OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
WASHINGTON, D.C. 20460

MEMORANDUM

DATE: June 27, 2024

SUBJECT: **Clothianidin.** Addendum to the Human Health Draft Risk Assessment in Support of Registration Review with Updated Occupational and Residential Exposure Assessment for Seed Treatment Uses.

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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: EPA's Scientific Integrity Policy. The full text of the EPA Scientific Integrity Program's *Approaches for Expressing and Resolving Differing Scientific Opinions* can be found here: Approaches for Expressing and Resolving Differing Scientific Opinions | US EPA.

Introduction

The Pesticide Re-evaluation Division (PRD) of the Office of Pesticide Programs (OPP) has requested the Health Effects Division (HED) evaluate the hazard and exposure data and conduct an updated assessment to estimate the risk to human health that will result from the currently registered seed treatment uses of clothianidin. This memorandum serves as an addendum to HED's 2017 Registration Review human health draft risk assessment (DRA). This memorandum, which supports the ongoing clothianidin Registration Review, incorporates new and updated exposure data and policies for seed treatment scenarios (Science Advisory Council for Exposure (ExpoSAC) Policies 14 and 15, January 2022) as well as comments received on the DRA related to assumptions used for corn seed treatment.

A summary of the findings and addendum to the assessment of human risk resulting from the registered seed treatment uses of clothianidin are provided in this document. Except as noted herein, the elements and conclusions of the 2017 DRA remain unchanged (D. Drew *et al.*, D439294, 09/07/2017).

In most cases, additional personal protective equipment (PPE) can be used to address risk estimates of concern for seed treatment scenarios. The exceptions are 1) occupational handler risks for on-farm seed treatment of potato seed pieces with a dust formulation; and 2) occupational handlers cleaning commercial seed treatment equipment for all formulations and numerous seed types.

Note: This memorandum was reviewed by the Exposure Science Advisory Committee (ExpoSAC) on 07/27/2023.

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1.0 Executive Summary

HED has conducted an updated occupational exposure assessment for the registered conventional seed uses of the active ingredient (ai), clothianidin, in support of Registration Review to incorporate new exposure monitoring data and science policies related to evaluating seed treatment uses of pesticides as well as updates to the seed treatment assumptions for corn as a result of comments received on the preliminary interim decision (PID). Clothianidin is a broad spectrum, systemic neonicotinoid insecticide (Group 4A insecticide) and is identical to the major metabolite (CGA-322704) of the ai insecticide, thiamethoxam. Clothianidin is currently registered for use to control a variety of indoor and outdoor pests found on agricultural crops, turf, ornamentals, and in residential and commercial settings (e.g., food handling establishments, schools, homes, etc.). This memorandum, which supports the ongoing clothianidin Registration Review, incorporates new and updated exposure data and policies for seed treatment scenarios (ExpoSAC Policies 14 and 15, January 2022). Therefore, the updated seed treatment assessment included here supersedes those assessed in the DRA (D. Drew *et al.*, D439294, 09/07/2017).

Except as noted herein, the elements and conclusions of the 2017 DRA remain unchanged (D. Drew *et al.*, D439294, 09/07/2017). For a detailed summary of the use and exposure profiles, hazard characterization and dose response, non-occupational spray drift, non-occupational post-application inhalation assessment, aggregate risks, occupational handler (agricultural, non-seed treatment), and occupational post-application risk assessment, available in the clothianidin registration review docket under docket EPA-HQ-OPP-2011-0865-0243.

<u>Use Profile</u>
Clothianidin is currently formulated as liquids, aerosol sprays, water dispersible granules, water dispersible powders (seed treatment), granules, gels/pastes, and baits containing between 0.25% and 50% ai. Clothianidin is currently registered for use on a wide variety of food/feed crops, as well as seed treatment uses for a variety of crops. It is also registered for use in a variety of commercial and residential settings (e.g., food handling establishments, warehouses, schools, homes, auditoriums, institutions, schools, supermarkets, parks, lawns, landscaping, nurseries, greenhouses, etc).

Agricultural seed treatment uses include several liquid and one water dispersible powder (WDP) formulations. These end-use products (EPs) can be applied at rates ranging from 0.0005 to 0.78 lb ai/lb seed (liquid) and 0.0002 to 0.21 lb ai/lb seed (WDP). The personal protective equipment (PPE) statements on the registered agricultural seed treatment labels require handlers to wear baseline attire (long-sleeve shirt, long pants, shoes, and socks or coveralls over short-sleeve shirt and short pants) with chemical-resistant gloves. Specific respirators are required on at least one label (EPA Reg. No. 264-1081).

All agricultural seed treatment labels list a restricted-entry interval (REI) of at least 12 hours, in accordance with the Worker Protection Standard (WPS), with the exception of EPA Reg No. 59639-204 and EPA Reg No. 264-1081 which do not list a re-entry interval(REI).

A summary of the registered agricultural seed treatment uses is provided in Table 4.1.

Exposure Profile

Occupational and residential handler (dermal and inhalation) exposures and post-application (dermal, inhalation, and incidental oral) exposures are anticipated based on the registered uses of clothianidin. Non-occupational spray drift exposure is also expected. Occupational handler and post-application exposure is expected to be both short- (1 to 30 days) and intermediate-term (1 to 6 months). Residential handler and post-application exposure is expected to be short-term only. Non-occupational exposures from spray drift (dermal and/or incidental oral) are expected to be short-term only. Chronic exposure is not expected for the registered use patterns.

Hazard Characterization

Toxicological points of departure (PODs) and endpoints for incidental oral, dermal, and inhalation exposure were selected from an oral two-generation reproduction study in rats and are appropriate for all exposure durations. In the study, the no observed adverse effect level (NOAEL) of 9.8 mg/kg/day was based on decreased body weight gain, delayed sexual maturation, decreased absolute thymus weights in F_1 pups, and an increase in stillbirths in both F_1 and F_2 generations seen at the lowest observed adverse effect level (LOAEL) of 31.2 mg/kg/day. A dermal absorption factor (DAF) of 1% was used for the dermal exposure assessment. HED has received and reviewed an acceptable subchronic inhalation toxicity study; however, increased quantitative susceptibility was observed in the database. Therefore, an oral point of departure was selected since the inhalation toxicity study did not evaluate developmental or reproductive endpoints. The two-generation reproduction study in the rat was selected instead because it was an appropriate exposure duration and is protective of all effects seen following subchronic exposures, including developmental and offspring effects, and effects observed in the rat following subchronic inhalation exposure.

Uncertainty Factors (UFs)/Levels of Concern (LOCs) for Risk Assessment: A level of concern (LOC) of 100 based on the 10X interspecies and 10X intraspecies uncertainty factors is used for all routes of exposure. The Food Quality Protection Act Safety Factor (FQPA SF) was reduced to 1X for dermal and inhalation pathways (D. Drew *et al.*, D439294, 09/07/2017).

Cancer Classification: Clothianidin is classified as "not likely to be carcinogenic in humans" based on the results from carcinogenicity studies in rats and mice.

Occupational Exposure and Risk Estimates

Many of the short- and intermediate-term occupational handler inhalation and dermal risk estimates are not of concern (i.e., Margins of Exposure (MOEs) ≥ the LOC of 100) with label-required attire and PPE (baseline attire, gloves, and no respirator). However, several seed treatment scenarios remain a risk of concern even when additional PPE (PF10 respirator) is added. Below are the commercial seed treatment uses that are below the LOC.

