sunflower. Exposure estimates for these crops are still of concern with the addition of additional PPE (double-layered clothing and PF-10 respirator). Combined risks are primarily driven by the dermal route of exposure.

For the registered on-farm seed treatment uses, occupational handler exposure and risk estimates indicate that the combined (dermal and inhalation) MOEs are not of concern to HED (i.e., MOE  $\geq$  LOC of 100) for crops with label-required baseline attire and PPE.

<u>Human Studies Review</u>: This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include the AHETF database and ExpoSAC Policy 14 (SOPs for Seed Treatment), are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency website<sup>2</sup>.

#### 2.0 Risk Assessment Conclusions and Recommendations

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<sup>&</sup>lt;sup>2</sup> Available online: Occupational Pesticide Handler Exposure Data | US EPA

#### 2.1 Summary of Risk Estimates

<u>Commercial Seed Treatments (All Formulations)</u>: Total (dermal and inhalation) MOEs are not of concern (MOEs ≥ LOC of 100) with label-required attire and PPE for all scenarios except:

- Treating: Safflower (MOE = 95), which is not of concern with the addition of double-layered clothing (MOE = 110). Combined risk is driven by the dermal route of exposure.
- Packaging: Safflower (MOE = 81), which is not of concern with the addition of a PF-10 respirator (MOE = 300). Combined risk is driven by the inhalation route of exposure.
- Loading/Planting: Navy beans (MOE = 47), which are not of concern with the addition of a PF-10 respirator (MOE = 110). Combined risk is driven by the inhalation route of exposure.
- Cleaning: Canola (MOE = 23), carrot (MOE = 92), corn (field, pop, and sweet; MOE = 92), cotton (MOE = 46), crambe (MOE = 23), flax (MOE = 23), millet (Japanese, pearl, and prose; MOE = 92), mustard seed (MOE = 23), safflower (MOE = 46), sorghum (MOE = 92), and sunflower (MOE = 46). Total MOEs are still of concern at the highest level of PPE (double-layered clothing and PF-10 respirators) Canola (MOE = 25), carrot (MOE = 99), corn (field, pop, and sweet; MOE = 99), cotton (MOE = 49), crambe (MOE = 25), flax (MOE = 25), millet (Japanese, pearl, and prose; MOE = 99), mustard seed (MOE = 25), safflower (MOE = 49), sorghum (MOE = 99), and sunflower (MOE = 49). Combined risks are primarily driven by the dermal route of exposure.

<u>On-farm Seed Treatments (Liquid Formulation Only)</u>: Total (dermal and inhalation) are not of concern (MOEs ≥ 100) using label-required baseline attire and PPE, with MOEs ranging from 450 to 7,300.

#### 2.2 Label Recommendations

None.

### 2.3 Data Deficiencies and Requirements

None.

#### 3.0 Hazard Characterization

<u>Acute Toxicity</u>: The acute toxicity of imidacloprid is summarized below in Table 3.1. Imidacloprid is classified as Toxicity Category II for acute oral toxicity and Category IV for acute dermal and acute inhalation toxicity, and for skin and eye irritation potential. Imidacloprid is not a dermal sensitizer.

Guideline No.	Study Type	MRID(s)	Results	Toxicity Category	
070 1100	Acret Coulded	42055331	LD <sub>50</sub> = 424 mg/kg (M) LD <sub>50</sub> > 450 mg/kg and < 475 mg/kg (F)	П	
370.1100	Acute Oral (rat)	46790604	LD <sub>50</sub> > 380 mg/kg and < 550 mg/kg (F)	III	
		46833503	LD <sub>50</sub> = 380 mg/kg (F)	11	
870.1200	Acute Dermal (rat)	42055332	LD <sub>50</sub> > 5000 mg/kg (M & F)	IV	
870.1300	Acute Inhalation (rat)	42256317	LC <sub>50</sub> > 5.33 mg/L (M & F)	IV	
870.2400	Primary Eye Irritation (rabbit)	42055334	Not an eye irritant	IV	
870.2500	Primary Skin Irritation (rabbit)	42055335	Not a dermal irritant	IV	

Table 3.1. Acute Toxicity of Imidacloprid.									
Guideline No.	Study Type		Results	Toxicity Category					
870.2600	Dermal Sensitization (guinea pig)	42055336	Not a dermal sensitizer (Maximization)	N/A					
870.2600	Dermai Sensitization (guinea pig)	47227011	Not a dermal sensitizer (Buehler)	N/A					

Toxicological Points of Departure (PODs) Used for Risk Assessment: A route-specific inhalation study is available and showed no effects up to the highest dose tested in adult animals. The POD for short- and intermediate-term dermal and inhalation exposures, the NOAEL of 8 mg/kg/day, is based on an increased incidence of tremors/trembling observed in the 90-day dog study at the LOAEL of 22 mg/kg/day. This study is appropriate for all durations and is protective of the decreased absolute body weights in the combined chronic carcinogenicity study where the hazard database shows that the effects do not progress with time from subchronic to chronic durations. Furthermore, imidacloprid's absorption, distribution, metabolism, and excretion (ADME) profile shows that the chemical is rapidly absorbed, excreted within 24 hours, and does not accumulate in the body, and thus corroborates the lack of progression of toxicity from subchronic to chronic durations. This study is appropriate for the route and durations of concern, and for young children in residential settings. Imidacloprid has been classified as a Group E chemical, "Evidence of non-carcinogenicity for humans," by the HED Reference Dosed (RfD)/Peer Review Committee (11/10/93). A summary of the toxicological doses and endpoints for occupational human health risk assessments are provided in Table 3.2.

Exposure/ Scenario	POD	Uncertainty/FQPA SF	LOC	Study and Toxicological Effects
Incidental Oral Short- (1-30 days) and Intermediate-Term (1-6 months), and Long-Term	NOAEL = 8 mg/kg/day	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF = 1X	LOC = 100	Callaborate and the
Dermal Short- (1-30 days), Intermediate- (1-6 months), and Long-Term (> 6 months)	NOAEL = 8 mg/kg/day DAF = 4.8%	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF = 1X	LOC = 100	Subchronic oral – dog LOAEL = 22 mg/kg/day based upon an increased
Inhalation Short- (1-30 days), Intermediate- (1-6 months), and Long-Term (>6 months)	NOAEL = 8 mg/kg/day	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF = 1X	LOC = 100	incidence of tremors.
Cancer (oral, dermal, inhalation)	Classification: "Not likely to be Carcinogenic to Humans."			

