Proposed Registration Decision PRD2020-06

Broflanilide, Cimegra, Teraxxa and Teraxxa F4

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Overview

Proposed Registration Decision for Broflanilide

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of Broflanilide Technical Insecticide, Cimegra, Teraxxa and Teraxxa F4 containing the technical grade active ingredient Broflanilide, to be used as a soil treatment to control wireworm in potatoes and wireworm and corn rootworm in corn, and as a seed treatment to control wireworm in small cereal grains and wheat.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Broflanilide Technical Insecticide, Cimegra, Teraxxa and Teraxxa F4.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the Health Canada regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides portion of the Canada.ca website.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act.*

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "…the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on Broflanilide, Cimegra, Teraxxa and Teraxxa F4 Health Canada's PMRA will consider any comments received from the public in response to this consultation document.[3] Health Canada will then publish a Registration Decision[4] on Broflanilide, Cimegra, Teraxxa and Teraxxa F4 which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Broflanilide?

The active ingredient broflanilide is a new non-systemic conventional insecticide with contact activity that affects the nervous system of insects. Broflanilide is used as a soil treatment to control wireworm in potatoes and wireworm and corn rootworm in corn, and as a seed treatment to control wireworm in small cereal grains and wheat. Broflanilide has value as a new mode of action for use in resistance management.

Health Considerations

Can Approved Uses of Broflanilide Affect Human Health?

Cimegra, Teraxxa, and Teraxxa F4, containing broflanilide, are unlikely to affect your health when used according to label directions.

Potential exposure to broflanilide may occur through the diet (food and drinking water), when handling and applying the end-use products, or when coming into contact with treated surfaces. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose level at which no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals, the technical grade active ingredient broflanilide was of low acute toxicity via the oral, dermal and inhalation routes of exposure. It was non-irritating to the eyes and skin, and did not cause an allergic skin reaction.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

The acute toxicity of the end-use products Cimegra and Teraxxa, containing broflanilide, was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes and skin and did not cause an allergic skin reaction.

The acute toxicity of the end-use product Teraxxa F4 containing broflanilide was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes and slightly irritating to the skin. Teraxxa F4 caused an allergic skin reaction; consequently the hazard statement "POTENTIAL SKIN SENSITIZER" is required on the product label.

Registrant-supplied short- and long-term (lifetime) animal toxicity tests, as well as information from the published scientific literature, were assessed for the potential of broflanilide to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment were effects on the adrenal glands and the ovaries. There was no evidence that broflanilide damaged genetic material; however, it did cause tumours of the ovaries, uterus, adrenal gland, and testes in rats. There was no evidence of increased sensitivity of the young compared to adult animals. The risk assessment protects against the effects noted above and other potential effects by ensuring that the level of exposure to humans is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and drinking water are not of health concern.

Animal studies revealed no acute health effects. Consequently, a single dose of broflanilide is not likely to cause acute health effects in the general population (including infants and children).

Aggregate dietary intake estimates (food plus drinking water) revealed that the general population and Children 1–2 years old, the subpopulation which would ingest the most broflanilide relative to body weight, are expected to be exposed to less than 6% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from broflanilide is not of health concern for all population subgroups.

The lifetime cancer risk from the use of broflanilide on potato, corn (all types) and small grains is not of health concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using broflanilide on potatoes, corn and small cereal grains are acceptable. The MRLs for this active ingredient can be found in the Science Evaluation of this consultation document.

Teraxxa F4 is also formulated with the active ingredients pyraclostrobin, triticonazole, metalaxyl and fluxapyroxad. These other active ingredients are currently registered for use in Canada at rates equivalent to or greater than those proposed.

Risks in Residential and Other Non-Occupational Environments

A residential assessment was not required since these products are not permitted for use by residential handlers or for use in residential areas.

Occupational Risks From Handling Cimegra, Teraxxa F4 and Teraxxa

Occupational risks are not of concern when broflanilide is used according to the proposed label directions for the end-use products, which include protective measures.

Workers who mix, load and apply Cimegra as an in-furrow and/or T-band treatment during planting of potato or corn can come in direct contact with broflanilide on the skin and or through inhalation. Therefore, the label specifies that anyone mixing/loading and applying broflanilide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. Gloves are not required during application within a closed cab. As Cimegra is applied to subsurface soil as an in-furrow and/or T-band, exposures to broflanilide during postapplication activities are considered negligible. As such, a restricted-entry interval is not required on the label.

Workers in commercial seed treatment facilities, mobile treaters, on-farm treaters and planters handling seed treated with Teraxxa F4 or Terraxxa can come into direct contact with broflanilide through residues on the skin and by inhaling dust. Therefore, the label states that workers in commercial seed treatment facilities and mobile treaters must wear coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, shoes, socks and a dust-mask. Workers cleaning or repairing seed treatment equipment must wear chemical-resistant coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, socks, chemical-resistant footwear and a dust-mask. Workers completing on-farm seed treatment must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. Workers planting and handling treated seed must wear coveralls over a long-sleeved shirt, long pants, shoes and socks and use only a closed cab tractor. A dust-mask must be worn during the on-farm transfer of treated seed to planters/seeders.

For bystanders, exposure is considered to be negligible and are not of concern when drift statements are added to the labels.

Environmental Considerations

What Happens When Broflanilide Is Introduced Into the Environment?

When broflanilide is used according to the label directions, the risks to the environment have been determined to be acceptable.

Broflanilide enters the environment when applied as a soil or seed treatment to potatoes, corn and small cereal grains to control insect pests. Broflanilide is persistent in soil, but is not expected to move through the soil and reach groundwater because it binds strongly to the soil surface. In water bodies, broflanilide will move to sediments where it may remain over time.

Broflanilide is not expected to be found in the air or to travel long distances from where it was applied. Broflanilide is not expected to build-up in the tissues of organisms. Broflanilide is not expected to be taken up by plants and move inside plant tissues (it is not systemic) and its residues will remain mostly in the soil.

When used according to the label directions, broflanilide poses acceptable risk to wild mammals, birds, beneficial insects, earthworms, terrestrial and aquatic plants, fish, or amphibians. Exposure to broflanilide may affect freshwater and marine invertebrates if they are exposed to high enough levels; therefore, precautionary label statements for aquatic organisms are required on product labels. Precautionary label statements and best management practices are also required for pollinators to minimize potential bee exposure to dust during planting of treated seed; however, when used according to label directions, minimal exposure or risk to bees is expected.

Value Considerations

What Is the Value of Cimegra?

Cimegra provides a new mode of action for controlling wireworm in potatoes and wireworm and corn rootworm in corn.

Cimegra has value for control of corn rootworm (western and northern) and wireworm, and to reduce wireworm populations in treated fields. Wireworms are major pests of potatoes and corn, and are difficult to kill with currently registered pest control products, and corn rootworms are a major pest of corn. Broflanilide has value as a new mode of action for use in resistance management; there are no reported cases of cross-resistance of broflanilide to currently registered insecticide modes of action.

What Is the Value of Teraxxa F4 and Teraxxa?

Teraxxa F4 and Teraxxa provide a new mode of action for controlling wireworm in small cereal grains (barley, buckwheat, pearl millet, proso millet, oats, rye, sorghum, triticale, canary seed, annual canarygrass (grown for human consumption)) and wheat (all types: winter, spring and durum).

Teraxxa F4 and Teraxxa have value for control of wireworms and to reduce wireworm populations in treated fields. Wireworms are major pests of small cereal grains and wheat, and are difficult to kill with currently registered pest control products. In addition, as Teraxxa F4 is a pre-mix formulation with pyraclostrobin, fluxapyroxad, triticonazole, and metalaxyl, it provides control or suppression of certain seed- and soil-borne diseases. Broflanilide has value as a new mode of action for use in resistance management; there are no reported cases of cross-resistance of broflanilide to currently registered insecticide modes of action.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Broflanilide Technical Insecticide, Cimegra, Teraxxa and Teraxxa F4 to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

As direct contact with broflanilide on the skin or through inhalation can occur, workers mixing, loading and applying Cimegra must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. Chemical-resistant gloves are not required during application within a closed cab.

Workers in commercial seed treatment facilities (and mobile treaters) must wear coveralls over a long-sleeved shirt, long pants, chemical resistant gloves, shoes and socks when applying or in contact with Teraxxa F4 or Teraxxa treated seed. Cleanout/repair personnel must wear chemical-resistant coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, chemical-resistant footwear, socks and a dust-mask. Workers treating cereal seed on farm must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. Workers planting and handling treated seed must wear coveralls over a long-sleeved shirt, long pants, shoes and socks and use only a closed cab tractor. A dust-mask must be worn during the on-farm transfer of treated seed to planters/seeder.