- Commercial Seed Treatment (CST) – Cleaning Equipment (MOE for Crop)
    - Beet, Sugar (25)
    - Broccoli (3)
    - Carrot (21)
    - Corn, pop (92)
    - Endive (26)

- Leek (19)
- Lettuce, head (2)
- Lettuce, leaf (2)
- Onion, bulb, dry (16)
- Onion, green (16)
- Parsley (37)

- On Farm Seed Treatment Planting with Solids (OFST/P-S) – Dust (MOE for Crop)
  - Potato (67)

Human Studies Review

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 agricultural handler exposure task force (AHETF) database and the ExpoSAC Policy 14 and 15 (standard operating procedures (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[1].

2.0 Risk Assessment Conclusions and Recommendations

2.1 Summary of Risk Estimates

Occupational Handler – Seed Treatments: Many of the occupational handler scenarios are not of concern (i.e., MOEs > the LOC) when assuming baseline attire and label-specified PPE (i.e., gloves and no respirator) is worn. However, several scenarios remain of concern when maximum PPE (i.e., double layer of clothing with gloves (DL/G) and PF10 respirators (PF10 R)) is considered.

- For commercial seed treatments, short- and intermediate-term combined (dermal and inhalation) MOEs range from 1.0 to 1,400,000 (LOC = 100). Several scenarios which result in risks of concern (MOEs < LOC of 100) with additional PPE (i.e., DL/G + PF10 R).
  - Risks for treating of corn, pop as well as packing of corn, pop and corn, field are of concern at label PPE and not of concern with the addition of a PF10 respirator and SL/G. (Table 5.1.1).
  - There are crops for which the cleaning scenarios are of concern. These risks cannot be mitigated with additional PPE (Table 5.1.2).
- For on-farm seed treatments, short- and intermediate-term combined (dermal and inhalation) MOEs range from 12 to 1,800,000 (LOC = 100) considering a single layer of clothing with gloves (SL/G) with No Respirator, based on label PPE for liquid formulations; and 60 to 6,700,000 (SL/G + PF10 based on label PPE for solid formulation). The treating/planting of potato seed pieces dust scenario results in risks of concern (MOEs < LOC of 100) with additional PPE (i.e., DL/G + PF10 R) (Table 5.1.3).

[1] Available online: Occupational Pesticide Handler Exposure Data | US EPA and Occupational Pesticide Post-application Exposure Data | US EPA

2.2 Label Recommendations

None.

2.3 Data Deficiencies and Requirements

HED recommends that the seed treatment equipment and any additional seed treatment processes (i.e., pelleting, encrusting, film coating, etc.) be specified on the end-use product labels.

3.0 Hazard Characterization

The toxicological database for clothianidin is complete. The available toxicological data indicate that there are no consistent specific target organs in mammals. The majority of studies show decreases in body weights and body weight gains. Decreased body weight gain and decreased food consumption were observed in subchronic and chronic feeding studies in multiple species. In subchronic studies, dogs were more sensitive than rats to decreased body weight gain and also displayed decreased white blood cells, albumin and total protein, as well as some anemia. In chronic studies, rats were more sensitive to decreased body weight gain than dogs and mice. Additional effects in the rat include interstitial gland hyperplasia in the ovary; increased lymphohistiocytic infiltrate and altered hepatocellular eosinophilic foci of the liver; slightly increased incidences of pelvic mineralization, and transitional cell hyperplasia in the kidney; and mottled livers.

Acute Toxicity

Clothianidin has low to moderate oral toxicity (Toxicity Category II), dermal, and inhalation toxicity (Toxicity Categories III to IV) in acute lethality (LD_{50}) studies. It is not a dermal or eye irritant (Toxicity Category IV) and is not a dermal sensitizer.

Table 3.1. Acute Toxicity Profile - Clothianidin Technical.

Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute Oral (mouse)	45422622	LD_{50} = 425 mg/kg (M & F)	II
	Acute Oral (rat)	45422621	LD_{50} > 5000 mg/kg (M & F)	IV
870.1200	Acute Dermal (rat)	45422634	LD_{50} > 2000 mg/kg (M & F)	III
870.1300	Acute Inhalation (rat)	45422636	LC_{50} > 6.14 mg/L (M & F)	IV
870.2400	Primary Eye Irritation (rabbit)	45422701	Slightly irritating to the eye	IV
870.2500	Primary Skin Irritation (rabbit)	45422703	Not irritating to the skin	IV
870.2600	Dermal Sensitization (guinea pig)	45422705	Not a dermal sensitizer (Maximization)	N/A

Toxicological PODs Used for Risk Assessment

Toxicological PODs and endpoints for dermal and inhalation exposure were selected from an oral two-generation reproduction study in rats and is appropriate for all exposure durations. In the study, the NOAEL of 9.8 mg/kg/day was based on decreased body weight gain, delayed sexual maturation, decreased absolute thymus weights in F_1 pups, and an increase in stillbirths in both F_1 and F_2 generations seen at the LOAEL of 31.2 mg/kg/day. Although a dermal toxicity study is available for clothianidin, the oral reproduction study was used to protect for offspring effects observed in both the developmental neurotoxicity (DNT) and the two-generation reproduction studies that were not evaluated in the dermal toxicity study. Additionally, HED has received and reviewed an acceptable

subchronic inhalation toxicity study; however, increased quantitative susceptibility was observed in the database. As a result, an oral POD was selected since the inhalation toxicity study did not evaluate developmental or reproductive endpoints. The two-generation reproduction study in the rat was selected instead because it was an appropriate exposure duration and is protective of all effects seen following subchronic exposures, including developmental and offspring effects, and effects observed in the rat following subchronic inhalation exposure.

An uncertainty factor of 100X was used in the occupational risk assessments for all routes of exposure, based on a 10X for inter-species extrapolations and a 10X for intra-species variations. The FQPA SF was reduced to 1X.

Table 3.2. Summary of Toxicological Endpoints and Doses for Clothianidin Occupational Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	Level of Concern (LOC) for Risk Assessment	Study and Toxicological Effects
Dermal (short- and intermediate-term)	Oral study NOAEL= 9.8 mg/kg/day DAF = 1%	UF_A = 10X UF_H = 10X FQPA SF = 1X	LOC for MOE = 100	**Rat two-generation reproduction study** LOAEL = 31.2 mg/kg/day based on decreased body weight gains and delayed sexual maturation, decreased absolute thymus weights in F1 pups and increased stillbirths in both generations.
Inhalation (short- and intermediate-term)	Oral study NOAEL= 9.8 mg/kg/day (Inhalation toxicity equivalent to oral toxicity.)	UF_A = 10x UF_H = 10x FQPA SF = 1X	LOC for MOE = 100	**Rat two-generation reproduction study** LOAEL = 31.2 mg/kg/day based on decreased body weight gains and delayed sexual maturation, decreased absolute thymus weights in F1 pups and increased stillbirths in both generations.
Cancer (oral, dermal, inhalation)	"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_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. DAF = dermal absorption factor. MOE = margin of exposure. LOC = level of concern.

Cancer Classification: Clothianidin is classified as "not likely to be carcinogenic in humans" based on the results from carcinogenicity studies in rats and mice.

Absorption: A DAF of 1% was used for exposure assessment and is based on a dermal absorption study with monkeys (K. Schumacher, *et al*, D331226, 11/28/2006). 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: Since the dermal and inhalation PODs are based on developmental and/or fetal effects, the body weight appropriate for dermal and inhalation assessments is 69 kg for adults.