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<sub>A</sub> = extrapolation from animal to human (interspecies). UF<sub>H</sub> = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. MOE = margin of exposure. LOC = level of concern. Dermal-absorption factor (DAF) of 4.8% based on results of dermal absorption study (MRID 50411202).

Dermal Absorption: The results of a dermal absorption study (MRID 50411201) supports a 4.8% DAF. Since no inhalation absorption data are available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure.

Body Weight: The standard body weight for the general population (80 kg) was used for all exposure scenarios covered in this risk assessment since the endpoints selected were not female-specific, developmental and/or fetal effects.

#### 4.0 Use Profile

Imidacloprid end use products registered for seed treatment are manufactured as dust and flowable concentrate formulations. Both labels specify the type of seed treatment equipment that will be used, as well as any additional seed treatment processes (i.e., pelleting, encrusting, film coating, etc.). Information pertaining to the registered end-use product is presented in Table 4.1. A summary of the registered use patterns is presented in Table 4.2.

Trade Name	EPA Reg. No.	Imidacloprid Concentration	Formulation Type	Restrictions
Gaucho <sup>®</sup> 600 Flowable	<mark>264-968</mark>	48.7% ai 5 lb ai/gal of product	FIC	-For use in commercial seed treaters only, with the exception of application to canola, cotton (delinted seed), field corn, sorghum, millet, wheat and barley, which may be made either by commercial seed treatment or as an end-use seed treatment on agricultural establishments at, or immediately before, planting. This product is to be used in liquid or slurry treaters.  -PPE: mixers, loaders, applicators and other handlers to wear long sleeved shirts, long pants, chemical-resistant gloves made of waterproof material, and shoes and socks.
Gaucho <sup>®</sup> 75 ST Insecticide	<mark>264-959</mark>	75% ai	D	-For use in commercial seed treaters only. Not for use on agricultural establishments in hopper-box, slurry-box, or other seed treatment applications at, or immediately before, planting. This product is to be used in treaters designed for pelleting or coating seed. Mix thoroughly before use or use entire container at one time. All mixes should be pretested to determine physical compatibility between formulations. Observe all cautions and limitations on labeling of all products used in mixtures.  -PPE: mixers, loaders, applicators and other handlers to wear long sleeved shirts, long pants, chemical-resistant gloves made of waterproof material, and shoes and socks.

<sup>1.</sup> PPE = personal protective equipment; NA = not applicable; D = Dust; FIC = Flowable Concentrate.

Crop	Formulation [EPA Reg. No.] <sup>1</sup>	Max. Applic. Rate (lb ai/lb seed)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/lb seed)
Barley	D [264-959]; FIC [264-968]	0.00094		0.00094
Beans	D [264-959]; FIC [264-968]	0.00125		0.00125
Borage	FIC [264-968]	0.01		0.001
Canola	D [264-959]; FIC [264-968]	0.01		0.001
Carrot	D [264-959]; FIC [264-968]	0.0025		0.0025
Corn (field, pop, sweet)	D [264-959]; FIC [264-968]	0.0025		0.0025
Cotton	D [264-959]; FIC [264-968]	0.005		0.005
Crambe	FIC [264-968]	0.01	1	0.001
Flax	FIC [264-968]	0.01		0.001
Millet	FIC [264-968]	0.0025		0.0025
Mustard	FIC [264-968]	0.01		0.001
Oats	FIC [264-968]	0.00094		0.00094
Peanuts	D [264-959]	0.000623		0.000623
Peas	D [264-959]; FIC [264-968]	0.00125		0.00125
Rye	FIC [264-968]	0.00094		0.00094

Crop	Formulation [EPA Reg. No.] <sup>1</sup>	Max. Applic. Rate (lb ai/lb seed)	Max. No. Applic. per Season	Max. Seasonal Applic Rate (lb ai/lb seed)
Safflower	FIC [264-968]	0.005	2	0.005
Sorghum	FIC [264-968]	0.0025		0.0025
Soybeans	FIC [264-968]	0.00125	Ī	0.00125
Sunflower	FIC [264-968]	0.005		0.005
Sugarbeets	D [264-959]; FIC [264-968]	0.002		0.002
Triticale	D [264-959]; FIC [264-968]	0.00094	1	0.00094
Wheat	D [264-959]; FIC [264-968]	0.00094		0.00094

<sup>1.</sup> NA = not applicable; D = Dust; FIC = Flowable Concentrate.

#### 5.0 Occupational Exposure and Risk Estimates

#### 5.1 Occupational Handler Exposure/Risk Estimates

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from the registered uses. Commercial worker activities are expected for both the D and FIC formulations; however, on-farm seed treatment work activities are only expected for the FIC formulation on barley, canola, corn, cotton, millet, sorghum, and wheat.

Since the 2017 DRA in support of Registration Review, the seed treatment policies and unit exposures have been updated (ExpoSAC Policy 14.1 and 15.2). The following commercial and on-farm seed treatment worker activities are anticipated and have been assessed:

Commercial Seed Treatment (CST) – Treating: The CST-Treating scenario represents worker exposure while performing any combination of packaging, treating, or cleanout tasks, but not exclusively packaging or exclusively cleanout. This scenario includes several tasks, such as mixing and loading chemical, calibrating the treater, treating/coating the seed and sampling "wet" treated seed, that are very critical to the CST process and generally involve just a few specially trained workers at each facility. Worker exposure associated with these scenario-specific tasks is predicted from the amount of ai handled (AaiH).

The CST-Treating dataset represents use of closed loading systems. HED does not have data to quantify exposure from the use of an open loading system. Exposure may be higher with use of an open loading system; however, it should be noted that workers did other activities beyond just loading chemical (e.g., calibrating treater, treating/coating seed, sampling "wet" treated seed). If open loading systems are used for commercial seed treatment, HED anticipates that the risk estimates may be higher than

what is presented here.

CST - Packaging: The CST-Packaging scenario represents worker exposure while performing one or more packaging tasks, but none of the treating or cleanout tasks. The packaging-related tasks identified include bagging, closing/sewing, tagging, stacking, and moving packaged seed via forklift. Worker exposure associated with these scenario-specific tasks is predicted from the amount of AaiH.