Environment

- Label statements indicating toxicity to bees and best management practices to minimize bee exposure to dust during planting of treated seed
- Precautionary label statements indicating toxicity to aquatic organisms
- Precautionary label statements to mitigate runoff

Next Steps

Before making a final registration decision on Broflanilide, Cimegra, Teraxxa and Teraxxa F4, Health Canada’s PMRA will consider any comments received from the public in response to this consultation document. Health Canada will accept written comments on this proposal up to 45 days from the date of publication of this document. Please note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to Publications (contact information on the cover page of this document). Health Canada will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and Health Canada’s response to these comments.

Other Information

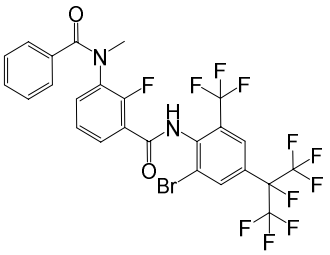
When the Health Canada makes its registration decision, it will publish a Registration Decision on Broflanilide, Cimegra, Teraxxa and Teraxxa F4 (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Broflanilide

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Broflanilide
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	6′-bromo-α,α,α,2-tetrafluoro-3-(N-methylbenzamido)-4′-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]benz-o-toluidide
2. Chemical Abstracts Service (CAS)	3-(benzoylmethylamino)-*N*-[2-bromo-4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-6-(trifluoromethyl)phenyl]-2-fluorobenzamide
CAS number	1207727-04-5
Molecular formula	$C_{25}H_{14}BrF_{11}N_2O_2$
Molecular weight	663.28
Structural formula	
Purity of the active ingredient	99.68%

1.2 Physical and Chemical Properties of the Active Ingredient and End-Use Product

Technical Product—Broflanilide Technical

Property	Result
Colour and physical state	Beige solid
Odour	No discernible odour
Melting range	154.0–155.5 °C
Boiling point or range	Not required for solid products
Density	1.6–1.7 g/cm^3
Vapour pressure at 25 °C	8.9×10^{-9} Pa

Property	Result
Ultraviolet (UV)-visible spectrum	pH / λmax (nm) / ε (L/mol^{-1}. cm^{-1}) 7.2 / 239 / 17 200 274 / 5000 282 / 4090 1.4 / 239 / 17 000 274 / 4980 282 / 4120 13.0 / 248 / 17 600 293 / 5560
Solubility in water at 20°C	0.71 mg/L
Solubility in organic solvents at 20 °C	Solvent / Solubility (g/L) n-hexane / 0.096 xylene / 6.0 n-octanol / 7.4 1,2-dichloroethane / 110 methanol / >250 acetone / >250 ethyl acetate / >250
n-Octanol-water partition coefficient (K_{ow})	pH / log K_{ow} 7 / 5.7
Dissociation constant (pK_a)	9.92
Stability (temperature, metal)	The product is stable for 14 days at 54 °C upon exposure to iron, iron acetate, aluminium, aluminium acetate, zinc and zinc acetate.

End-Use Product—Cimegra

Property	Result
Colour	Milky white
Odour	Slight smell
Physical state	Liquid
Formulation type	SU (suspension)
Label concentration	Broflanilide…….100 g/L
Container material and description	HDPE jugs, drum or totes
Density	1.034–1.069 g/mL at 20 °C
pH of 1% dispersion in water	6.0–8.0
Oxidizing or reducing action	The product was determined to be compatible with oxidizing agents, reducing agents, fire extinguishing agents and water.
Storage stability	Stable for 2 weeks when stored in HDPE containers at 54 °C.
Corrosion characteristics	No corrosion to HDPE containers was observed after 2 weeks storage at 54 °C.
Explodability	Not explosive

End-Use Product—Teraxxa F4

Property	Result
Colour	Red
Odour	Odourless
Physical state	Liquid
Formulation type	SU (suspension)
Label concentration	Broflanilide……..16.7 g/L Pyraclostrobin……..16.7 g/L Triticonazole……16.7 g/L Metalaxyl…….10.0 g/L Fluxapyroxad……...8.35 g/L
Container material and description	HDPE jugs, drums, totes, 0.1 L to bulk
Density	1.064–1.086 g/mL at 20 °C
pH of 1% dispersion in water	6.86
Oxidizing or reducing action	The product is not an oxidizing, but a reducing agent.
Storage stability	The product was stored at a temperature of 40 °C for a period of 8 weeks in HDPE containers.
Corrosion characteristics	After storage for 8 weeks in HDPE containers at a temperature of 40 °C, the product did not have any adverse effects on its commercial packaging.
Explodability	Not explosive

End-Use Product—Teraxxa

Property	Result
Colour	Cream
Odour	Slight smell
Physical state	Liquid
Formulation type	SU (suspension)
Label concentration	Broflanilide ……. 300 g/L
Container material and description	HDPE jugs, drums, totes, 0.1 L to bulk
Density	1.144–1.166 g/mL at 20 °C
pH of 1% dispersion in water	6.0–8.0
Oxidizing or reducing action	The product was determined to be compatible with oxidizing agents, reducing agents, fire extinguishing agents and water.
Storage stability	The product was stable for 14 days when stored at 54 °C or stable for 2 years when stored at 25 °C in HDPE containers.
Corrosion characteristics	No corrosion of the HDPE container was observed.
Explodability	Not explosive

1.3 Directions for Use

Cimegra

Cimegra provides control of wireworm in potatoes and wireworm and corn rootworm (western and northern) in corn when applied at planting at an application rate of 250 mL product (25 g broflanilide) per hectare. Cimegra is applied in a minimum application volume of 50 L per hectare. Potato applications are applied in-furrow, while corn applications are applied in-furrow or as a 10 to 20 cm T-band spray over the top of the open seed furrow.

Teraxxa

Terraxxa is applied as a seed treatment at 16.7 mL product (5 g broflanilide) per 100 kg seed to small cereal grains (barley, buckwheat, pearl millet, proso millet, oats, rye, sorghum, triticale, canary seed, and annual canarygrass (grown for human consumption)), and wheat (all types: winter, spring and durum) to control wireworm.

Teraxxa F4

Teraxxa F4 is applied as a seed treatment at 300 mL product (5 g broflanilide; 5 g pyraclostrobin; 2.5 g fluxapyroxad; 5 g triticonazole; and 3 g metalaxyl) per 100 kg seed to small cereal grains (barley, oats, rye, triticale, canary seed, and annual canarygrass (grown for human consumption)), and wheat (all types: winter, spring and durum) to control wireworm and to control or suppress certain seed- and soil-borne diseases of small cereal grains and wheat.

1.4 Mode of Action

The active ingredient broflanilide is a new non-systemic conventional insecticide with contact activity that affects the nervous system of insects. Broflanilide binds to an inter-subunit allosteric site on the GABA (Gamma-amino butyric acid) receptor, resulting in a block of inhibitory neurotransmission, convulsions and death of target insect. It is classified by the Insecticide Resistance Action Committee (IRAC) as a Group 30 insecticide (GABA-gated chloride channel allosteric modulators) and represents a new mode of action with no known cross resistance.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and impurities in the technical product have been validated and assessed to be acceptable.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

High-performance liquid chromatography methods with tandem mass spectrometry (HPLC-MS/MS) were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

High performance liquid chromatography methods with tandem mass spectrometric detection (HPLC-MS/MS; Method D1417/01 in plant matrices and Method D1604/01 in animal matrices) were developed and proposed for data gathering and enforcement purposes. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limits of quantitation. Acceptable recoveries (70–120%) were obtained in plant and animal matrices. The proposed enforcement methods for plant and animal matrices were successfully validated by independent laboratories. Extraction solvents used in the methods were similar to those used in the metabolism studies; thus, further demonstration of extraction efficiency with bioincurred residues of broflanilide in plant and animal matrices was not required for the enforcement methods.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Broflanilide, also identified as MCI-8007, is a meta-diamide insecticide. Its metabolite, des-methyl broflanilide (DM-8007), is considered the insecticidally active compound. The proposed insecticidal mode of action (MOA) involves binding to an inter-subunit allosteric site on the gamma-aminobutyric acid (GABA) receptor, resulting in a block of inhibitory neurotransmission, convulsions, and death of target insects. GABA binding is expected to be highly specific to invertebrates given interspecies differences in subunit amino acid positioning.

A detailed review of the toxicological database for broflanilide was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. Additional studies included a dietary repeat-dose study investigating hormonal effects to support a proposed MOA for Leydig cell tumour formation in rats. The applicant submitted a position paper that discussed the carcinogenic potential of broflanilide and a proposed MOA for Leydig cell tumour formation in rats, as well as the human relevance of toxicological effects that occurred at dose levels above a proposed kinetically-derived maximum dose (KMD). Finally, acute oral toxicity studies, repeat-dose dietary studies as well as genotoxicity studies for several broflanilide metabolites were conducted. The required studies in the broflanilide database were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to characterize the potential health hazards associated with broflanilide.