4.0 Use Profile

Clothianidin is currently formulated as liquids, aerosol sprays, water dispersible granules, water dispersible powders (seed treatment), granules, gels/pastes, and baits containing between 0.25% and 50% ai. Clothianidin is currently registered for use on a wide variety of food/feed crops, as well as many different seed treatment uses. It is also registered for use in a variety of commercial and residential settings (e.g., food handling establishments, warehouses, schools, homes, auditoriums, institutions, schools, supermarkets, parks, lawns, landscaping, nurseries, greenhouses, etc.). Agricultural, seed treatment uses include several liquid and one WDP formulations. These (EPs can be applied at rates ranging from 0.0005 to 0.78 lb ai/lb seed (liquid) and 0.0002 to 0.21 lb ai/lb seed (WDP).

A summary of the registered occupational seed treatment uses is listed in Table 4.1.

The PPE statement on the registered agricultural seed treatment labels requires handlers to wear baseline attire (long-sleeve shirt, long pants, shoes, and socks or coveralls over short-sleeve shirt and short pants) with chemical-resistant gloves. Specific respirators are required on at least one label (EPA Reg. No. 264-1081).

All agricultural, seed treatment labels list an REI of at least 12 hours, in accordance with the worker protection standard (WPS), with the exception of EPA Reg No. 59639-204 and EPA Reg No. 264-1081 which do not list an REI.

In the process of Registration Review, HED has agreed to break out the rates for corn into individual rates lb ai/lb seed for corn, field (0.0055), corn, pop (0.0131), and corn, sweet (0.0050). These rates are reflected in the exposure assessment below.

Table 4.1 Summary of Directions for Occupational Seed Treatment Uses of Clothianidin.

Crop	Application Equipment	Formulation [EPA Reg. No.][1]	App Rate (lb ai/lb seed)	PPE
Broccoli	Commercial seed treatment equipment	Liquid [264-789] (5 lb ai/gallon)	0.39 lb ai/lb seed* 1.1925 g ai/1000 seed	Chemical-resistant gloves
Canola/ Rapeseed			0.0046 lb ai/lb seed* 0.018 mg ai/seed	
Cereal grains (except corn, rice, sorghum, and wild rice)	Commercial and On-farm		0.0009 lb ai/lb seed* 0.02318 mg ai/seed	
Corn[1]	Commercial seed treatment equipment	Liquid [59639-197]	0.014 lb ai/lb seed* 1.25 mg ai/seed	Chemical-resistant gloves
Cotton	Commercial seed treatment equipment	Liquid [264-789] (5 lb ai/gallon)	0.0035 lb ai/lb seed* 0.353 mg ai/seed	Chemical-resistant gloves
Carrot			0.059 lb ai/lb seed 0.0675 g ai/1,000 seeds	

Table 4.1 Summary of Directions for Occupational Seed Treatment Uses of Clothianidin.				
Crop	**Application Equipment**	**Formulation [EPA Reg. No.][1]**	**App Rate (lb ai/lb seed)**	**PPE**
Leafy Greens[2]			0.78 lb ai/lb seed* 0.75 mg ai/seed	
Leek			0.0.064 lb ai/lb seed**	
Mustard	Commercial seed treatment equipment	Liquid [264-1034] (2.38 lb ai/gallon)	0.004 lb ai/lb seed	Chemical-resistant gloves
Onion	Commercial seed treatment equipment	Liquid [264-789] (5 lb ai/gallon)	0.075 lb ai/lb seed* 0.18 g ai/1000 seeds	
Rice			0.00075 lb ai/lb seed	
Sorghum			0.0025 lb ai/lb seed 0.06 mg ai/seed	
Soybean	Commercial seed treatment equipment	Liquid [59639-204] (2.08 lb ai/gallon)	0.0005 lb ai/lb seed 0.081 mg ai/seed	Chemical-resistant gloves
Sugar beet	Commercial seed treatment equipment	Liquid [264-789] (5 lb ai/gallon)	0.05 lb ai/lb seed 0.603 mg ai/seed	Chemical-resistant gloves
Tuberous and Corm	Commercial and On-farm	Liquid [59639-150]	0.001 lb ai/lb seed	Chemical-resistant gloves
Broccoli	Commercial seed treatment equipment	Water dispersible powder [264-1081] (56.25% ai)	0.21 lb ai/lb seed 1.1925 g ai/1000 seeds	Chemical-resistant gloves and TC-21C respirator
Carrot			0.06 lb ai/lb seed 0.0675 g ai/1000 seeds	
Leek			0.064 lb ai/lb seed 0.2 g ai/1000 seeds	
Onion			0.076 lb ai/lb seed 0.18 g ai/1000 seeds	
Cereal grains (except Rice)	Commercial and On-farm		0.00125 lb ai/lb seed	
Potato	On-farm; Seed Dust Metering Applicator		0.0002 lb ai/lb seed	

*Calculated using BEAD data from "Acres Planted per Day and Seeding Rates of Crops Grown in the United States" (Becker, J. and Ratnayake, S., 2011).

**Calculated using #seeds/lb data in 2017 Revised [DRAFT] ExpoSAC Policy 15.1.

1. In the process of Registration Review, HED has agreed to break out the rates for corn into individual rates lb ai/lb seed for corn, field (0.0055), corn, pop (0.0131), and corn, sweet (0.0050). These rates are reflected in the exposure assessment below.
2. HED does not have specific seed treatment related information for each crop in the leafy green category However, HED does have specific seed treatment related information for lettuce (head and leaf), spinach, endive, and parsley and considers these scenarios to be representative and protective of all other leafy green scenarios where the lb ai/lb seed rate is the same.

5.0 Updated Occupational Exposure and Risk Estimates – Seed Treatments

5.1 Updated Occupational Handler Exposure/Risk Estimates – Seed Treatments

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. Except as noted below, the elements and conclusions of the 2017 DRA assessment remain unchanged (D. Drew *et al.*, D439294, 09/07/2017).

Since the DRA, the seed treatment policies and unit exposures have been updated. Therefore, the seed treatment risk estimates included in this memorandum supersede risk estimates for seed treatment discussed in the DRA. 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 seed treater equipment, treating/coating the seed and sampling “wet” treated seed, which are very critical to the CST process but 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, as described above. If open loading systems are used for commercial seed treatment, HED anticipates that the risk estimates will be higher than what is presented here.

CST - Packaging: The CST-Packaging scenario represents exposure while workers are 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 active ingredient'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 comes 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 active ingredient handled.

On-Farm Seed Treatment and Planting with Solids (OFST/P-S): The OFST/P-S scenario involves workers that operate any on-farm seed treating equipment, including mixing, loading and application of solid pesticides to untreated seed, and any associated tasks such as maintaining the treating equipment and then planting the treated seed. The OFST/P-S scenario is representative of hopper box (or similar "at-plant" equipment) as well as commercial-style equipment used on-farm. The workers often perform tasks other than treating and planting during the monitoring period, including quickly cleaning the auger (mixing) system or planter after treatment was finished, shoveling treated seed into the auger or directly into a planter, fixing auger problems, spreading untreated seed in seed hopper, 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 active ingredient handled.

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 presented here.

The quantitative exposure/risk assessment developed for occupational handlers is based on the scenarios presented in Tables 5.1.4 and 5.1.5.

Occupational Handler Exposure Data and Assumptions

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: A screening-level approach was used for the assessment of occupational exposures by evaluation of the maximum registered application rate per crop for all possible occupational handler seed treatment exposure scenarios of clothianidin. The quantitative exposure/risk assessment developed for occupational handlers treating seed is based on the maximum registered application rate per crop as listed in Table 4.1.

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, 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: Standard Operating Procedures for Seed Treatment[2], which, along with additional information on seed treatment exposure assessment, can be found at the Agency website[3].

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 clothianidin, 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

[2] Available online: US EPA - Standard Operating Procedures for Seed Treatment

[3] Available online: Occupational Pesticide Exposure - Seed Treatment | US EPA

risk assessment are protective of any intermediate-term exposures.