CST - Cleaning: The CST-Cleaning scenario represents worker exposure while performing cleanout-related tasks. Cleanout of seed-treating equipment is a task that can involve intensive contact with residue on equipment surfaces. Cleanout tasks might occupy a worker anywhere from a few minutes up to a large portion of the workday. The cleanout activity frequently involves intermittent cleanout tasks that occur for short durations periodically during a workday. If such workdays involve packaging and/or treating tasks as well, then total workday exposure would be described by the CST-Treating scenario. The CST-Cleaning scenario represents only those workers whose workday is exclusively devoted to cleanout activity. Worker exposure associated with these scenario-specific tasks is predicted from the ai's seed treatment application rate (AR) and the cleanout activity duration (AD) (AR x AD).

CST - Loader/Planter: The CST-Loader/Planter scenario consists of handling purchased bags of commercially treated seed, loading the treated seed to a hopper or similar planting equipment, and planting seed in fields. During planting, the planter typically performs other tasks in addition to operating the equipment by driving the tractor through the field, such as making sure that the seed is properly planted (e.g., by checking seed depth and making adjustments or repairs as needed) or leveling the seed in the hopper as needed. It would also include any 'background' exposure such as contact with contaminated surfaces or equipment in the workday environment. Even though this scenario is identified as involving enclosed cab tractors only, the assumption is that there would be no meaningful difference in planter exposure between open versus closed cabs, and therefore, the same dataset is used for both. This assumption is based on the likelihood that most worker exposure while planting treated seeds is coming from activities occurring outside the planter/tractor cab (i.e., maintenance activities). Worker exposure associated with these scenario-specific tasks is predicted from the amount of ai handled.

On-Farm Seed Treatment and Planting with Liquids (OFST/P-L): The OFST/P-L scenario involves workers that operate any on-farm seed treating equipment, including mixing, loading and application of liquid pesticides to untreated seed, and any associated tasks such as maintaining the treating equipment, and then planting the treated seed. The OFST/P-L scenario represents treatment of seed at or immediately before planting using manual-style treating/planting equipment such as hopper-box, planter-box, and slurry-boxes as well as using commercial-style treatment equipment. The workers often perform tasks other than treating and planting during the monitoring period, including cleaning auger (mixing) systems or planters after treatment was finished, shoveling treated seed into augers or directly into a planter, checking augers or spray nozzle operation, fixing auger problems, spreading untreated seed in seed hoppers, checking seed depth during planting, adjusting seed equipment, and removing dirt build-up on the planter. Worker exposure associated with these scenario-specific tasks is predicted from the amount of ai handled.

presented here.

The on-farm seed treatment datasets represent use of open loading systems. HED does not have data to quantify exposure from the use of a closed loading system. Exposure may be lower with use of a closed loading system; however, it should be noted that workers did other activities beyond just loading chemical (e.g., loading treated seed into planters and planting). If closed loading systems are used for on-farm seed treatment, HED anticipates that the risk estimates may be lower than what is

The quantitative exposure/risk assessment developed for occupational handlers is based on the scenarios presented in Tables 5.1.1 and 5.1.2.

<u>Occupational Handler Exposure Data and Assumptions</u>: A series of assumptions and exposure factors served as the basis for completing the occupational handler risk assessments. Each assumption and factor is detailed below on an individual basis.

Application Rate: The quantitative exposure/risk assessment developed for occupational handlers treating seed is based on the registered application rates listed in Table 4.2.

Unit Exposures: It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include PHED 1.1, the AHETF database, the Outdoor Residential Exposure Task Force (ORETF) database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary (e.g., AHETF data), and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures", are outlined in HED's Exposure Science Advisory Council Policy 14 (Version 14.1): Standard Operating Procedures for Seed Treatment<sup>3</sup>, which, along with additional information on seed treatment exposure assessment, can be found at the Agency website<sup>4</sup>.

Area Treated or Amount Handled: The inputs for area treated/amount handled were based on information in ExpoSAC Policy 15.

Exposure Duration: HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. Exposure duration is determined by many things, including the exposed population, the use site, the pest pressure triggering the use of the pesticide, and the cultural practices surrounding that use site. For most agricultural uses, it is reasonable to believe that occupational handlers will not apply the same chemical every day for more than a one-month time frame; however, there may be a large agribusiness and/or commercial applicators who may apply a product over a period of weeks (e.g., completing multiple applications for multiple clients within a region). For imidacloprid, based on the existing registered commercial seed treatment uses, both short- and intermediate-term exposures are expected for occupational handlers because a product could be applied multiple times per season. On-farm seed treatment exposures are anticipated to be short-term only in duration. Since short- and intermediate-term PODs are the same, the results of the short-term risk assessment are protective of any intermediate-term exposures.

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<sup>&</sup>lt;sup>3</sup> Available online: <u>US EPA - Standard Operating Procedures for Seed Treatment</u>

<sup>&</sup>lt;sup>4</sup> Available online: Occupational Pesticide Exposure - Seed Treatment | US EPA

*PPE*: Estimates of dermal and inhalation exposure were calculated considering the PPE listed on product labels, and any additional PPE necessary to identify risk estimates not of concern. The attire and/or PPE that was considered and assessed, as needed, include: (1) baseline with gloves and no respirator, (2) double layer with gloves and no respirator, (3) baseline with gloves and PF10 respirator, and (5) double layer with gloves and PF10 respirator. The imidacloprid product labels for seed treatments direct mixers, loaders, applicators and other handlers to wear baseline attire with PPE consisting of chemical-resistant gloves.

Estimates of inhalation exposure and risk for occupational handler exposure assessments consider the reduction in exposure afforded by respirators. Typically, results are presented for "baseline," defined as no respirator, and then, because they are the occupational standard in the pesticide industry, for half-face filtering facepiece or elastomeric respirators, quantified via application of their corresponding assigned protection factor (APF) of 10 (90% exposure reduction). This format, in some cases along with risk estimates for engineering controls, provides a variety of options for risk management decisions. This risk assessment presents potential inhalation risk estimates of concern when using a half-face filtering facepiece or elastomeric respirator (i.e., a PF10 respirator) for all scenarios.