Metabolism and toxicokinetic studies were conducted in rats via the oral route. In these studies, broflanilide was carbon (C)14-radiolabelled on the phenyl ring (identified as the C-ring) or the trifluorophenyl ring (identified as the B-ring) portion of the broflanilide molecule. Broflanilide was rapidly but poorly absorbed and widely distributed to tissues following single low- or high-

dose gavage administration. The plasma elimination half-lives were 42–79 hours and 8–58 hours, for low- and high-dose groups, respectively. Highest levels of radioactivity were observed in the liver, pancreas, adrenal gland, thyroid gland, epididymides and ovaries at 4 hours with the B-ring label, and in the kidney and liver at 1 hour with the C-ring label. Concentrations of radioactivity in tissues were generally greater in males than in females.

Radioactivity was readily excreted within 48–72 hours of administration of a single dose, with the majority of radioactivity excreted via the faeces and lower amounts excreted via the urine. Results from bile duct-cannulated rats suggested that biliary excretion accounted for very little of the eliminated radioactivity when compared to the excretion via feces. The levels of radioactivity in urine and bile decreased as the dose increased, whereas those in faeces increased as the dose increased (only tested in males). In these studies, bioavailability was not significantly different between sexes.

The toxicokinetics of C14- radiolabelled broflanilide were also examined following 14 days of gavage administration to rats. Maximum plasma and whole blood concentrations occurred at 4 hours after the final dose. Peak tissue concentrations occurred 24 hours after the final dose with greatest concentrations in the fat, and notable concentrations also present in liver, pancreas, adrenal gland, thyroid gland, epididymides and ovaries. Concentrations of radioactivity observed in tissues following repeated dosing were generally greater than those in plasma except for whole blood, blood cells, brain, testes and bone. This observation was similar to findings observed in tissues following single dosing. Levels of radioactivity retained in tissues following repeat dosing of a low dose level of the B-ring radiolabel were higher when compared to the single dose study, suggesting increased tissue retention with repeated dosing. There was no notable sex difference in the distribution of radioactivity in the repeat-dose study, and the majority of the administered radioactivity was excreted via the feces.

Broflanilide was only partially metabolised in the rat with no significant sex differences identified. Following single gavage dosing with a low- or high-dose of C14-radiolabelled test material, unchanged broflanilide was the major component in fecal extracts. Other metabolites detected in the feces included DM-(C-H2O)-8007, DM-(A,C-diOH)-8007, DC-DM-(A-OH)-8007, and DM-8007. In urine, hippuric acid was the predominant metabolite. The proposed metabolic pathway involves the metabolism of broflanilide to either S(PFP-OH)-8007 or DM-8007, followed by hydroxylation and conjugation of DM-8007 to form DM-(C-H2O)-8007 cysteine conjugate, or hydroxylation of DM-8007 to form DM-(A,C-OH)-8007 and DM-(A,C-diOH)-8007. DM-8007 was also subject to hydrolysis of the amide bond to form DC-DM-8007, followed by hydroxylation to form DC-DM-(A-OH)-8007, and conjugation to form DC-DM-(A-OH)-8007 cysteine conjugate. Additionally, hydrolysis of DM-8007 also resulted in the formation of benzoic acid, which was subsequently metabolized to hippuric acid. The identity of metabolites that were further characterized are presented in Appendix I, Table 2.

Plasma concentrations of non-radiolabelled broflanilide and metabolite DM-8007 were determined in select repeat-dose oral toxicity studies conducted with rats, mice, and dogs. DM-8007 was generally detected at much higher concentrations than broflanilide. Unchanged broflanilide and DM-8007 levels increased with increasing dose level, but not in a dose-proportional manner.

Plasma concentrations of broflanilide and DM-8007 generally showed a sublinear dose-response compared to external dose, a trend which was more profound at higher concentrations. Based on the plasma level analyses of broflanilide and DM-8007, there was some evidence to support the occurrence of saturation of absorption. There were no clear or consistent differences between sexes in any species.

The applicant suggested that nonlinear kinetics resulting in saturation of absorption were observed in the database at oral dose levels greater than 16–20 mg/kg bw/day in rats. This, it was argued, would lead to a lower than expected increase in plasma concentration of broflanilide with increasing dose levels based on an assumption of linear kinetics. The applicant reasoned that toxicological effects that occur at dose levels above a KMD would be of questionable human relevance. The available toxicokinetic data did not demonstrate complete saturation of oral absorption. The toxicokinetics studies demonstrated that the proportion of radioactive dose administered to rats that was absorbed following oral administration decreased with increasing dose level. However, maximum serum concentration (Cmax) and area-under-the-curve (AUC) data presented by the applicant showed that these parameters increased with increasing dose level, although not proportional to dose level, suggesting a change in oral absorption and not a complete saturation of oral absorption. In addition, despite lower relative oral absorption at higher dose levels, there were clear treatment-related dose-responsive toxic effects observed throughout the database. The utility of the plasma kinetic data from the repeat-dose oral toxicity studies was limited by the fact that only broflanilide and the metabolite DM-8007 were measured, and that analysis was limited to the plasma. The kinetics of other metabolites were not accounted for, and plasma levels of broflanilide or the DM-8007 metabolite may not have provided a reliable indication of the internal dose given that greater levels of radioactivity in tissues when compared to plasma were observed in the toxicokinetic data. It was concluded that the applicant's position regarding the lack of human relevance for effects observed at dose levels above a KMD could not be supported.

In acute toxicity testing, broflanilide was of low acute toxicity to rats via the oral, dermal and inhalation routes of exposure, not irritating to the eyes or skin of rabbits, and negative for skin sensitization in guinea pigs using the Maximization test protocol and in mice using the local lymph node assay.

The end-use products Cimegra, Teraxxa, and Teraxxa F4, each containing broflanilide, were of low acute toxicity to rats via the oral, dermal and inhalation routes of exposure, and minimally irritating to the eyes of rabbits. Cimegra and Teraxxa were minimally irritating to the skin of rabbits, and negative for skin sensitization in guinea pigs using the Buehler test protocol. Teraxxa F4 was slightly irritating to the skin of rabbits, and was a potential skin sensitizer in guinea pigs according to the Buehler test protocol.

Repeat-dose dietary toxicity studies with broflanilide were available in mice and rats, and capsule administration studies were available in dogs. In these studies, which involved short-term to longer-term testing, the most sensitive species for toxicity appeared to be the rat, followed by the dog and the mouse. The adrenal gland was the primary target tissue following repeated oral dosing in the three test species. Adrenal gland toxicity was evidenced by increased organ weight, adrenal gland enlargement and vacuolation. In the dog and rat, adrenal gland hypertrophy was also observed, whereas adrenal gland accessory nodules and inflammatory cell

foci were observed in the mouse. Discoloration, the presence of masses, fatty changes, as well as cystic degeneration, were additional findings in rat adrenal glands. Additional findings outside of the adrenal included decreases in red blood cell counts, hemoglobin concentrations, and hematocrit concentrations in rats; increases in alkaline phosphatase and triglycerides in dogs; and increased cholesterol in rats and dogs.

Effects on several reproductive organs were also observed following repeated oral dosing with broflanilide. Increased ovarian weight and ovarian cysts were observed in rats and mice, and ovarian vacuolation was observed in rats. In rats, uterine hyperplasia was observed, as well as increased testicular and epididymal weights. At high dose levels in rats, discoloration, foci, and masses of the testes were also observed.

There was some evidence to suggest a slight increase in toxicity with extended duration of dosing in the rat and dog studies. In rats, increased adrenal gland weight and adrenal gland vacuolation were observed at lower dose levels in the long-term study when compared to studies of shorter duration, although this comparison is hindered by the dose levels selected for testing in these studies. The dose levels at which ovarian vacuolation was observed were more clearly affected by dosing duration. Furthermore, uterine glandular hyperplasia, and testes effects (discolouration, foci, and masses) were observed in rats only at terminal sacrifice in the long-term dietary study. In dogs, 12 months of dosing resulted in additional findings not seen after 90 days of dosing, such as adrenal gland hypertrophy and vacuolation and reduced body weight. Additionally in dogs, some effects that were observed in both studies were observed at a lower dose level in the longer-term study.

In a 28-day dermal toxicity study in rats, there was no indication of systemic toxicity up to the limit dose of testing. In a 28-day inhalation toxicity study in rats, there were a number of findings that were consistent with those observed in the repeat-dose dietary toxicity studies, namely, increases in adrenal gland and ovary weights, as well as adrenal gland and ovary vacuolation. There were findings specific to the inhalation route of administration, such as effects in the lung, which included increased organ weight, regenerative bronchiolar hyperplasia, alveolar histiocytosis, and debris, as well as larynx epithelial alteration. Additionally in the 28-day inhalation toxicity there were effects noted in the spleen, namely, an increase in the severity of the organ pigment storage, as well as extramedullary hematopoiesis.

There was no indication of neurotoxicity in an acute neurotoxicity study in rats conducted via oral gavage, or in a 90-day dietary neurotoxicity study rats. Decreases in offspring brain weight were noted in the 2-generation reproductive toxicity study, which are discussed in greater detail below. No other nervous system effects were noted in the database.