Personal Protective Equipment: 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 considered and assessed include: (1) baseline, defined as a single layer of clothing consisting of a long-sleeved shirt, long pants, shoes plus socks, no protective gloves, (2) baseline with gloves, (3) double layer clothing (i.e., single layer plus coveralls) with gloves, (4) no respirator, and (5) PF10 respirator. The clothianidin product labels for seed treatments direct mixers, loaders, applicators, and other handlers to wear baseline attire with PPE consisting of chemical-resistant gloves. For one product label (EPA Reg. No. 264-1081), a respirator is also required.

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.

Occupational Handler Non-Cancer Exposure and Risk Estimate Equations

The algorithms used to estimate non-cancer exposure and dose for occupational handlers can be found in Appendix A.

Combining Exposures/Risk Estimates

Occupational handler dermal and inhalation exposure is anticipated from the registered clothianidin use. 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) ÷ Combined dermal + inhalation dose (mg/kg/day)

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates

Many of the occupational handler scenarios are not of concern (i.e., MOEs ≥ the LOC) when assuming baseline clothing (e.g., single layer of clothing, and no respirator) and gloves (label-required PPE) are worn.

In commercial seed treatment facilities, seed is professionally treated and packaged in small bags, mini-bulk containers (e.g., bins or large bags), or loose bulk containers (e.g., seed wagons or trucks), and then delivered later to growers. Downstream facilities process much of their seed as loose bulk, where treated seed is conveyed into a grower's truck or wagon directly from the treater. This is distinctly different from on-farm seed treating where seed is treated more locally (e.g., at a specific farm), and planted without bagging.

All on-farm seed treatment systems have a method to transfer and treat clean untreated seed from bulk storage to a seed wagon or truck, or from a truck or wagon to the planter. On-farm seed treatment generally involves workers that operate any on-farm seed treating equipment, including mixing, loading and application of a pesticide to untreated seed, and any associated tasks such as maintaining the treating equipment and planting the treated seed. This scenario applies to any seed type labeled for on-farm seed treatment. Treating equipment for this scenario includes both open and closed systems. On-farm seed treating equipment typically involves some type of mechanical conveying or augering system that accommodates treatment as the seed is moved into equipment such as a seed truck (such as for transport to the field), onto a conveyor (such as for transport into temporary storage), or directly into a planter. All on-farm seed treaters are continuous flow treaters, meaning the seed treatment process continues until the seed supply is depleted. On-farm systems are manual in design and require an operator to stop and start the seed treating process.

Thus, commercial seed treatments and on-farm seed treatments are assessed separately.

For commercial seed treatments, short- and intermediate-term combined (dermal and inhalation) MOEs range from 1.0 to 1,400,000 (LOC = 100). Several scenarios result in risks of concern (MOEs < LOC of 100) with additional PPE (i.e., DL/G + PF10 R). See Tables 5.1.1, 5.1.2, and 5.1.3 below.

Table 5.1.1 Summary of Combined (Dermal and Inhalation) Scenarios at Label PPE (SL/G) that can be Mitigated with Additional PPE (i.e., PF10 R).

CST-Treating (MOE for crop(s))	CST-Packaging (MOE for crop(s))

• Corn, pop (SL/G No R (91))
  ○ Corn, pop (SL/G + PF10 R (240))
	• Corn, pop (SL/G No R (40))
	  ○ Corn, pop (SL/G + PF10 R (290))
	• Corn, field (SL/G No R (84))
	  ○ Corn, field (SL/G + PF10 R (680))

Table 5.1.2. Summary of Combined (Dermal and Inhalation) Scenarios that Remain Risks of Concern with Additional PPE (i.e., DL/G + PF10 R).

CST-Cleaning Equipment (MOE for crop(s))		
• Beet, Sugar (25)	• Endive (26)	• Onion, bulb, dry (16)
• Broccoli (3)	• Leek (19)	• Onion, green (16)
• Carrot (21)	• Lettuce, head (2)	• Parsley (37)
• Corn, pop (92)	• Lettuce, leaf (2)	

For on-farm seed treatments, short- and intermediate-term combined (dermal and inhalation) MOEs range from 12 to 1,800,000 (LOC = 100) (SL/G + No R – label PPE for liquid formulations) and 60 to 6,700,000 (SL/G + PF10 – label PPE for solid formulation). The treating/planting of potato seed pieces dust scenario results in risks of concern (MOEs < LOC of 100) with additional PPE (i.e., DL/G + PF10 R).

Table 5.1.3. Summary of Combined (Dermal and Inhalation) Scenarios that Remain Risks of Concern with Additional PPE (i.e., DL/G + PF10 R).

OFST/P-S (Dust) (MOE for crop)
Potato (67)

Table 5.1.4. Updated Occupational Handler Non-Cancer Exposure and Risk Estimates for Clothianidin – Commercial Seed Treatments.

Crop or Target	Specialized Treatment/ Formulation	App Rate (lb ai/lb seed)[2]	Amount Seed Treated (lb seed/day*)/ Planted per Day (seeds planted/day§)/ Activity Duration (activity hours/day╧)[3]	Dermal[4] MOE[5] (LOC = 100)		Inhalation[6] MOE[7] (LOC = 100)		Combined[8] MOE[10] (LOC =100)			
				SL/G	DL/G	No-R	PF10	SL/G + No-R	DL/G + No-R	SL/G + PF10 R	DL/G + PF10 R
Treating (CST-T)[1]											
Barley	N/A	0.00125	360,000*	2,900	3,600	1,300	13,000	**900**	960	2400	2,800
Beet, sugar	Film-coated	0.05	3,000*	8,800	11,000	3,800	38,000	2,700	2,800	**7,100**	8,500
Broccoli	Film-coated	0.39	3,000*	1,100	1,400	480	4,800	330	360	**890**	1,100
Broccoli	Encrusted/Pelleted	0.39	225*	15,000	18,000	6,400	64,000	4,500	4,700	**12,000**	14,000
Canola	N/A	0.0046	125,000*	2,300	2,800	980	9,800	**690**	730	1,900	2,200
Carrot	Film-coated	0.059	3,000*	7,500	9,100	3,200	32,000	2,200	2,400	**6,100**	7,100
Carrot	Encrusted/Pelleted	0.059	225*	99,000	120,000	43,000	430,000	30,000	32,000	**80,000**	94,000
Celery	Film-coated	0.00125	3,000*	350,000	430,000	150,000	1,500,000	110,000	110,000	**280,000**	330,000
Celery	Encrusted/Pelleted	0.00125	225*	4,700,000	5,700,000	2,000,000	20,000,000	1,400,000	1,500,000	**3,800,000**	4,400,000
Corn, field	N/A	0.0055	339,500*	710	860	300	3,000	**210**	220	570	670
Corn, pop	N/A	0.0131	339,500*	300	360	130	1,300	**91**	96	240	280
Corn, sweet	N/A	0.005	339,500*	780	940	330	3,300	**230**	240	630	730
Cotton	N/A	0.0035	125,000*	3,000	3,700	1,300	13,000	**910**	960	2,400	2,900
Endive	Film-coated	0.047	3,000*	9,300	11,000	4,000	40,000	2,800	2,900	**7,500**	8,600
Endive	Encrusted/Pelleted	0.047	225*	130,000	150,000	53,000	530,000	38,000	39,000	**100,000**	120,000
Leek	Film-coated	0.064	3,000*	6,900	8,400	2,900	29,000	2,000	2,200	**5,600**	6,500
Leek	Encrusted/Pelleted	0.064	225*	92,000	110,000	39,000	390,000	27,000	29,000	**74,000**	86,000
Lettuce, head	Film-coated	0.78	3,000*	560	690	240	2,400	170	180	**450**	540
Lettuce, head	Encrusted/Pelleted	0.78	225*	7,500	9,200	3,200	32,000	2,200	2,400	**6,100**	7,100
Lettuce, leaf	Film-coated	0.78	3,000*	560	690	240	2,400	170	180	**450**	540
Lettuce, leaf	Encrusted/Pelleted	0.78	225*	7,500	9,200	3,200	32,000	2,200	2,400	**6,100**	7,100
Millet, pearl	N/A	0.00125	360,000*	2,900	3,600	1,300	13,000	**900**	960	2,400	2,800
Millet, proso	N/A	0.00125	360,000*	2,900	3,600	1,300	13,000	**900**	960	2,400	2,800

Table 5.1.4. Updated Occupational Handler Non-Cancer Exposure and Risk Estimates for Clothianidin – Commercial Seed Treatments.