<u>Combining Exposures/Risk Estimates</u>: Dermal and inhalation risk estimates were combined in this assessment, since the toxicological effects for these exposure routes were similar. Dermal and inhalation risk estimates were combined using the following formula:

Total  $MOE = Point of Departure (mg/kg/day) \div Combined dermal + inhalation dose (mg/kg/day)$ 

<u>Occupational Handler Non-Cancer Exposure and Risk Estimate Equations</u>: The algorithms used to estimate non-cancer exposure and dose for occupational handlers can be found in Appendix A.

<u>Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates</u>: Summaries of dermal and inhalation risk estimates for occupational handlers for commercial and on-farm seed treatments can be found in Tables 5.1.4 and 5.1.5, respectively.

Commercial Seed Treatments (All Formulations): Combined (dermal and inhalation) MOEs range from 21 to 310,000 (LOC = 100) assuming label-required attire and PPE (baseline attire and gloves). Additional PPE (e.g., double layer clothing and respirators) may be used to mitigate some of the risk estimates of concern. However, some scenarios still result in risks of concern (MOEs < LOC of 100) with additional PPE (double layer of clothing and PF10 respirator). See Tables 5.1.1-5.1.3.

On-farm Seed Treatments (Liquid Formulations): Combined (dermal and inhalation) MOEs range from 450 to 7,300 and are not of concern (MOEs ≥ 100) with label-required attire and PPE (baseline attire and gloves). See Table 5.1.1.

	On-Farm Seed Treatment (Liquid Formulation)					
Treating (MOE)	Packaging (MOE)	Cleaning (MOE)	Loading/Planting (MOE)	Treating/Planting (MOE)		
<ul> <li>Barley (520)</li> <li>Bean, dry (500)</li> <li>Bean, lima (420)</li> <li>Bean, navy (420)</li> <li>Bean, snap (420)</li> <li>Beet, sugar (29,000)</li> <li>Canola (140)</li> <li>Carrot, film-coated (23,000)</li> <li>Carrot, encrusted/pelleted (310,000)</li> <li>Corn, field (210)</li> <li>Corn, pop (210)</li> <li>Corn, sweet (210)</li> <li>Cotton (280)</li> <li>Crambe, film-coated (6,400)</li> <li>Flax (140)</li> <li>Millet, Japanese (190)</li> <li>Millet, pearl (190)</li> <li>Millet, proso (190)</li> <li>Mustard seed, film-coated (5,900)</li> <li>Mustard seed, encrusted/pelleted (80,000)</li> <li>Mustard seed (140)</li> <li>Oat (520)</li> <li>Pea, garden (420)</li> <li>Peanut (2,200)</li> <li>Rye (520)</li> <li>Sorghum, grain (190)</li> <li>Soybean (500)</li> <li>Sunflower (430)</li> <li>Triticale (520)</li> <li>Wheat (520)</li> </ul>	Barley (420) Bean, dry (410) Bean, lima (340) Bean, navy (340) Bean, snap (340) Beet, sugar (24,000) Canola (110) Carrot, film-coated (19,000) Carrot, encrusted/pelleted (250,000) Corn, field (170) Corn, pop (170) Corn, sweet (170) Cotton (230) Crambe, film-coated (64,000) Thax (110) Millet, Japanese (160) Millet, pearl (160) Millet, pearl (160) Millet, proso (160) Mustard seed, film-coated (4,800) Mustard seed, encrusted/pelleted (64,000) Mustard seed (110) Oat (420) Pea, garden (420) Peanut (1,900) Rye (420) Sorghum, grain (160) Soybean (410) Sunflower (360) Triticale (420)	<ul> <li>Barley (220)</li> <li>Bean, dry (160)</li> <li>Bean, lima (160)</li> <li>Bean, navy (160)</li> <li>Bean, snap (160)</li> <li>Beet, sugar (100)</li> <li>Oat (220)</li> <li>Pea, garden (160)</li> <li>Peanut (340)</li> <li>Rye (220)</li> <li>Soybean (410)</li> <li>Triticale (220)</li> <li>Wheat (220)</li> </ul>	<ul> <li>Barley (330)</li> <li>Bean, dry (150)</li> <li>Bean, lima (230)</li> <li>Bean, snap (120)</li> <li>Beet, sugar (760)</li> <li>Canola (370)</li> <li>Carrot, film-coated (2,500)</li> <li>Carrot, encrusted/pelleted (2,500),</li> <li>Corn, field (410)</li> <li>Corn, pop (550)</li> <li>Corn, sweet (940)</li> <li>Cotton (320)</li> <li>Crambe (370)</li> <li>Flax (150)</li> <li>Millet, Japanese (1,200)</li> <li>Millet, pearl (1,500)</li> <li>Millet, proso (1,600)</li> <li>Mustard seed, film-coated (1,100)</li> <li>Mustard seed, encrusted/pelleted (1,100)</li> <li>Mustard seed (1,100)</li> <li>Oat (360)</li> <li>Pea, garden (150)</li> <li>Peanut (540)</li> <li>Rye (360)</li> <li>Safflower (440)</li> <li>Sorghum, grain (2,500)</li> <li>Sunflower (3,800)</li> <li>Triticale (300)</li> <li>Wheat (210)</li> </ul>	Barley (730)     Canola (920)     Corn, field (700)     Cotton (7,800)     Millet, Japanese (2,600)     Millet, pearl (3,300)     Millet, proso (2,200)     Sorghum, grain (5,600)     Wheat (450)		

Table 5.1.2. Summary of <u>Combined</u> (Dermal and Inhalation) Scenarios with <u>No Risks of Concern</u> Assuming Double Layer Clothing and Gloves (DL/G).								
Commercial Seed Treatment								
Treating (MOE)	Packaging (MOE)	Loading/Planting (MOE)						
Safflower (110)	Safflower (300)	• Beans, Navy (110)						

	Commercial Seed Treatment
	Cleaning Equipment
	(MOE)
Canola (25)	Millet, Japanese (99)
Carrot, film-coated (99)	Millet, pearl (99)
Carrot, encrusted/pelleted (99)	Millet, proso (99)
Corn, field (99)	Mustard seed, film-coated (25)
Corn, pop (99)	<ul> <li>Mustard seed, encrusted/pelleted (25)</li> </ul>
Corn, sweet (99)	Mustard seed (25)
Cotton (49)	Safflower (49)
Crambe, film-coated (25)	Sorghum, grain (99)
Crambe, encrusted/pelleted (25)	Sunflower (49)
Flax (25)	