In a 28-day dietary immunotoxicity study in rats dosed with broflanilide, no treatment-related effects were identified. There was no evidence of immune dysregulation noted in this study, or in other studies in the broflanilide database.

In a 2-generation dietary reproductive toxicity study conducted in rats, the systemic toxicity observed in parental animals was generally consistent with findings reported in other repeat-dose dietary studies in rats, and included increased adrenal gland and ovary weights, as well as adrenal gland and ovary vacuolation, and adrenal gland hypertrophy. Effects on reproductive

tissues were observed at dose levels that were toxic to the parental animals. Reproductive effects included increased epididymides, cauda epididymides, and testes weight, as well as the previously mentioned increase in ovary weight, and ovary vacuolation. Of note, the effects observed in the testes and epididymides were in F1 males, but not in P males, suggesting that the second generation of males is more sensitive to these effects than the first generation. Effects noted in the offspring were observed at higher dose levels than those resulting parental toxicity. Effects in the offspring included decreased body weight and body weight gain, as well as decreases in thymus, brain, and spleen weight. The effect on brain weight was a unique effect seen in offspring that was not observed in parental animals. However, concern for this unique finding was tempered by the fact that it was observed at a much higher dose level (approximately 15-fold) than that which resulted in toxic effects in parental animals. Increased pup death in the early post-natal period was noted at the highest dose level tested, resulting in a lower viability index. This effect was only observed above the limit dose and in the presence of maternal toxicity. The findings identified in the 2-generation reproductive toxicity study conducted in rats suggested that there was no increased sensitivity of the young animal when compared to the adult animal.

A supplemental developmental/reproductive toxicity screening study was conducted in rats. Parental animals administered broflanilide in the diet exhibited increased adrenal gland weight (both sexes) and adrenal gland hypertrophy (females only). There were no treatment-related effects on reproductive performance, although there was one complete litter loss that occurred in the early post-natal period at a dose level in excess of the limit dose of testing. Additionally at this dose level, there was an increase in the number of pup deaths between post-natal days 1 and 4. Similar to the findings from the 2-generation reproductive toxicity study conducted in rats, the reproductive and offspring effects noted in the developmental/reproductive toxicity screening study occurred at the limit dose and in the presence of parental toxicity.

Developmental toxicity studies were conducted via oral gavage in rats and rabbits. No adverse maternal or developmental effects were identified up to the limit dose of testing in either species, suggesting that there was no sensitivity of the young animal.

Broflanilide was negative in a genotoxicity testing battery which included a bacterial reverse mutation assay in S. typhimurium and E. coli, an in vitro chromosomal aberration assay in Chinese hamster lung cells, an in vitro forward mutation assay in Chinese hamster ovary cells, and an in vivo micronucleus assay in mice.

There was no evidence of oncogenicity in an 18-month dietary oncogenicity study conducted in mice. In a 24-month dietary chronic toxicity/oncogenicity study conducted in rats, there was a statistically significant increase in the incidence of Leydig cell adenomas in males at the highest dose level tested. At the highest dose level tested in females, there were non-statistically significant increases in the incidences of ovarian luteomas and the combined incidence of ovarian tumours of sex cord stromal origin (luteomas, thecomas, granulosa cell tumours, and sex cord stromal tumours), as well as adrenal cortex carcinomas. Additionally in females at the two highest dose levels, there were increases in ovarian granulosa cell tumours which were only statistically significant at the next-to-highest dose level, and in uterine adenocarcinomas which were statistically significant at the highest dose level. A statistically significant linear trend was observed for these tumours, except for the ovarian granulosa cell tumours. The provided

historical control data for these tumour types, when available, indicated that incidences in broflanilide-exposed rats at the above-noted dose levels exceeded the upper end of the historical control ranges and that the concurrent control incidences were generally similar to the historical control means, suggesting they were related to treatment.

The applicant submitted a proposed MOA and a human relevance framework analysis for the rat Leydig cell adenomas. The proposed MOA involves the following key events (KE): KE 1) a transient decrease in serum testosterone (T) levels; KE 2) increased serum luteinizing hormone (LH) levels with subsequent LH binding to LH receptors on Leydig cells; KE 3) the promotion of Leydig cell hyperplasia; and KE 4) the promotion/progression to Leydig cell tumours.

In support of the proposed MOA, a non-guideline subchronic toxicity study investigating effects on various hormone levels was performed in Wistar rats exposed to either a low- or high-dose level of broflanilide via the diet for 91 days. Although there appeared to be a slight decrease in serum T levels observed towards the end of the study period, which would support KE 1, the more apparent observation was a large increase in T observed at the beginning of the dosing period (study day 10). Additionally, there appeared to be an increase in LH observed towards the end of the study period, which provided some supporting evidence for KE 2. It should be noted that the interpretation of these findings is confounded by the fact that hormone levels were not measured prior to the initiation of the dosing period, there was a high degree of variability in the data, and the group sizes were relatively small when considering the sample size recommended for the reliable detection of changes in T levels in rats. Moreover, in regards to the increased LH levels, this is a KE that is common to various hormone-based MOAs for the formation of Leydig cell tumours and is not specific to the applicant's proposed MOA. Although there was a clear increase in Leydig cell hyperplasia observed in the 24-month rat chronic/oncogenicity study, which supported KE 3, the findings from the non-guideline subchronic toxicity study investigating effects on various hormone levels were not considered adequate to support KEs 1 or 2. Therefore, the submitted data were not considered adequate to support the proposed MOA for Leydig cell tumours in rats. No MOAs were proposed by the applicant for the other tumour types identified in the rat (ovarian luteomas, ovarian tumours of sex cord stromal origin, ovarian granulosa cell tumours, adrenal cortex carcinomas, and uterine adenocarcinoma). Overall, a quantitative linear low-dose extrapolation approach was deemed appropriate for the cancer risk assessment.

A number of studies were provided for seven broflanilide metabolites: DM-8007, DC-DM-8007, S(PFP-OH)-8007, DC-8007, MFBA, AB-oxa, and S(Br-OH)-8007. All seven metabolites were found to be of low acute toxicity via the oral route in rats, and negative in bacterial reverse mutation assays in S. typhimurium and E. coli. In an in vitro assay in Chinese hamster lung cells with MFBA, an increase in chromosomal aberrations was observed but only in the presence of test compound precipitation, and without a dose-response. Additionally, MFBA was negative for clastogenicity in an in vivo micronucleus assay.

Repeat-dose dietary toxicity studies in rats of 28 or 90 days duration were provided for DM-8007, DC-DM-8007, and S(PFP-OH)-8007, which allowed a comparison of toxic effects with the 90-day repeat-dose dietary toxicity with broflanilide. For metabolite MFBA, only a 28-day repeat-dose gavage toxicity study in rats was provided.

In the repeat-dose dietary toxicity studies, no toxic effects were observed with DM-8007 when tested at higher dose levels than broflanilide. DC-DM-8007 produced toxic effects at a similar dose level and in the same tissues when compared to broflanilide, with the addition of spleen as a target tissue as evidenced by increased spleen weight, enlarged spleen, and extramedullary hematopoiesis. Dosing with S(PFP-OH)-8007 resulted in a similar spectrum of toxicity to broflanilide but at a lower dose level. However, when considering the dose spacing and the magnitude of the effects following repeated dosing with S(PFP-OH)-8007 and broflanilide, S(PFP-OH)-8007 was considered to be of comparable toxicity to broflanilide. In the 28-day rat gavage study with MFBA, effects occurred only at the limit dose of testing. Although a comparable 28-day oral toxicity study was not available for broflanilide, the effect levels in the available repeat-dose oral toxicity studies in rats with broflanilide were orders of magnitude lower than those determined in the 28-day study with MFBA.

Based on the available information, it was concluded that metabolites DM-8007, DC-DM-8007, S(PFP-OH)-8007, DC-8007, MFBA, AB-oxa, and S(Br-OH)-8007 are to be considered of equal toxicity as broflanilide.

The identification of select broflanilide metabolites is presented in Appendix I, Table 2. Results of the toxicology studies conducted on laboratory animals with broflanilide, its metabolites, and its associated end-use products, are summarized in Appendix I, Tables 3, 4 and 5. The toxicological reference values for use in the human health risk assessment are summarized in Appendix I, Table 6.

Incident Reports

Broflanilide is a new active ingredient pending registration for use in Canada and the United States, and as of 4 September 2019, no incident reports involving broflanilide had been submitted to the PMRA.