Crop or Target	Specialized Treatment/ Formulation	App Rate (lb ai/lb seed)[2]	Amount Seed Treated (lb seed/day*)/ Planted per Day (seeds planted/day§)/ Activity Duration (activity hours/day⊥)[3]	Dermal[4] MOE[5] (LOC = 100)		Inhalation[6] MOE[7] (LOC = 100)		Combined[8] MOE[10] (LOC =100)			
				SL/G	DL/G	No-R	PF10	SL/G + No-R	DL/G + No-R	SL/G + PF10 R	DL/G + PF10 R
Mustard seed	Film-coated	0.004	3,000*	110,000	130,000	47,000	470,000	33,000	35,000	**89,000**	100,000
Mustard seed	Encrusted/Pelleted	0.004	225*	1,500,000	1,800,000	620,000	6,200,000	440,000	460,000	**1,200,000**	1,400,000
Mustard seed	N/A	0.004	125,000*	2,600	3,200	1,100	11,000	**770**	820	2,100	2,500
Oat	N/A	0.00125	360,000*	2,900	3,600	1,300	13,000	**900**	960	2,400	2,800
Onion, dry, bulb	Film-coated	0.075	3,000*	5,900	7,100	2,500	25,000	1,800	1,800	**4,800**	5,500
Onion, dry, bulb	Encrusted/Pelleted	0.075	225*	78,000	95,000	33,000	330,000	23,000	24,000	**63,000**	74,000
Onion, green	Film-coated	0.075	3,000*	5,900	7,100	2,500	25,000	1,800	1,800	**4,800**	5,500
Onion, green	Encrusted/Pelleted	0.075	225*	78,000	95,000	33,000	330,000	23,000	24,000	**63,000**	74,000
Parsley	Film-coated	0.0325	3,000*	14,000	16,000	5,800	58,000	4,100	4,300	**11,000**	13,000
Parsley	Encrusted/Pelleted	0.0325	225*	180,000	220,000	77,000	770,000	54,000	57,000	**150,000**	170,000
Potato	N/A	0.0002	800,000*	8,200	10,000	3,500	35,000	**2,500**	2,600	6,600	7,800
Rice	N/A	0.00075	302,500*	5,800	7,100	2,500	25,000	**1,700**	1,800	4,700	5,500
Rye	N/A	0.00125	360,000*	2,900	3,600	1,300	13,000	**900**	960	2,400	2,800
Sorghum, grain	N/A	0.0025	360,000*	1,500	1,800	620	6,200	**440**	460	1,200	1,400
Soybean	N/A	0.0005	281,250*	9,400	11,000	4,000	40,000	**2,800**	2,900	7,600	8,600
Spinach	Film-coated	0.005	3,000*	88,000	110,000	38,000	380,000	27,000	28,000	**71,000**	85,000
Spinach	Encrusted/Pelleted	0.005	225*	1,200,000	1,400,000	500,000	5,000,000	350,000	370,000	**970,000**	1,100,000
Triticale	N/A	0.00125	360,000*	2,900	3,600	1,300	13,000	**900**	960	2,400	2,800
Wheat	N/A	0.00125	360,000*	2,900	3,600	1,300	13,000	**900**	960	2,400	2,800
Packaging (CST-P)[1]											
Barley	N/A	0.00125	360,000*	8,900	11,000	420	4,200	**400**	400	2,900	3,000
Beet, sugar	Film-coated	0.05	3,000*	27,000	34,000	1,300	13,000	1,200	1,300	**8,800**	9,400
Broccoli	Film-coated	0.39	3,000*	3,400	4,400	160	1,600	150	150	**1,100**	1,200
Broccoli	Encrusted/Pelleted	0.39	225*	46,000	59,000	2,100	21,000	2,000	2,000	**14,000**	15,000

Table 5.1.4. Updated Occupational Handler Non-Cancer Exposure and Risk Estimates for Clothianidin – Commercial Seed Treatments.

Crop or Target	Specialized Treatment/ Formulation	App Rate (lb ai/lb seed)[2]	Amount Seed Treated (lb seed/day*)/ Planted per Day (seeds planted/day§)/ Activity Duration (activity hours/day╧)[3]	Dermal[4] MOE[5] (LOC = 100)		Inhalation[6] MOE[7] (LOC = 100)		Combined[8] MOE[10] (LOC =100)			
				SL/G	DL/G	No-R	PF10	SL/G + No-R	DL/G + No-R	SL/G + PF10 R	DL/G + PF10 R
Canola	N/A	0.0046	125,000*	7,000	9,000	330	3,300	**320**	320	2,200	2,400
Carrot	Film-coated	0.059	3,000*	23,000	29,000	1,100	11,000	1,000	1,100	**7,400**	8,000
Carrot	Encrusted/Pelleted	0.059	225*	300,000	390,000	14,000	140,000	13,000	14,000	**95,000**	100,000
Celery	Film-coated	0.00125	3,000*	1,100,000	1,400,000	50,000	500,000	48,000	48,000	**340,000**	370,000
Celery	Encrusted/Pelleted	0.00125	225*	14,000,000	18,000,000	670,000	6,700,000	640,000	650,000	**4,500,000**	4,900,000
Corn, field	N/A	0.0055	339,500*	2,100	2,800	100	1,000	**95**	97	680	740
Corn, pop	N/A	0.0131	339,500*	900	1,200	42	420	**40**	41	290	310
Corn, sweet	N/A	0.005	339,500*	2,400	3,000	110	1,100	**110**	110	750	800
Cotton	N/A	0.0035	125,000*	9,200	12,000	430	4,300	**410**	420	2,900	3,200
Endive	Film-coated	0.047	3,000*	28,000	37,000	1,300	13,000	1,200	1,300	**8,900**	9,600
Endive	Encrusted/Pelleted	0.047	225*	380,000	490,000	18,000	180,000	17,000	17,000	**120,000**	130,000
Leek	Film-coated	0.064	3,000*	21,000	27,000	980	9,800	940	950	**6,700**	7,200
Leek	Encrusted/Pelleted	0.064	225*	280,000	360,000	13,000	130,000	12,000	13,000	**89,000**	96,000
Lettuce, head	Film-coated	0.78	3,000*	1,700	2,200	80	800	76	77	**540**	590
Lettuce, head	Encrusted/Pelleted	0.78	225*	23,000	29,000	1,100	11,000	1,000	1,100	**7,400**	8,000
Lettuce, leaf	Film-coated	0.78	3,000*	1,700	2,200	80	800	76	77	**540**	590
Lettuce, leaf	Encrusted/Pelleted	0.78	225*	23,000	29,000	1,100	11,000	**1,000**	1,100	7,400	8,000
Millet, pearl	N/A	0.00125	360,000*	8,900	11,000	420	4,200	**400**	400	2,900	3,000
Millet, proso	N/A	0.00125	360,000*	8,900	11,000	420	4,200	**400**	400	2,900	3,000
Mustard seed	Film-coated	0.004	3,000*	330,000	430,000	16,000	160,000	15,000	15,000	**110,000**	120,000
Mustard seed	Encrusted/Pelleted	0.004	225*	4,500,000	5,700,000	210,000	2,100,000	200,000	200,000	**1,400,000**	1,500,000
Mustard seed	N/A	0.004	125,000*	8,000	10,000	380	3,800	**360**	370	2,600	2,800
Oat	N/A	0.00125	360,000*	8,900	11,000	420	4,200	**400**	400	2,900	3,000
Onion, dry, bulb	Film-coated	0.075	3,000*	18,000	23,000	840	8,400	800	810	**5,700**	6,200

Table 5.1.4. Updated Occupational Handler Non-Cancer Exposure and Risk Estimates for Clothianidin – Commercial Seed Treatments.