Table 5.1.4. Revised	Occupational Handler	Non-Cancer Expo	sure and Risk Estimates	for Imidaclo	prid – Com	mercial Se	ed Treatmer	nt – <u>All Form</u> ul	ations.		
			Exposure Variable	Dern			lation <sup>3</sup>	Total MOE <sup>6</sup> (LOC = 100)			
Crop or	Specialized	App Rate	(AST, activity duration,	MOE⁴ (LO	C = 100)	MOE⁵ (L	OC = 100)		Total IVIO	)E (LOC = 100)	
Target	Treatment	(lb ai/lb seed)1	or NSP) <sup>2</sup>	SL/G	DL/G	No-R	PF10 R	SL/G; No-R	DL/G; No-R	SL/G; PF10 R	DL/G; PF10 R
				Treating	(CST-T)						
Barley	N/A	0.00094	360,000	770	930	1,600	16,000	520	590	730	880
Bean, dry	N/A	0.00125	281,250	740	900	1,500	15,000	500	560	710	850
Beans, lima											
Beans, navy	N/A	0.00125	339,500	620	750	1,300	13,000	420	480	590	710
Bean, snap											
Beet, sugar	Film-coated	0.002	3,000	43,000	53,000	89,000	890,000	29,000	33,000	41,000	50,000
Canola	N/A	0.01	125,000	210	250	430	4,300	140	160	200	240
Carrot	Film-coated	0.0025	3,000	35,000	42,000	71,000	710,000	23,000	26,000	33,000	40,000
6 611	Encrusted/Pelleted		225	460,000	560,000	950,000	9,500,000	310,000	350,000	440,000	530,000
Corn, field	N/A	0.0025	339,500	310	370	630	6,300	210	230	300	350
Corn, pop Corn, sweet	N/A	0.0025	339,300	310	370	630	6,300	210	230	300	350
Cotton	N/A	0.005	125 000	420	510	850	8,500	280	320	400	480
Cotton		0.005	125,000								9,500
Crambe <sup>7</sup>	Film-coated Encrusted/Pelleted	0.01	3,000 225	8,700 120,000	10,000 140,000	18,000 240,000	180,000 2,400,000	5,900 80,000	6,400 88,000	8,300 110,000	130,000
Flax	N/A	0.01	125,000	210	250	430	4,300	140	220	280	330
Millet, Japanese	IN/A	0.01	123,000	210	230	430	4,300	140	220	280	330
Millet , pearl	N/A	0.0025	360,000	290	350	590	5,900	190	220	280	330
Millet, proso	1 .,,,,	0.0025	500,000	250	555		3,300				
minety proso	Film-coated		3,000	8,700	10,000	18,000	180,000	5,900	6400	8,300	9,500
Mustard seed	Encrusted/Pelleted	0.01	225	120,000	140,000	240,000	2,400,000	80,000	88,000	110,000	130,000
	N/A		125,000	210	250	430	4,300	140	160	200	240
Oat	N/A	0.00094	360,000	770	930	1,600	16,000	520	590	730	880
Pea, garden	N/A	0.00125	339,500	620	750	1,300	13,000	420	480	590	710
Peanut	N/A	0.000623	126,000	3,300	4,000	6,800	68,000	2,200	2,500	3,100	3,800
Rye	N/A	0.00094	360,000	770	930	1,600	16,000	520	590	730	880
Safflower	N/A	0.005	360,000	140	180	300	3,000	95	110	130	170
Sorghum, grain	N/A	0.0025	360,000	290	350	590	5,900	190	220	280	330
Soybean	N/A	0.00125	281,250	740	900	1,500	15,000	500	560	710	850
Sunflower	N/A	0.005	80,000	650	790	1,300	13,000	430	490	620	740
Triticale	N/A	0.00094	360,000	770	930	1,600	16,000	520	590	730	880
Wheat	N/A	0.00094	360,000	770	930	1,600	16,000	520	590	730	880
_	т .	•	T	Packagin							ı
Barley	N/A	0.00094	360,000	2,300	3,000	520	5,200	420	440	1,600	1,900
Bean, dry	N/A	0.00125	281,250	2,200	2,900	500	5,000	410	430	1,500	1,800
Beans, lima	N/A	0.00135	220 500	1 000	2.400	420	4 200	340	360	1 200	1 500
Beans, navy	N/A	0.00125	339,500	1,900	2,400	420	4,200	340	360	1,300	1,500
Bean, snap	Film coated	0.002	3,000	130,000	170,000	30,000	300,000	24,000	26,000	91,000	110 000
Beet, sugar	Film-coated N/A	<b>L</b>		630	810	140		110	26,000 120	430	110,000 510
Canola	N/A Film-coated	0.01	125,000 3,000	100,000	140,000	24,000	1,400 240,000	19,000	20,000	71,000	88,000
Carrot	Encrusted/Pelleted	0.0025	225	1,400,000	1,800,000	_	3,100,000	250,000	260,000	960,000	1,100,000
	Encrusted/Pelleted	L	225	1,400,000	1,000,000	310,000	3,100,000	250,000	200,000	900,000	1,100,000