There was a repeated exposure scenario of animals accidentally ingesting seed treated with seed treatment products containing other registered active ingredients that are present in Terexxa F4 Seed Treatment. Of the incidents considered to be associated with the pesticide exposure, the majority of the reported effects were minor to moderate in severity and included effects such as vomiting, tremors and lethargy; a low number of animal deaths were also reported. The presence of multiple active ingredients in the reported products introduces confounding elements due to the simultaneous exposure to other pesticides. Therefore, it is not possible to determine which pesticide may have contributed to the reported health effects in animals. In addition, the concern for the serious effects in animals is tempered by the low acute toxicity potential of Terexxa F4 Seed Treatment. Based on the health concerns identified from incident reports related to seed treatment products, it is proposed that the tags and bags of treated seed include a statement “Keep out of reach of children and animals” to reduce the likelihood of exposure of children and pets to treated seed.

3.1.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database contains the full complement of required studies including gavage developmental toxicity studies in rats and rabbits, and a dietary 2-generation reproductive toxicity study in rats. A supplemental developmental and reproductive toxicity screening study, in which rats were exposed to broflanilide via the diet, was also available.

With respect to potential prenatal and postnatal toxicity, there was no indication of increased sensitivity of fetuses or offspring compared to parental animals in the reproductive or developmental toxicity studies. In the 2-generation rat reproductive toxicity study, there was a decrease in offspring bodyweight, and decreases in offspring brain, thymus and spleen weights; however, these effects occurred in the presence of maternal toxicity. Additionally, increased pup death was noted at the highest dose level in the early post-natal period, resulting in a lower viability index. Concern for this serious finding was low given that it was only observed above the limit dose of testing and in the presence of maternal toxicity. Similarly, in the supplemental developmental/reproductive toxicity screening study there were reproductive and offspring effects (one litter loss and increased pup death) observed only at the limit dose and in the presence of maternal toxicity.

Overall, the database is adequate for determining the sensitivity of the young. There is a low level of concern for sensitivity of the young as effects in the young are well-characterized and occurred in the presence of maternal toxicity. On the basis of this information, the *Pest Control Products Act* factor (PCPA factor) was reduced to onefold.

3.2 Acute Reference Dose (ARfD)

Establishment of an acute reference dose is not required, as an endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies.

3.3 Acceptable Daily Intake (ADI)

To estimate risk following repeated dietary exposure, the dermal no observed adverse effect level (NOAEL) of 1.7 mg/kg bw/day from the 12-month interim sacrifice group in the 24-month dietary chronic toxicity/oncogenicity study in the rat was selected. It is worth noting that the lower NOAEL from the 12-month interim sacrifice group, when compared to the 24-month sacrifice group, was due to dose selection as the 12-month group included an additional low-dose level that was not tested in the 24-month portion of the study. At the lowest observed adverse effect level (LOAEL) of 5.7 mg/kg bw/day, increases in adrenal gland vacuolation and adrenal gland and heart weight, as well as in reticulocytes and cholesterol were observed. This study provides the lowest NOAEL in the database. The selection of this study for use in risk

assessment is supported by a similar parental NOAEL of 2.3 mg/kg bw/day observed in the 2-generation reproductive toxicity study in rats. At the LOAEL of 7.5 mg/kg bw/day in the 2-generation reproductive toxicity study, increases in adrenal gland vacuolation and adrenal gland weight were observed. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the PCPA factor was reduced to onefold. The composite assessment factor (CAF) is thus 100.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{1.7 \text{ mg/kg bw/day}}{100} = 0.02 \text{ mg/kg bw/day of broflanilide}$$

The ADI provides a margin of over 50 000 to the dose levels at which increased pup deaths were observed in the supplemental reproductive/developmental toxicity screening study and the 2-generation dietary reproductive toxicity study in rats.

Cancer Assessment

Broflanilide is considered to have carcinogenic potential based on the weight of evidence. There was evidence of treatment-related tumours in rats in the form of increased incidences of Leydig cell adenomas in males, and increased incidences of ovarian luteomas, ovarian granulosa cell tumours, and ovarian tumours of sex cord stromal origin (combined incidences of luteomas, thecomas, granulosa cell tumours, and sex cord stromal tumours), as well as adrenal cortex carcinomas and uterine adenocarcinoma in females. The supporting data for the proposed Leydig cell adenoma MOA were not considered adequate due to inconsistent results and a paucity of data to support certain key events. The applicant did not propose a MOA for the other tumour types identified. Furthermore, the applicant's argument that tumours were observed at high dose levels that exceeded a KMD, and were, therefore, not relevant to human health, was not supported. Therefore, a linear low-dose extrapolation (non-threshold approach) was deemed appropriate for the cancer risk assessment. A cancer potency factor (q^1*) of 2.1×10^{-3} (mg/kg bw/day)$^{-1}$ was derived based on the incidence of Leydig cell adenomas in male rats treated orally with broflanilide. This cancer potency factor was selected as it reflected the most conservative potency factor for the various tumour types and was considered relevant to all routes of exposure except for the inhalation route. Given the low oral absorption demonstrated for broflanilide at the dose levels tested in the oral toxicity studies, a 10-fold factor was applied to the inhalation cancer risk assessment to account for differences in absorption when extrapolating from an oral toxicity study to the inhalation route of exposure, for which absorption is assumed to be near 100%. Therefore, for the inhalation cancer risk assessment a q^1* of 2.1×10^{-2} (mg/kg bw/day)$^{-1}$ was determined to be appropriate. The cancer potency factor was not adjusted for assessing cancer risks via the dermal route of exposure, as the available data suggested that absorption of broflanilide via the dermal route is also quite low and similar to absorption via the oral route.

3.4 Occupational and Residential Risk Assessment

3.4.1 Occupational and Residential Routes and Durations of Exposure

Cimegra

Workers are expected to be exposed via the dermal and inhalation routes during mixing, loading and application of Cimegra during in-furrow and/or T-band application at planting to potato or corn. The duration of exposure is expected to be short-term in duration. Due to the use pattern of Cimegra, where it is applied to subsurface soil during in-furrow and/or T-band application at planting, exposure to postapplication workers entering fields is expected to be negligible.

Teraxxa F4 and Teraxxa

Commercial seed treatment workers, mobile treaters, on-farm treaters, planters and anyone handling seed treated with Teraxxa F4 or Teraxxa are expected to be exposed via the dermal and inhalation routes. The duration of exposure for those working in commercial seed treatment facilities is expected to be intermediate-term and short-term for mobile and on-farm treaters and those planting and handling treated seed on-farm.

3.4.2 Toxicological Reference Values

Short- and Intermediate-term Dermal

For short- and intermediate-term dermal occupational exposures, the NOAEL of 1000 mg/kg bw/day from the 28-day dermal toxicity study in rats was selected for risk assessment. A LOAEL was not established since there were no adverse effects observed up to the highest dose level tested.

The target margin of exposure (MOE) is 100 for short-term occupational exposure scenarios, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The target MOE is 300 for intermediate-term occupational exposure scenarios, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, as well as an additional threefold factor to account for uncertainty in extrapolating from a short-term study to a longer-term exposure scenario, given evidence in the database suggesting a slight increase in toxicity with an extended duration of dosing. The selection of this study is protective of all populations, including nursing infants and the unborn children of exposed female workers.

Short- and Intermediate-term Inhalation

For short- and intermediate-term inhalation occupational exposures, the no observed adverse effect concentration (NOAEC) of 0.041 mg/L (equivalent to 8.4 mg/kg bw/day) from the 28-day inhalation toxicity study in rats was selected for risk assessment. At the lowest observed adverse effect concentration (LOAEC) of 0.193 mg/L (equivalent to 52 mg/kg bw/day), adrenal gland and ovarian vacuolation, extramedullary hematopoiesis of the spleen, and increased adrenal gland and heart weight were observed. The target MOE is 100 for short-term occupational exposure scenarios, which includes uncertainty factors of 10-fold for interspecies extrapolation

and 10-fold for intraspecies variability. The target MOE is 300 for intermediate-term occupational exposure scenarios, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, as well as an additional threefold factor to account for uncertainty in extrapolating from a short-term study to a longer-term exposure scenario, given evidence in the database suggesting a slight increase in toxicity with an extended duration of dosing. The selection of this study is protective of all populations, including nursing infants and the unborn children of exposed female workers.

Aggregate Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from dietary (food and drinking water), residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation). For broflanilide, the aggregate assessment consisted of combining food and drinking water exposure only, since residential exposure is not expected. An endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies; therefore, an acute oral aggregate risk assessment is not required. The most relevant toxicological endpoint and assessment factors for chronic oral aggregate exposure are the same as those selected for the ADI (see Section 3.3).