Crop or Target	Specialized Treatment/ Formulation	App Rate (lb ai/lb seed)[2]	Amount Seed Treated (lb seed/day*)/ Planted per Day (seeds planted/day§)/ Activity Duration (activity hours/day↓)[3]	Dermal[4] MOE[5] (LOC = 100)		Inhalation[6] MOE[7] (LOC = 100)		Combined[8] MOE[10] (LOC =100)			
				SL/G	DL/G	No-R	PF10	SL/G + No-R	DL/G + No-R	SL/G + PF10 R	DL/G + PF10 R
Onion, dry, bulb	Encrusted/Pelleted	0.075	225*	240,000	310,000	11,000	110,000	11,000	11,000	**75,000**	81,000
Onion, green	Film-coated	0.075	3,000*	18,000	23,000	840	8,400	800	810	**5,700**	6,200
Onion, green	Encrusted/Pelleted	0.075	225*	240,000	310,000	11,000	110,000	11,000	11,000	**75,000**	81,000
Parsley	Film-coated	0.0325	3,000*	41,000	53,000	1,900	19,000	1,800	1,800	**13,000**	14,000
Parsley	Encrusted/Pelleted	0.0325	225*	540,000	710,000	26,000	260,000	25,000	25,000	**180,000**	190,000
Potato	N/A	0.0002	800,000*	25,000	32,000	1,200	12,000	**1,100**	1,200	8,100	8,700
Rice	N/A	0.00075	302,500*	18,000	23,000	830	8,300	**790**	800	5,700	6,100
Rye	N/A	0.00125	360,000*	8,900	11,000	420	4,200	**400**	400	2,900	3,000
Sorghum, grain	N/A	0.0025	360,000*	4,500	5,700	210	2,100	**200**	200	1,400	1,500
Soybean	N/A	0.0005	281,250*	28,000	37,000	1,300	13,000	**1,200**	1,300	8,900	9,600
Spinach	Film-coated	0.005	3,000*	270,000	340,000	13,000	130,000	**12,000**	13,000	88,000	94,000
Spinach	Encrusted/Pelleted	0.005	225*	3,600,000	4,600,000	170,000	1,700,000	160,000	160,000	**1,200,000**	1,200,000
Triticale	N/A	0.00125	360,000*	8,900	11,000	420	4,200	**400**	400	2,900	3,000
Wheat	N/A	0.00125	360,000*	8,900	11,000	420	4,200	**400**	400	2,900	3,000
Barley	N/A	0.00125	360,000*	8,900	11,000	420	4,200	**400**	400	2,900	3,000
Cleaning (CST-CI)[1]											
Barley	N/A	0.00125	2.5↓	930	1,000	2,000	20,000	**630**	670	890	950
Beet, sugar	Film-coated	0.05		23	26	51	510	16	17	**22**	25
Broccoli	Film-coated	0.39		3.0	3.3	6.6	66	2.1	2.2	**2.9**	3.1
Broccoli	Encrusted/Pelleted	0.39		3.0	3.3	6.6	66	2.1	2.2	**2.9**	3.1
Canola	N/A	0.0046		250	280	550	5,500	**170**	190	240	270
Carrot	Film-coated	0.059		20	22	43	430	14	15	**19**	21
Carrot	Encrusted/Pelleted	0.059		20	22	43	430	14	15	**19**	21
Celery	Film-coated	0.00125		930	1,000	2,000	20,000	630	670	**890**	950

Table 5.1.4. Updated Occupational Handler Non-Cancer Exposure and Risk Estimates for Clothianidin – Commercial Seed Treatments.

Crop or Target	Specialized Treatment/ Formulation	App Rate (lb ai/lb seed)[2]	Amount Seed Treated (lb seed/day*)/ Planted per Day (seeds planted/day§)/ Activity Duration (activity hours/day↓)[3]	Dermal[4] MOE[5] (LOC = 100)		Inhalation[6] MOE[7] (LOC = 100)		Combined[8] MOE[10] (LOC =100)			
				SL/G	DL/G	No-R	PF10	SL/G + No-R	DL/G + No-R	SL/G + PF10 R	DL/G + PF10 R
Celery	Encrusted/Pelleted	0.00125		930	1,000	2,000	20,000	630	670	**890**	950
Corn, field	N/A	0.0055		210	230	460	4,600	**140**	150	200	220
Corn, pop	N/A	0.0131		89	97	190	1,900	**61**	64	85	92
Corn, sweet	N/A	0.005		230	260	510	5,100	**160**	170	220	250
Cotton	N/A	0.0035		330	360	730	7,300	**230**	240	320	340
Endive	Film-coated	0.047		25	27	54	540	17	18	**24**	26
Endive	Encrusted/Pelleted	0.047		25	27	54	540	17	18	**24**	26
Leek	Film-coated	0.064		18	20	40	400	12	13	**17**	19
Leek	Encrusted/Pelleted	0.064		18	20	40	400	12	13	**17**	19
Lettuce, head	Film-coated	0.78		1.5	1.6	3.3	33	1.0	1.1	**1.4**	1.5
Lettuce, head	Encrusted/Pelleted	0.78		1.5	1.6	3.3	33	1.0	1.1	**1.4**	1.5
Lettuce, leaf	Film-coated	0.78		1.5	1.6	3.3	33	1.0	1.1	**1.4**	1.5
Lettuce, leaf	Encrusted/Pelleted	0.78		1.5	1.6	3.3	33	1.0	1.1	**1.4**	1.5
Millet, pearl	N/A	0.00125		930	1,000	2,000	20,000	**630**	670	890	950
Millet, proso	N/A	0.00125		930	1,000	2,000	20,000	**630**	670	890	950
Mustard seed	Film-coated	0.004		290	320	640	6,400	200	210	**280**	300
Mustard seed	Encrusted/Pelleted	0.004		290	320	640	6,400	200	210	**280**	300
Mustard seed	N/A	0.004		290	320	640	6,400	**200**	210	280	300
Oat	N/A	0.00125		930	1,000	2,000	20,000	**630**	670	890	950
Onion, dry, bulb	Film-coated	0.075		16	17	34	340	11	11	**15**	16
Onion, dry, bulb	Encrusted/Pelleted	0.075		16	17	34	340	11	11	**15**	16
Onion, green	Film-coated	0.075		16	17	34	340	11	11	**15**	16
Onion, green	Encrusted/Pelleted	0.075		16	17	34	340	11	11	**15**	16
Parsley	Film-coated	0.0325		36	39	78	780	25	26	**34**	37

Table 5.1.4. Updated Occupational Handler Non-Cancer Exposure and Risk Estimates for Clothianidin – Commercial Seed Treatments.