Table 5.1.4. Revised	Occupational Handler	Non-Cancer Expo	sure and Risk Estimates	for Imidaclo	prid – Com	mercial Se	ed Treatmer	nt – <u>All Formul</u>	ations.		
_			Exposure Variable	Dermal <sup>3</sup> Inhalation <sup>3</sup>			Total MOE <sup>6</sup> (LOC = 100)				
Crop or	Specialized	App Rate	(AST, activity duration,	MOE⁴ (LO	C = 100)	MOE⁵ (L	OC = 100)		l otal IVIO	)E- (LOC = 100)	
Target	Treatment	(lb ai/lb seed)1	or NSP) <sup>2</sup>	SL/G	DL/G	No-R	PF10 R	SL/G; No-R	DL/G; No-R	SL/G; PF10 R	DL/G; PF10 R
Corn, field											
Corn, pop	N/A	0.0025	339,500	930	1,200	210	2,100	170	180	640	760
Corn, sweet											
Cotton	N/A	0.005	125,000	1,300	1,600	280	2,800	230	240	890	1,000
Crambe <sup>7</sup>	Film-coated	0.01	3,000	350,000	450,000	79,000	790,000	64,000	67,000	240,000	290,000
	Encrusted/Pelleted		225	26,000	34,000	5,900	59,000	4,800	5,000	18,000	22,000
Flax	N/A	0.01	125,000	630	810	140	1,400	110	170	610	710
Millet, Japanese											
Millet , pearl	N/A	0.0025	360,000	880	1,100	200	2,000	160	170	610	710
Millet, proso											
l	Film-coated		3,000	26,000	34,000	5,900	59,000	4,800	5,000	180,00	22,000
Mustard seed	Encrusted/Pelleted	0.01	225	350,000	450,000	79,000	790,000	64,000	67,000	240,000	290,000
0.	N/A	0.00004	125,000	630	810	140	14,000	110	120	430	510
Oat	N/A	0.00094	360,000	2,300	3,000	520	5,200	420	440	1,600	1,900
Pea, garden	N/A	0.00125	339,500	1,900	2,400	420	4,200	340	360	1,300	1,500
Peanut	N/A	0.000623	126,000	10,000	13,000	2,300	23,000	1,900	2,000	7,000	8,300
Rye	N/A	0.00094	360,000	2,300 440	3,000	520 99	5,200	420 81	440 84	1,600	1,900
Safflower	N/A	0.005	360,000		560		990			300	360
Sorghum, grain	N/A	0.0025	360,000	880	1,100	200	2,000	160 410	170	610	710
Soybean	N/A	0.00125	281,250	2,200	2,900	500	5,000	360	430 370	1,500	1,800
Sunflower Triticale	N/A N/A	0.005 0.00094	80,000 360,000	2,000 2,300	2,500 3,000	440 520	4,400 5,200	420	440	1,400 1,600	1,600 1,900
Wheat	N/A	0.00094	360,000	2,300	3,000	520	5,200	420	440	1,600	1,900
Wileat	NA	0.00034	300,000	Cleaning		320	3,200	420	440	1,000	1,500
Barley	N/A	0.00094		240	270	2,600	26,000	220	240	240	270
Bean, dry	N/A	0.00125		180	200	1,900	19,000	160	180	180	200
Beans, lima						,	,				
Beans, navy	N/A	0.00125		180	200	1,900	19,000	160	180	180	200
Bean, snap	i '					,	,				
Beet, sugar	Film-coated	0.002		110	130	1,200	12,000	100	120	110	130
Canola	N/A	0.01		23	25	240	24,000	21	23	23	25
	Film-coated	0.0005			400	070	0.700				
Carrot	Encrusted/Pelleted	0.0025		92	100	970	9,700	84	91	91	99
Corn, field			2.5								
Corn, pop	N/A	0.0025		92	100	970	9,700	84	91	91	99
Corn, sweet											
Cotton	N/A	0.005		46	50	480	4,800	42	45	46	49
Crambe <sup>7</sup>	Film-coated	0.01		23	25	240	24,000	21	23	23	25
	Encrusted/Pelleted										
Flax	N/A	0.01		23	25	240	2,400	21	23	23	25
Millet, Japanese											
Millet , pearl	N/A	0.0025		92	100	970	9,700	84	91	91	99
Millet, proso											

Table 5.1.4. Revised	Occupational Handler	Non-Cancer Expo	sure and Risk Estimates	for Imidaclo	prid – Com	mercial Se	ed Treatmer	nt – <u>All Formul</u>	ations.		
	Specialized	App Rate (Ib ai/lb seed)1	Exposure Variable	Dermal <sup>3</sup> Inhalation <sup>3</sup>		T . [14076/100 - 400)					
Crop or			(AST, activity duration, or NSP) <sup>2</sup>	MOE4 (LOC = 100)		MOE <sup>5</sup> (LOC = 100)		Total MOE <sup>6</sup> (LOC = 100)			
Target	Treatment			SL/G	DL/G	No-R	PF10 R	SL/G; No-R	DL/G; No-R	SL/G; PF10 R	DL/G; PF10 R
	Film-coated										
Mustard seed	Encrusted/Pelleted	0.01		23	25	240	2,400	21	23	23	25
	N/A										
Oat	N/A	0.00094		240	270	2,600	26,000	220	240	240	270
Pea, garden	N/A	0.00125		180	200	1,900	19,000	160	180	180	200
Peanut	N/A	0.000623		370	400	3,900	39,000	340	360	370	400
Rye	N/A	0.00094		240	270	2,600	26,000	220	240	240	270
Safflower	N/A	0.005		46	50	480	4,800	42	45	46	49
Sorghum, grain	N/A	0.0025		92	100	970	9,700	84	91	91	99
Soybean	N/A	0.00125		180	200	1,900	19,000	160	180	180	200
Sunflower	N/A	0.005		46	50	480	4,800	42	45	46	49
Triticale	N/A	0.00094		240	270	2,600	26,000	220	240	240	270
Wheat	N/A	0.00094		240	270	2,600	26,000	220	240	240	270
		•	Lo	ading/Plant	ing (CST-L/	P)				•	
Barley	N/A	0.00094	184,240,000	910	1,400	520	5,200	330	380	770	1,100
Bean, dry	N/A	0.00125	26,136,000	410	620	2,400	24,000	150	170	350	490
Beans, lima			19,008,00	640	960	370	3,700	230	270	550	760
Beans, navy	N/A	0.00125	83,635,200	130	190	74	740	47	53	110	150
Bean, snap			33,454,080	320	480	190	1,900	120	140	270	380
Beet, sugar	Film-coated	0.002	87,120,000	2,100	3,200	1,200	12,000	760	870	1,800	2,500
Canola	N/A	0.01	148,104,000	1,000	1,500	590	5,900	370	420	860	1,200
Carrot	Film-coated	0.0025		7,000	10,000	4,000	40,000	2,500	2,900	6,000	8,000
Carrot	Encrusted/Pelleted		167,270,400	7,000	10,000	4,000	40,000	2,500	2,900	6,000	8,000
Corn, field			8,050,000	1,100	10,000	660	6,600	410	480	940	1,400
Corn, pop	N/A	0.0025	6,000,000	1,500	1,700	880	8,800	550	640	1,300	3,000
Corn, sweet			4,779,120	2,500	2,300	1,500	15,000	940	1,100	2,100	3,000
Cotton	N/A	0.005	17,000,000	880	3,800	510	5,100	320	370	750	1,000
Crambe <sup>7</sup>	Film-coated Encrusted/Pelleted	0.01	46,080,000	7,900	12,000	4,600	46,000	2,900	3.300	6,700	9,500
Flax	N/A	0.01	243,936,000	420	630	240	2,400	150	370	750	1,000
Millet, Japanese			310,00,000	3,300	5,000	1,900	19,000	1,200	170	360	500
Millet, pearl	N/A	0.0025	136,000,000	4,200	6,300	2,400	24,000	1,500	1,400	2,800	4,000
Millet, proso			112,000,000	2,800	4,200	2,800	28,000	1,600	1,700	3,600	5,000
	Film-coated										
Mustard seed	Encrusted/Pelleted	0.01	101,360,000	3,000	4,500	1,700	17,000	1,100	1,200	2,600	3,600
	N/A	]									
Oat	N/A	0.00094	234,000,000	990	1,500	570	5,700	360	410	840	1,200
Pea, garden	N/A	0.00125	44,804,560	410	610	240	2,400	150	170	350	490
Peanut	N/A	0.000623	8,400,000	1,500	2,200	850	8,500	540	610	1,300	1,700
Rye	N/A	0.00094	324,000,000	990	1,500	570	5,700	360	410	840	1,200
Safflower	N/A	0.005	38,102,400	1,200	1,800	690	6,900	440	500	1,000	1,400
Sorghum, grain	N/A	0.0025	8,000,000	7,000	10,000	4,000	4,000	2,500	2,900	6,000	8,000
Soybean	N/A	0.00125	50,000,000	400	600	230	2,300	150	170	340	480
Sunflower	N/A	0.005	640,000	10,000	16,000	6,000	60,000	3,800	4,400	8,600	13,000