Cumulative Assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pesticides was undertaken for broflanilide. Based on its pesticidal MOA, broflanilide has been classified into IRAC Group 30: GABA-gated chloride channel allosteric modulators. The only other active ingredient included in IRAC Group 30 is fluxametamide. Fluxametamide is a novel insecticide belonging to the isoxazoline class of chemicals; exposure to this pesticide is not expected to occur in Canada. As previously noted, binding of broflanilide to GABA receptors is expected to be highly specific to invertebrates given interspecies differences in subunit amino acid. There was no evidence in the toxicological database to suggest that broflanilide exerts its toxic action in mammals via GABA-receptor binding. Broflanilide has also been classified as a diamide insecticide based on its chemical structure (the presence of two amide groups substituted on a benzene ring), along with other insecticides registered for use in Canada, including chlorantraniliprole, cyantraniliprole, and cyclaniliprole. However, broflanilide is further sub-categorized as a meta-diamide, meaning that the amide groups are located in the meta-substituted positions of the benzene ring, whereas chlorantraniliprole, cyantraniliprole, and cyclaniliprole are considered anthranilic diamides. Anthranilic diamides have their amide groups in the ortho-substituted positions of the benzene ring and are known to target insect ryanodine receptors. It has been determined that there is insufficient evidence to link the apical endpoints observed in the toxicology databases for the anthranilic diamide class of pesticides to a common mechanism. Overall, for the current evaluation, the PMRA did not identify information indicating that broflanilide shares a common mechanism of toxicity with other pest control products. Therefore, no cumulative health risk assessment is required at this time.

3.4.2.1 Dermal Absorption

The applicant submitted an in vivo dermal absorption study where male Wistar Han IGS rats were administered nominal doses of 1.25, 2.5 or 1000 µg/cm^2 of ^{14}C-MCI 8007 in BAS 450 00 I and monitored up to 120 hours post-dosing. The total exposure duration was 8 hours prior to conducting the first skin wash. Excreta (feces and urine) were collected at multiple time points from the time of dosing to the time of sacrifice for all exposure groups. Analyzed matrices included excreta, cage wash, blood cells, plasma, carcass, protective cover, skin wash, skin (at and surrounding the application site) and tape strips. Overall mean group recoveries of the applied dose of ^{14}C-MCI 8007 ranged from 93–109%.

Estimates of dermal absorption (total absorbed dose) were calculated by summing the amount recovered (% of the applied dose) in the stratum corneum (tape strips), application skin test site, untreated skin, cage wash, urine, faeces, blood and carcass. The study authors did not include the skin at the application site and surrounding area or the tape strips (stratum corneum) in the dermal absorption estimates but these have been incorporated into the estimates as the data demonstrated that the skin bound residues continued to be bioavailable. Mean group residues found in the stratum corneum ranged from 0.07–1.07%, while mean group residues in the application skin site ranged from 0.65 to 8.19%. Mean dermal absorption values for the group sacrificed at 120 hours (n=4), were 5.2%, 5.3% and 2.4% at the low, mid and high doses respectively.

Mean group total absorbed doses with a skin wash at 8 hours ranged from 4.4–7.8%, 4.6–10.4% and 2.3–5.7% of the applied doses from the low, mid and high dose groups, respectively. Maximum mean percent absorption values were observed for the groups of rats sacrificed at 8 hours for all dose groups due to residues remaining in the skin at the application site. While some of the residues remaining in the skin after 8 hours were absorbed, as evidenced by increasing percentages of the applied dose in the faeces and carcass over time, some of the residues were also recovered in the second skin wash. These results indicate that the dermal absorption values from the groups sacrificed after 8 hours likely overestimate the percent of the dose that will be taken up into the body. The observed pattern of dermal absorption suggests that ^{14}C-MC1 8007 might reach a threshold of absorption with increasing dose as the amount of total absorbed dose decreases as the applied dose concentration increases.

Given the variability in the mean dermal absorption between the various exposure groups, in order to select a conservative value to represent dermal absorption, the maximum group mean dermal absorption was chosen. The maximum mean dermal absorption (10.4%) was observed for the mid dose (2.5 µg/cm^2) exposure group when sacrificed immediately after the 8 hour exposure period. Therefore, a dermal absorption value of 10% was selected for risk assessment purposes. Additionally, there were some minor limitations to the study; however, these limitations did not impact the confidence in the selected dermal absorption value.

The dermal absorption study was not required in the non-cancer risk assessment as the NOAEL was derived from a dermal toxicological study representing the durations of exposure relevant to the proposed end-use products. The dermal absorption value is typically included in the calculation of the absorbed daily dose (ADD) when estimating the cancer risk. However, in a toxicokinetic study, where Wistar rats were given a single dose (gavage) of radiolabelled

broflanilide at 5 mg/kg bw or 500 mg/kg bw, oral absorption of the administered dose was 14–23% and 2% for the low and high dose, respectively. The rat in vivo dermal absorption study demonstrated that absorption of broflanilide ranged from 2.3–10.4%, which is within the range of oral absorption demonstrated in the toxicokinetic study. As such, dermal and oral absorption are considered to be similar and thus, the dermal absorption value of 10% will not be applied to the dermal exposure calculations since an oral toxicity study was relied upon to determine the cancer potency factor.

3.4.3 Occupational Exposure and Risk

3.4.3.1 Mixer/loader/applicator Exposure and Risk Assessment

Cimegra

Non-Cancer Risk Assessment

Exposure estimates were derived for mixers/loaders/applicators handling Cimegra for the in-furrow and/or T-band treatment of potato and corn. The dermal and inhalation exposure estimates are based on workers wearing a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes and were generated using the unit exposure values from the Agricultural Handlers Exposure Task Force (AHETF) database.

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted.

Dermal and inhalation exposures were estimated by combining the unit exposure values with the amount of product handled per day. Exposures were normalized to mg/kg bw/day by using 80 kg adult body weight.

Exposure estimates were compared to the toxicological reference values to obtain the margin of exposure (MOE); the target MOE is 100 for short-term exposures (Appendix I, Table 6). Calculated MOEs are above the target MOE of 100 for M/L/A scenarios for potato and corn and are, therefore, not of concern (Appendix I, Table 7).

Cancer Risk

In addition, a cancer risk assessment was conducted for M/L/As of Cimegra. The cancer risk was calculated separately for both the dermal and inhalation routes by estimating the ADD and then the lifetime average daily dose (LADD). The ADD was based on exposure estimates from the non-cancer risk assessment as presented in Appendix I, Table 7. The LADD was calculated by amortizing the ADD over the number of exposure days per year and the working lifetime of an agricultural worker. The LADD for each route was multiplied by the route-specific cancer potency factors (q^1*) prior to being combined for the total cancer risk.

For occupational workers, lifetime cancer risks of less than 1×10^{-5} is considered acceptable and as the total cancer risk for Cimegra is less than 2×10^{-7}, cancer risks are not of concern (Appendix I, Table 8).

Teraxxa F4 and Teraxxa

Non-Cancer Risk Assessment

Commercial Facilities and Mobile Treaters

Broflanilide is proposed as a seed treatment of barley, buckwheat, pearl millet, proso millet, oats, rye, sorghum, triticale, canary seed, annual canarygrass (grown for human consumption) and wheat (winter, spring and durum). Individuals have the potential for exposure to broflanilide while treating seed in commercial seed treatment facilities and by mobile treaters as well as while bagging, sewing and stacking of treated seed in commercial treatment facilities and during clean-up and repair of treatment equipment. Occupational exposure to Teraxxa F4 or Teraxxa is characterized as intermediate-term in duration for seed treatment workers in commercial facilities and short-term for mobile treaters and occurs predominantly by the dermal and inhalation routes.

To estimate exposure to those mixing/loading, treating and calibrating and other workers in commercial facilities (including mobile treaters), two different wheat passive dosimetry studies were used. Wheat was used as the surrogate seed for all cereal seeds. An open pour passive dosimetry study was used for treaters in commercial facilities and mobile treaters. This type of study may overestimate exposure to treaters in commercial facilities, as they typically use closed mix/load/treatment/calibration systems; however, it is representative of mobile treaters who may use open mix/load systems. The unit exposure values for treaters were based on subjects wearing a single layer of personal protectice equipment (PPE) (long-sleeved shirt and long pants) and chemical-resistant gloves. This is less PPE than that on the proposed label, which includes coveralls over a single layer, so the latter will be maintained.

For workers in commercial facilities bagging/sewing/stacking treated cereals and cleaning seed treatment equipment, the passive dosimetry study was selected based on the similarity between the use pattern of the study and the new end-use products. Workers in the study were monitored wearing a single layer and no chemical resistant gloves. This is also less PPE than that on the proposed label, which includes coveralls over a single layer. The cleaners from this surrogate study wore chemical-resistant coveralls and chemical-resistant gloves which is greater PPE than the coveralls over a single layer on the proposed label. As such, the PPE on the label will be amended to match that of the study.

The risk assessment is presented for wheat only but is representative of exposure to the other cereals. Similarly, exposure to workers in commercial treatment facilities is representative of that of mobile treaters because of the larger seed throughput capacities in commercial facilities.

Dermal and inhalation exposures were calculated by combining unit exposure values with the maximum application rate and the AHETF throughput values for wheat. Exposures were normalized to mg/kg bw/day by using 80 kg adult body weight. The calculated MOEs were greater than the intermediate-term target MOE of 300 and the short-term target MOE of 100 for both dermal and inhalation routes (Appendix I, Table 9). As such, no health risks of concern are expected for workers in commercial treatment facilities or mobile treaters provided they wear the PPE specified on the proposed label.