Crop or Target	Specialized Treatment/ Formulation	App Rate (lb ai/lb seed)[2]	Amount Seed Treated (lb seed/day*)/ Planted per Day (seeds planted/day§)/ Activity Duration (activity hours/day┴)[3]	Dermal[4] MOE[5] (LOC = 100)		Inhalation[6] MOE[7] (LOC = 100)		Combined[8] MOE[10] (LOC =100)			
				SL/G	DL/G	No-R	PF10	SL/G + No-R	DL/G + No-R	SL/G + PF10 R	DL/G + PF10 R
Parsley	Encrusted/Pelleted	0.0325		36	39	78	780	25	26	**34**	37
Potato	N/A	0.0002		5,800	6,400	13,000	130,000	**4,000**	4,300	5,600	6,100
Rice	N/A	0.00075		1,600	1,700	3,400	34,000	**1,100**	1,100	1,500	1,600
Rye	N/A	0.00125		930	1,000	2,000	20,000	**630**	670	890	950
Sorghum, grain	N/A	0.0025		470	510	1,000	10,000	**320**	340	450	490
Soybean	N/A	0.0005		2,300	2,600	5,100	51,000	**1,600**	1,700	2,200	2,500
Spinach	Film-coated	0.005		230	260	510	5,100	160	170	**220**	250
Spinach	Encrusted/Pelleted	0.005		230	260	510	5,100	160	170	**220**	250
Triticale	N/A	0.00125		930	1,000	2,000	20,000	**630**	670	890	950
Wheat	N/A	0.00125		930	1,000	2,000	20,000	**630**	670	890	950
Loading/Planting (CST-L/P)[1]											
Barley	N/A	0.00125	184,240,000§	3,500	5,200	420	4,200	**380**	390	1,900	2,300
Beet, sugar	Film-coated	0.05	87,120,000§	430	640	52	520	46	48	**240**	290
Broccoli	Film-coated	0.39	16,867,600§	1,000	1,600	120	1,200	110	110	**550**	690
Broccoli	Encrusted/Pelleted	0.39	16,867,600§	1,000	1,600	120	1,200	110	110	**550**	690
Canola	N/A	0.0046	148,104,000§	11,000	17,000	1,400	14,000	**1,200**	1,300	6,200	7,700
Carrot	Film-coated	0.059	167,270,400§	1,500	2,300	180	1,800	160	170	**820**	1,000
Carrot	Encrusted/Pelleted	0.059	167,270,400§	1,500	2,300	180	1,800	160	170	**820**	1,000
Celery[8]	Film-coated	0.00125	5,575,680§	12,000,000	18,000,000	1,500,000	15,000,000	1,300,000	1,400,000	**6,700,000**	8,200,000
Celery[8]	Encrusted/Pelleted	0.00125	5,575,680§	12,000,000	18,000,000	1,500,000	15,000,000	1,300,000	1,400,000	**6,700,000**	8,200,000
Corn, field[8]	N/A	0.0055	8,050,000§	2,600	3,900	310	3,100	**280**	290	1,400	1,700
Corn, pop	N/A	0.0131	6,000,000§	1,500	2,200	180	1,800	**160**	170	820	990
Corn, sweet	N/A	0.005	4,779,120§	6,400	9,600	770	7,700	**690**	710	3,500	4,300
Cotton	N/A	0.0035	17,000,000§	6,400	9,600	770	7,700	**690**	710	3,500	4,300

Table 5.1.4. Updated Occupational Handler Non-Cancer Exposure and Risk Estimates for Clothianidin – Commercial Seed Treatments.

Crop or Target	Specialized Treatment/ Formulation	App Rate (lb ai/lb seed)[2]	Amount Seed Treated (lb seed/day*)/ Planted per Day (seeds planted/day§)/ Activity Duration (activity hours/day⊥)[3]	Dermal[4] MOE[5] (LOC = 100)		Inhalation[6] MOE[7] (LOC = 100)		Combined[8] MOE[10] (LOC =100)			
				SL/G	DL/G	No-R	PF10	SL/G + No-R	DL/G + No-R	SL/G + PF10 R	DL/G + PF10 R
Endive	Film-coated	0.047	4,181,760§	5,600	8,400	680	6,800	610	630	**3,100**	3,800
Endive	Encrusted/Pelleted	0.047	4,181,760§	5,600	8,400	680	6,800	610	630	**3,100**	3,800
Leek	Film-coated	0.064	11,947,920§	18,000	27,000	2,100	21,000	1,900	1,900	**9,700**	12,000
Leek	Encrusted/Pelleted	0.064	11,947,920§	18,000	27,000	2,100	21,000	1,900	1,900	**9,700**	12,000
Lettuce, head	Film-coated	0.78	25,090,560§	1,700	2,600	210	2,100	190	190	**940**	1,200
Lettuce, head	Encrusted/Pelleted	0.78	25,090,560§	1,700	2,600	210	2,100	190	190	**940**	1,200
Lettuce, leaf	Film-coated	0.78	12,560,000§	3,500	5,200	420	4,200	380	390	**1,900**	2,300
Lettuce, leaf	Encrusted/Pelleted	0.78	12,560,000§	3,500	5,200	420	4,200	380	390	**1,900**	2,300
Millet, pearl	N/A	0.00125	136,000,000§	43,000	64,000	5,100	51,000	**4,600**	4,700	23,000	28,000
Millet, proso	N/A	0.00125	112,000,000§	28,000	43,000	3,400	34,000	**3,000**	3,200	15,000	19,000
Mustard seed	Film-coated	0.004	101,360,000§	38,000	57,000	4,600	46,000	4,100	4,300	**21,000**	25,000
Mustard seed	Encrusted/Pelleted	0.004	101,360,000§	38,000	57,000	4,600	46,000	4,100	4,300	**21,000**	25,000
Mustard seed	N/A	0.004	101,360,000§	38,000	57,000	4,600	46,000	**4,100**	4,300	21,000	25,000
Oat	N/A	0.00125	234,000,000§	3,800	5,700	450	4,500	**400**	420	2,100	2,500
Onion, dry, bulb	Film-coated	0.075	32,000,000§	3,500	5,300	430	4,300	380	400	**1,900**	2,400
Onion, dry, bulb	Encrusted/Pelleted	0.075	32,000,000§	3,500	5,300	430	4,300	380	400	**1,900**	2,400
Onion, green	Film-coated	0.075	200,000,000§	560	850	69	690	61	64	**310**	380
Onion, green	Encrusted/Pelleted	0.075	200,000,000§	560	850	69	690	61	64	**310**	380
Parsley	Film-coated	0.0325	480,000,000§	820	1,200	99	990	88	91	**450**	540
Parsley	Encrusted/Pelleted	0.0325	480,000,000§	820	1,200	99	990	88	91	**450**	540
Potato	N/A	0.0002	2,125,728§	1,000	1,500	120	1,200	**110**	110	550	670
Rice	N/A	0.00075	487,672,000§	3,600	5,400	440	4,400	**390**	410	2,000	2,400
Rye	N/A	0.00125	324,000,000§	3,800	5,700	450	4,500	**400**	420	2,100	2,500
Sorghum, grain	N/A	0.0025	8,000,000§	35,000	53,000	4,300	43,000	**3,800**	4,000	19,000	24,000

Table 5.1.4. Updated Occupational Handler Non-Cancer Exposure and Risk Estimates for Clothianidin – Commercial Seed Treatments.