Table 5.1.4. Revised Occupational Handler Non-Cancer Exposure and Risk Estimates for Imidacloprid – Commercial Seed Treatment – All Formulations.											
Crop or Target	Specialized Treatment	App Rate (lb ai/lb seed)¹	Exposure Variable	Dern	Dermal <sup>3</sup> Inhalation <sup>3</sup> Total M			DE <sup>6</sup> (LOC = 100)			
			(AST, activity duration, or NSP) <sup>2</sup>	MOE4 (LOC = 100)		MOE <sup>5</sup> (LOC = 100)		Total MOE <sup>6</sup> (LOC = 100)			
				SL/G	DL/G	No-R	PF10 R	SL/G; No-R	DL/G; No-R	SL/G; PF10 R	DL/G; PF10 R
Triticale	N/A	0.00094	327,000,000	820	1,200	470	4,700	300	340	700	960
Wheat	N/A	0.00094	300,000,000	570	850	330	3,300	210	240	490	680

- 1. Maximum Application Rate: Based on registered labels (see Table 4.2).
- 2. Area Treated or Amount Handled: ExpoSAC Policy 15 and 2011 BEAD memo, "Acres Planted Per Day and Seeding Rates of Crops Grown in the United States" (J. Becker, March 2011). Exposure Variable:
- a. Treating = amount of seed treated (AST).
- b. Packaging = amount of seed treated (AST).
- c. Cleaning = activity duration (hours).
- d. Loading/Planting = number of seeds planted (NSP).
- 3. Unit Exposures from HED Exposure Science Advisory Council Policy 14: Standard Operating Procedures for Seed Treatment (<a href="https://www.epa.gov/system/files/documents/2022-01/exposac-policy-14\_seed-treatment-exposure-data.pdf">https://www.epa.gov/system/files/documents/2022-01/exposac-policy-14\_seed-treatment-exposure-data.pdf</a>). Level of PPE: SL/G = single layer, gloves; DL/G = double layer, gloves; No-R = no respirator; PF10 = respirator assumed to reduce inhalation exposure by 90%. Dose calculations, where DAF = 4.8% for dermal dose calculations and BW = 80 kg for dermal dose calculations and 80 kg for inhalation dose calculations.
- a. Treating and Packaging Dose (mg/kg/day) = Unit Exposure (μg/lb ai) × Conversion Factor (0.001 mg/μg) × Application Rate (lb ai/lb seed) × AST (lb seed/day) × DAF (4.8%, if necessary) ÷ BW (kg).
- b. Cleaning Dose (mg/kg/day) = Unit Exposure [(ug ai/hr)/(lb ai/lb seed)] × Conversion Factor (0.001 mg/μg) × Application Rate (lb ai/lb seed) × Activity Duration (hours/day) × AF (4.8%, if necessary) ÷ BW (80 kg).
- c. Loading/Planting Dose (mg/kg/day) = Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/seed) × NSP (seeds/day) × DAF (4.8%, if necessary) ÷ BW (80 kg).
- 4. Dermal MOE = Dermal POD (8 mg/kg/day) ÷ Dermal Dose (mg/kg/day). LOC = 100.
- 5. Inhalation MOE = Inhalation NOAEL (8 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). LOC = 100.
- 6. Combined MOE: Total MOE = POD (8 mg/kg/day) + Dermal Dose + Inhalation Dose OR Total MOE = 1 + (1/Dermal MOE + 1/Inhalation MOE).
- 7. Kale was used as a surrogate for crambe.