On-Farm Treatment and Planting

Exposures to workers treating cereal seeds on-farm and then planting or only planting seeds treated in commercial facilities were represented through two surrogate passive dosimetry studies. The on-farm treating and planting study monitored workers wearing a single layer of PPE and chemical-resistant gloves and the planting study monitored workers wearing coveralls over a single layer of PPE and chemical-resistant gloves. The non-cancer risk was calculated by combining the application rate, the seeding rate for wheat and the maximum planting area per day with unit exposure values. The exposure and risk estimates for on-farm treaters and planters are presented in Appendix I, Table 10. As the calculated MOEs are above the short-term target MOE of 100, there are no health risks of concern for on-farm treaters when wearing a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks or for planters when wearing coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. As the dermal and inhalation unit exposure values for planters are derived from studies which used closed cab tractors, this restriction will be added to the label.

Cancer Risk Assessment

A cancer risk assessment was conducted for workers in direct contact with Teraxxa F4 and Teraxxa or with seeds treated with the end-use products. The cancer risk was calculated separately for both the dermal and inhalation routes by estimating the ADD and then the LADD. The ADD was based on exposure estimates from the non-cancer risk assessment but amended using a lower seed throughput in commercial facilities. The LADD was calculated by amortizing the ADD over the number of exposure days per year and the working lifetime of an agricultural worker. The LADD for each route was multiplied by the route-specific cancer potency factors (q^1*) prior to being combined for the total cancer risk.

For occupational workers, lifetime cancer risks of less than 1×10^{-5} are considered acceptable and as the total cancer risk for Teraxxa F4 and Teraxxa is less than 4×10^{-6}, cancer risks are not of concern (Appendix I, Table 11).

3.4.3.2 Exposure and Risk Assessment for Workers Entering Treated Areas

Postapplication exposure to workers is expected to be negligible following soil in-furrow and/or T-band application of Cimegra at planting.

3.4.4 Residential Exposure and Risk Assessment

3.4.4.1 Handler Exposure and Risk

As the end-use products containing broflanilide are proposed as commercial marketing class products, a residential handler risk assessment is not required.

3.4.4.2 Postapplication Exposure and Risk

The end-use products containing broflanilide are not proposed for use in residential areas, therefore a postapplication residential risk assessment is not required.

3.4.4.3 Bystander Exposure and Risk

Bystander exposure is expected to be negligible since the potential for drift is expected to be minimal and label restrictions to minimize drift are to be added to the labels.

3.5 Exposure from Drinking Water

3.5.1 Concentrations in Drinking Water

For the human health assessment, estimated environmental concentrations (EEC) in potential drinking water sources are calculated for both groundwater and surface water. For surface water, Pesticide in Water Calculator (PWC) calculates the amount of pesticide entering a water body by runoff and drift, and the subsequent degradation of the pesticide in the water system. EECs are calculated by modelling a total land area of 173 ha draining into a 5.3 ha reservoir with a depth of 2.7 m. Groundwater EECs are calculated by simulating leaching through a layered soil profile and reporting the average concentration in the top 1 meter of a water table.

Drinking water modelling follows a tiered approach consisting of progressive levels of refinement. Level 1 EECs are conservative values intended to screen out pesticides that are not expected to pose any concern related to drinking water. These are calculated using conservative inputs with respect to application rate, application timing, and geographic scenario. Level 2 EECs are based on a narrower range of application timing, methods, and geographic scenarios, and are not considered conservative values that cover all regions of Canada. Only Level 1 modelling was required for broflanilide.

The residue definition consisted of parent broflanilide only. EECs for surface water were calculated based on a single standard scenario. EECs in groundwater were calculated for several scenarios representing different regions of Canada; only the highest EECs from across these scenarios are reported. The surface scenario was run for 50 years, and groundwater scenarios were run for 100 years due to the slower breakthrough of broflanilide in the soil. The major fate inputs used for the modelling are presented in Table 3.5.1. Level 1 EECs of broflanilide are reported in Table 3.5.2. Further details of water modelling inputs and calculations are available upon request.

Table 3.5.1 Major fate inputs for the modelling of broflanilide

Fate Parameter	Value
K_{oc} (L/kg)	5735[1]
Aerobic water half-life (d) at 20 °C	1430[2]
Anaerobic water half-life life (d) at 20 °C	1411[2]
Photolysis half-life (d) at 40 °N	80
Hydrolysis life (d) at pH 7 and 20 °C	Stable
Soil half-life (d) at 25 °C	4168[3]

1 20^{th} percentile of 7 values
2 Longer of 2 available values
3 90^{th} percentile confidence bound on the mean of four soil half-lives

Table 3.5.2 EECs (µg a.i./L) for the drinking water risk assessment of broflanilide

Use pattern	Groundwater (µg a.i./L)		Surface Water (µg a.i./L)	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
A single application of 25 g a.i./ha	0.72	0.72	0.97	0.39

[1] 90th percentile of daily average concentrations
[2] 90th percentile of 365-day moving average concentrations
[3] 90th percentile of the peak concentrations from each year
[4] 90th percentile of yearly average concentrations

3.6 Food Residues Exposure Assessment

3.6.1 Residues in Plant and Animal Foodstuffs

The residue definition for risk assessment and enforcement in plant products is broflanilide. The residue definition for enforcement and risk assessment in animal commodities is broflanilide and the metabolite DM-8007, expressed as parent equivalents. The data gathering/enforcement analytical methods are valid for the quantitation of broflanilide in plant matrices, and broflanilide and the metabolite DM-8007 residues in livestock matrices. The residues of broflanilide are stable in five crop commodity categories (high water, high oil, high protein, high starch and high acid content) for up to 24 months when stored at approximately -20 °C. Therefore, broflanilide residues are considered stable in all plant matrices and processed fractions for up to 24 months. Broflanilide and the metabolite DM-8007 residues are stable in all livestock matrices for up to 60 days. The raw agricultural commodities of potato, field corn and wheat were processed. Adequate feeding studies were carried out to assess the anticipated residues in livestock matrices resulting from the current uses. Crop field trials conducted throughout Canada and the United States using end-use products containing broflanilide at exaggerated rates in or on potato, field corn, sweet corn, wheat and barley are sufficient to support the proposed maximum residue limits.

3.6.2 Dietary Risk Assessment

Chronic (non-cancer and cancer) dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™).

3.6.2.1 Acute Dietary Exposure Results and Characterization

No appropriate toxicological reference value attributable to a single dose for the general population (including children and infants) was identified.

3.6.2.2 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the basic chronic non-cancer analysis for broflanilide: 100% crop treated, default processing factors (where available), the proposed MRLs for the plant and animal commodities. The basic chronic dietary exposure from all supported broflanilide food

uses (alone) for the total population, including infants and children, and all representative population subgroups is 5.6% of the ADI. Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that chronic dietary exposure to broflanilide from food and drinking water is 1.3% (0.000253 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for Children 1–2 years old at 5.7% (0.001134 mg/kg bw/day) of the ADI.

The basic chronic cancer risk assessment was conducted with the same criteria used for the chronic non-cancer assessment. The lifetime cancer risk from exposure to broflanilide in food and drinking water was estimated to be 5×10^{-7} for the general population, which is not of health concern.

3.6.3 Aggregate Exposure and Risk

The aggregate risk for broflanilide consists of exposure from food and drinking water sources only; there are no residential uses.

3.6.4 Maximum Residue Limits

Table 3.6.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Tuberous and corm vegetables (Crop Subgroup 1C)	0.04
Eggs, fat, meat, and meat byproducts of cattle, goats, hogs, horses, sheep and poultry, milk	0.02
Cereal grains (CG 15), except rice and wild rice, amaranth grain, annual canarygrass seeds, cañihua grain, chia grain, cram-cram grain, huauzontle grain, quinoa, spelt grain, teff grain	0.01[1]
Food commodities (other than those listed in this item)	0.01[1]

[1] The uses are not on the Canadian label. Proposed MRLs are to allow importation from the United States.

MRLs are proposed for each commodity included in the listed crop groupings in accordance with the Residue Chemistry Crop Groups webpage in the Pesticides section of Canada.ca

For additional information on Maximum Residue Limits (MRLs) in terms of the international situation and trade implications, refer to Appendix II.

The nature of the residues in animal and plant matrices, analytical methodologies, field trial data, and acute and chronic dietary risk estimates are summarized in Appendix I, Tables 1, 12 and 13.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Hydrolysis is not expected to be an important route of dissipation for broflanilide in the environment as < 10% hydrolyzed after 5 days at 50 °C in pH 4, 7, and 9 buffer solutions. Phototransformation on soil is also not expected to be an important route of dissipation for

broflanilide as <10% was transformed after 14 days of continuous irradiation. Similarly, phototransformation in water under neutral conditions (pH 7) is not expected to be an important route of dissipation for broflanilide (half-life = 80 days). Under acidic and basic conditions there is a potential for phototransformation (half-lives = 17 and 4 days at pH 5 and 9, respectively). Four major aqueous phototransformation products were identified: AB-oxa, S(BR-OH)-8007, MFBA and benzoic acid.