Crop or Target	Specialized Treatment/ Formulation	App Rate (lb ai/lb seed)[2]	Amount Seed Treated (lb seed/day*)/ Planted per Day (seeds planted/day§)/ Activity Duration (activity hours/day⊥)[3]	Dermal[4] MOE[5] (LOC = 100)		Inhalation[6] MOE[7] (LOC = 100)		Combined[8] MOE[10] (LOC =100)			
				SL/G	DL/G	No-R	PF10	SL/G + No-R	DL/G + No-R	SL/G + PF10 R	DL/G + PF10 R
Soybean	N/A	0.0005	50,000,000§	5,100	7,700	620	6,200	**550**	570	2,800	3,400
Spinach	Film-coated	0.005	80,000,000§	8,400	13,000	1,000	10,000	890	930	**4,600**	5,700
Spinach	Encrusted/Pelleted	0.005	80,000,000§	8,400	13,000	1,000	10,000	890	930	**4,600**	5,700
Triticale	N/A	0.00125	327,000,000§	3,100	4,700	380	3,800	**340**	350	1,700	2,100
Wheat	N/A	0.00125	300,000,000§	2,200	3,300	260	2,600	**230**	240	1,200	1,500

Bolded values indicate MOEs at current label PPE.

1. Unit Exposures: Based on the ExpoSAC Policy 14 (US EPA - Standard Operating Procedures for Seed Treatment); 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%.
2. Maximum Application Rate: Based on registered labels (see Table 4.1).
3. 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).
4. Commercial Seed Treaters and Packagers 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 (1 %) ÷ BW (69 kg).
   Commercial Seed Treatment Cleaners Dermal Dose = Dermal Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/lb seed) × Activity Duration (2.5 hr) × DAF (1 %) ÷ BW (69 kg).
5. Dermal MOE = Dermal POD (9.8 mg/kg/day) ÷ Dermal Dose (mg/kg/day). LOC = 100.
6. Commercial Seed Treaters and Packagers Inhalation Dose = Inhalation Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/lb seed) × Amount of Seed Treated (lb seed/day) ÷ BW (69 kg).
   Commercial Seed Treatment Cleaners Inhalation Dose = Inhalation Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/lb seed) × Activity Duration (2.5 hr) ÷ BW (69 kg).
7. Inhalation MOE = Inhalation POD (9.8 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). LOC = 100.
8. Buckwheat is a similar crop to rhubarb and they have similar seed types. Celery is the recommended surrogate for rhubarb. Therefore, celery was a surrogate for buckwheat. In addition, Corn, field was selected as the surrogate for Tesonite (cereal grain (Tesonite rate is 0.02318 mg ai/seed and 0.0009 lb ai/lb seed)). The rate used for field corn is higher and therefore, tesonite would be covered.

Table 5.1.5. Updated Occupational Handler Non-Cancer Exposure and Risk Estimates for Clothianidin – On-Farm Seed Treatments.

Crop or Target	App Rate (lb ai/lb seed)[2]	Amount Seed Treated (lb seed/day) 3	Planted per Day (seeds planted/day)[3]	Dermal[4] MOE[5] (LOC = 100)		Inhalation[6] MOE[7] (LOC = 100)		Combined[8] MOE[9] (LOC =100)			
				SL/G	DL/G	No-R	PF10	SL/G + No-R	DL/G + No-R	SL/G + PF10 R	DL/G + PF10 R
Treating/Planting (OFST/P-L)[1,2]											
Barley	0.0009	19,600	184,240,000	17,000	21,000	1,000	10,000	**940**	950	6,300	6,800
Oat	0.0009	18,000	234,000,000	18,000	22,000	1,100	11,000	**1,000**	1,000	6,800	7,300
Potato	0.0002	425,000	2,125,728	3,500	4,300	210	2,100	**200**	200	1,300	1,400
Rye	0.0009	18,000	324,000,000	18,000	22,000	1,100	11,000	**1,000**	1,000	6,800	7,300
Triticale	0.0009	21,800	327,000,000	15,000	19,000	920	9,200	**870**	880	5,700	6,200
Wheat	0.0009	31,400	300,000,000	11,000	13,000	640	6,400	**600**	610	4,000	4,300
Celery[11]	0.0009	3,000	5,575,680	17,000,000	25,000,000	2,000,000	20,000,000	**1,800,000**	1,900,000	9,200,000	11,000,000
Treating/Planting (OFST/P-S)[1,2]											
Barley	0.00125	19,600	184,240,000	360	500	44	440	39	40	**200**	230
Corn, field[10]	0.00125	5,910	8,050,000	1,200	1,700	140	1,400	130	130	**650**	770
Oat	0.00125	18,000	234,000,000	400	540	48	480	43	44	**220**	250
Potato	0.0002	425,000	2,125,728	110	140	13	130	12	12	**60**	67
Rye	0.00125	18,000	324,000,000	400	540	48	480	43	44	**220**	250
Sorghum, grain	0.00125	960	8,000,000	7,400	10,000	890	8,900	790	820	**4,000**	4,700
Triticale	0.00125	21,800	327,000,000	330	450	39	390	35	36	**180**	210
Wheat	0.00125	31,400	300,000,000	230	310	27	270	24	25	**120**	140
Celery[11]	0.00125	3,000	5,575,680	12,000,000	18,000,000	1,500,000	15,000,000	1,300,000	1,400,000	**6,700,000**	8,200,000

1. **Bolded values indicate MOEs at current label PPE.**OFST/P-L = on-farm seed treatment/planting with liquid. OFST/P-S = on-farm seed treatment/planting with solid (dust).
2. Maximum Application Rate: Based on registered labels (see Table 4.1).
3. Unit Exposures: Based on the ExpoSAC Policy 14 (US EPA - Standard Operating Procedures for Seed Treatment); 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.
4. 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).
5. 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 (1 %) ÷ BW (69 kg).
6. Dermal MOE = Dermal POD (9.8 mg/kg/day) ÷ Dermal Dose (mg/kg/day). LOC = 100.
7. On-Farm Seed Treaters and Planters Inhalation Dose = Inhalation Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/lb seed) × Amount of Seed Treated (lb seed/day) ÷ BW (69 kg).
8. Inhalation MOE = Inhalation POD (9.8 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). LOC = 100.
9. Total MOE = 1÷ [(1 ÷ Dermal MOE) + (1 ÷ Inhalation MOE)].
10. Corn, field was selected as the surrogate for Tesonite (cereal grain (Tesonite rate is 0.02318 mg ai/seed and 0.0009 lb ai/lb seed)). Rate used for field corn is higher and therefore, tesonite would be covered.
11. Buckwheat is a similar crop to rhubarb and they have similar seed types. Celery is the recommended surrogate for rhubarb. Therefore, celery was a surrogate for buckwheat.

Appendix A. Summary of Occupational Non-cancer Algorithms

Occupational Non-cancer Algorithms for Commercial Seed Treaters and Packagers

Potential daily exposures for occupational seed treaters and packagers are calculated using the following formulas:

$$E=UE * AR * AST * 0.001\ mg/ug$$

where:

E	=	exposure (mg ai/day)
UE	=	unit exposure (µg ai/lb ai)
AR	=	maximum application rate according to proposed label (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)
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)
ADD	=	average daily dose absorbed in a given scenario (mg ai/kg/day)

Occupational Non-cancer Algorithms for Commercial Seed Treatment Cleaners

Potential daily exposures for occupational seed treatment cleaners are calculated using the following formulas:

$$E=UE * AR * AD * 0.001\ mg/ug$$

where:

E	=	exposure (mg ai/day)
UE	=	unit exposure [(µg ai/hr)/(lb ai/lb seed)]
AR	=	maximum application rate according to proposed label (lb ai/lb seed)
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)
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)
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 On-farm 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)
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)
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)
ADD	=	average daily dose absorbed in a given scenario (mg ai/kg/day)