	App Rate (lb ai/lb	Amount of Seed Treated		Dermal <sup>3</sup>	Inhalation <sup>3</sup> MOE <sup>5</sup> (LOC = 100)		Total MOE <sup>6</sup> (LOC = 100)	
Crop or			Planted per Day (# of seeds	MOE <sup>4</sup> (LOC = 100)				
Target	seed)1	(lb seed/day) <sup>2</sup>	planted/day) <sup>2</sup>	SL/G	No-R	PF10 R	SL/G, No-R	SL/G, PF10
			Treating/Planting (OF	ST/P-L)				
Barley	0.00094	19,600	184,240,000	3,200	940	9,400	730	2,400
Canola	0.001	1,650	148,104,000	4,000	1,200	12,00 0	920	3,000
Corn, field	0.0025	5,910	8,050,000	3,100	910	9,100	700	2,300
Cotton	0.005	3,780	17,000,000	36,000	10,000	100,0 00	7,800	26,000
Millet, Japanese	0.0025	2,000	310,000,000	12,000	3,400	34,00 0	2,600	8,900
Millet, pearl	0.0025	1,600	136,000,000	15,000	4,300	43,00 0	3,300	11,000
Millet, proso	0.0025	2,400	112,000,000	9,800	2,900	29,00 0	2,200	7,300
Sorghum, grain	0.0025	960	8,000,000	25,000	7,200	72,00 0	5,600	19,000
Wheat	0.00094	31,400	300,000,000	2,000	580	5,800	450	1,500

<sup>1</sup> Application Rate provided in Table 4.1

- 4 Dermal MOE = Dermal NOAEL (8mg/kg/day) ÷ Dermal Dose (mg/kg/day). LOC = 100
- 5 Inhalation MOE = Inhalation NOAEL (8 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). LOC = 100
- 6 Combined MOE: Total MOE = POD (8 mg/kg/day) + Dermal Dose + Inhalation Dose OR Total MOE = 1 + (1/Dermal MOE + 1/Inhalation MOE).

<sup>2</sup> Area Treated or Amount Handled: ExpoSAC Policy 15 and 2011 BEAD memo, "Acres Planted Per Day and Seeding Rates of Crops Grown in the United States" (J. Becker, March 2011).

<sup>3</sup> Unit Exposures from HED Exposure Science Advisory Council Policy 14: Standard Operating Procedures for Seed Treatment (https://www.epa.gov/system/files/documents/2022-01/exposac-policy-14\_seed-treatment-exposure-data.pdf). Level of PPE: SL/G = single layer, gloves; DL/G = double layer, gloves; No-R = no respirator; PF10 = respirator assumed to reduce inhalation exposure by 90%. Dose calculations, where DAF = 4.8% for dermal dose calculations and BW = 80 kg for dermal dose calculations and 80 kg for inhalation dose calculations:

a. On-Farm Seed Treaters and Planters Dermal Dose = Dermal Unit Exposure (μg/lb ai) × Conversion Factor (0.001 mg/μg) × Application Rate (lb ai/lb seed) × Amount of Seed Treated (lb seed/day) × DAF (4.8%, if necessary) ÷ BW (80 kg).

## Appendix A. Summary of Occupational and Residential Non-cancer Algorithms

<u>Occupational Non-cancer Algorithms for Commercial Seed Treaters and Packagers</u>: Potential daily exposures for occupational seed treaters and packagers are calculated using the following formulas:

where:

E = exposure (mg ai/day), UE = unit exposure (μg ai/lb ai),

AR = maximum application rate according to proposed label (lb ai/lb seed)

AST = amount of seed treated (lb seed/day).

The daily doses are calculated using the following formula:

$$ADD = \frac{E * AF}{BW}$$

where:

ADD = average daily dose absorbed in a given scenario (mg ai/kg/day),

E = exposure (mg ai/day),

AF = absorption factor (dermal and/or inhalation), and

BW = body weight (kg).

Margin of Exposure: Non-cancer risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. The daily dermal and inhalation dose received by occupational handlers are compared to the appropriate POD (i.e., NOAEL) to assess the risk to occupational handlers for each exposure route. All MOE values are calculated using the following formula:

$$MOE = \frac{POD}{ADD}$$

where:

MOE = margin of exposure: value used by HED to represent risk estimates

(unitless),

POD = point of departure (mg/kg/day), and

ADD = average daily dose absorbed in a given scenario (mg ai/kg/day).

<u>Occupational Non-cancer Algorithms for Commercial Seed Treatment Cleaners</u>: Potential daily exposures for occupational seed treatment cleaners are calculated using the following formulas:

where:

E = exposure (mg ai/day),

UE = unit exposure  $[(\mu g \text{ ai/hr})/(\text{lb ai/lb seed})]$ ,

AR = maximum application rate according to proposed label (lb ai/lb seed)

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AD = activity duration (2.5 hr).

The daily doses are calculated using the following formula:

$$ADD = \frac{E * AF}{BW}$$

where:

ADD = average daily dose absorbed in a given scenario (mg ai/kg/day),

E = exposure (mg ai/day),

AF = absorption factor (dermal and/or inhalation), and

BW = body weight (kg).

Margin of Exposure: Non-cancer risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. The daily dermal and inhalation dose received by occupational handlers are compared to the appropriate POD (i.e., NOAEL) to assess the risk to occupational handlers for each exposure route. All MOE values are calculated using the following formula:

$$MOE = \frac{POD}{ADD}$$

where:

MOE = margin of exposure: value used by HED to represent risk estimates

(unitless),

POD = point of departure (mg/kg/day), and

ADD = average daily dose absorbed in a given scenario (mg ai/kg/day).

Occupational Non-cancer Algorithms for Loaders/Planters of Commercially Treated Seed and for Onfarm Seed Treatment/Planting: Potential daily exposures for occupational loaders/planters of commercially treated seed and for on-farm seed treatment/planting are calculated using the following formulas:

$$E=UE*AR*2.2x10^{-6}$$
 lb/mg\*ASP\*0.001 mg/ug

where:

E = exposure (mg ai/day),

UE = unit exposure (μg ai/lb ai),

AR = maximum application rate according to proposed label (mg ai/seed), and

ASP = amount of seed planted or, for on-farm, amount of seed treated and then planted (# seeds/day).

The daily doses are calculated using the following formula:

$$ADD = \frac{E * AF}{BW}$$

where:

ADD = average daily dose absorbed in a given scenario (mg ai/kg/day),

E = exposure (mg ai/day),

AF = absorption factor (dermal and/or inhalation), and

BW = body weight (kg).

Margin of Exposure: Non-cancer risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. The daily dermal and inhalation dose received by occupational handlers are compared to the appropriate POD (i.e., NOAEL) to assess the risk to occupational handlers for each exposure route. All MOE values are calculated using the following formula:

$$MOE = \frac{POD}{ADD}$$

where:

MOE = margin of exposure: value used by HED to represent risk estimates

(unitless),

POD = point of departure (mg/kg/day), and

ADD = average daily dose absorbed in a given scenario (mg ai/kg/day).