Biotransformation is not an important route of dissipation for broflanilide based on laboratory studies. Broflanilide is persistent in both soil and aquatic systems. In laboratory aerobic and anaerobic biotransformation studies, the DT_{50} values for broflanilide were 157–5742 days in soil and 871–1411 days in aquatic systems. The only major transformation product identified was DC-8007. Broflanilide was found to be strongly bound to soil and sediment.

Terrestrial field studies showed that the dissipation of broflanilide was significantly faster under field conditions compared to the laboratory, with field DT_{50} values of 3.3–182 days. All transformation products observed under field conditions were minor (<10% applied radioactivity (AR)) and were the same as those observed in the laboratory studies. Broflanilide and its transformation products were not detected below the 15 cm soil depth, indicating that movement to groundwater is not anticipated. Overall, taking into consideration results of laboratory studies, sorption data, assessments using Groundwater Ubiquity Scores (GUS) and criteria of Cohen et al. (1984), and terrestrial field dissipation studies, broflanilide and its residues are unlikely to leach to groundwater. Broflanilide and its residues are persistent, however, are likely irreversibly bound to soil and therefore not bioavailable. The residue definition was parent only for both drinking water and ecoscenario, as all transformation products were excluded on the basis of exposure.

The log octanol-water partition coefficients (K_{ow}) of 4.34–5.75 for broflanilide suggest a potential for bioaccumulation; however, bioconcentration factors (BCF) of 96–119 demonstrated that broflanilide did not bioconcentrate appreciably in fish tissue.

Broflanilide is non-systemic. Therefore, broflanilide applied as an in-furrow spray or seed treatment is expected to mostly remain in the soil at the point of application.

The transformation products of broflanilide detected in laboratory and field dissipation studies are summarized in Appendix I, Table 14. The fate and behaviour of broflanilide and its transformation products in the environment is summarized in Appendix I, Table 15.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. The EECs are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated by taking into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including

invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC). If the screening level risk quotient is below the LOC, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the LOC, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and may consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

The individual fungicide components comprising the proposed end-use product, Teraxxa F4 Insecticide and Fungicide Seed Treatment, are all registered in Canada. The proposed use pattern, including application rates and crops, are consistent with the current registered use pattern for the registered co-formulated active ingredients. Only risk characterization from the proposed new active ingredient, broflanilide is discussed here.

4.2.1 Risks to Terrestrial Organisms

A risk assessment for broflanilide was conducted for terrestrial organisms based on available toxicity data. For acute toxicity studies, uncertainty factors (UF) of 1/2 and 1/10 of the EC_{50} (LC_{50}) are typically used in modifying the toxicity values for terrestrial invertebrates, birds, and mammals when calculating risk quotients. No uncertainty factors are applied to chronic NOEC endpoints. A summary of terrestrial toxicity data for broflanilide, its transformation products, and end-use products is presented in Appendix I, Table 16. The screening level risk assessment for broflanilide is presented in Appendix I, Table 17, for terrestrial organisms other than birds and mammals, and Appendix I, Table 18, for birds and mammals.

Earthworms: The EEC for a direct application on soil was calculated using the maximum proposed application rate of Cimegra Insecticide (25 g a.i./ha). There are also two proposed seed treatment products; however, seed treatments are expected to result in much lower soil levels of broflanilide than spray applications and are thus considered to be covered by the soil application EECs. As a conservative estimate, all endpoints were compared to the Cimegra application rate.

Broflanilide, its transformation products, and end-use products were not acutely toxic to earthworms at concentrations up to 1000 mg/kg dw soil. Chronic exposure to broflanilide can affect reproduction at rates greater than 30 mg a.i./kg dw soil.

The risk quotients for earthworms resulting from acute and chronic exposure to broflanilide, its end-use products and its transformation products do not exceed the level of concern at the screening level. The use of broflanilide is not expected to pose an acute or chronic risk to earthworms.

Other soil-dwelling invertebrates: Chronic broflanilide exposure in soils significantly affected the survival and reproduction of the soil mite, *Hypoaspis aculeifer*, at concentrations of 0.36 mg a.i./kg dry soil and greater. The risk quotient for *Hypoaspis aculeifer* resulting from chronic exposure to broflanilide does not exceed the level of concern at the screening level. The use of broflanilide is not expected to pose a chronic risk to soil-dwelling invertebrates.

Bees: The pollinator risk assessment followed the tiered framework developed jointly by the PMRA, USEPA (United States Environmental Protection Agency) and CDPR (California Department of Pesticide Regulation) in 2012 with guidance published in 2014 (*Guidance for Assessing Pesticide Risks to Bees*). The tiered risk assessment framework consists of exposure and effects characterization relative to bees and moves from a highly conservative risk assessment at lower tiers to a more realistic assessment at higher tiers.

Tier I screening level assessment

Broflanilide, its transformation product, DM-8007, and end-use products, Cimegra and Teraxxa, were highly toxic to bees on an acute and contact basis. However, other tested transformation products were practically nontoxic. Broflanilide was also toxic to both adult and larval bees on a chronic basis, with NOAEL values based on mortality of 0.62 ng a.i./bee/day and 0.088 ng a.i./larva/day, respectively. The Tier I effects information indicated that bumble bees (a non-*Apis* bee) and honey bees have similar acute oral sensitivity to broflanilide exposure, and bumble bees may be less sensitive from contact exposure. Effect endpoints derived from the Tier I honey bee laboratory studies are considered suitable as a surrogate for non-*Apis* bees, and the results of the Tier I screening and refined risk assessment for *Apis* bees are considered relevant to non-*Apis* bees.

The Tier I risk assessment for oral exposure through pollen and nectar was based on default exposure values and assumed the pesticide might be systemic (Appendix I, Table 17). There was negligible risk to adult bees from acute oral exposure to soil applications. There was a potential risk to adult bees from acute oral exposure to seed treatment applications. There was potential risk identified for adult bees from chronic oral exposure to both soil and seed treatment applications. There was also a potential risk to larval bees from acute oral exposure to seed treatment applications and from chronic oral exposure to both soil and seed treatment applications. In the conservative Tier I approach, it is assumed that all soil-applied and seed-treated pesticides are systemic and able to be transported to pollen and nectar. Broflanilide is not a systemic pesticide, and contact toxicity is its mode of action. Therefore, the risk assessment from oral exposure through pollen and nectar from soil and seed treatments was further refined considering the evidence that broflanilide is not systemic.

For the proposed soil application types (in-furrow and T-band), it is assumed that honey bees will not be directly exposed through contact because they are not expected to be present on the surface of the soil. However, some non-*Apis* bees may be exposed through contact with soil, for

example if they nest in soil. There is not currently an established quantitative method to assess exposure to non-*Apis* bees through soil. Qualitatively, for these proposed uses, there is expected to be minimal exposure of bees nesting in soil, as applications are made in limited areas via in-furrow and T-band, and only to potato and corn. Therefore, it is not likely that broflanilide will be found in important nesting areas for non-*Apis* bees.

For some seed types, bees may also be exposed through pesticide-containing dust generated during planting of treated seed. Generation of dust from planting of treated seed is related to many factors, including the planting equipment and seed type. The proposed seeds to be treated in Canada include small cereal grains only (in other words, wheat, barley, buckwheat, oats, etc.). Small cereal seeds are not typically planted with equipment likely to generate dust during planting. Due to the type of seeds being treated, there is no requirement for use of a dust-reducing fluency agent. Because of the high toxicity of broflanilide to bees, it was determined that best management practices to minimize dust exposure during planting of treated seed will be required to be followed.

Tier II refined assessment

Physical-chemical data: The mobility of a chemical in the environment depends largely on its physical-chemical parameters, including water solubility, octanol/water partition coefficient (log K_{ow}), and coefficient of dissociation (pKa). Broflanilide has low water solubility (0.71 mg/L at 20 °C), as do its transformation products (0.006–1.6 mg/L at 20 °C).

Broflanilide log K_{ow} values range from 4.34–5.91. The Briggs' model used to estimate dietary exposure from soil applications is applicable only for chemicals with log $K_{ow} \leq 5$. Soil partition coefficient (K_{oc}) values for broflanilide range from 3261–23 342 in different soil types, with an average K_{oc} value of 9274. Based on its high K_{oc} and log K_{ow} values, broflanilide's mobility in aqueous environments and across plant root membranes is expected to be very low. Broflanilide's transformation products are also expected to show very low mobility based on the available physical-chemical data.

Overall, the physical-chemical properties of broflanilide and its transformation products indicate that they are unlikely to move systemically through translocation in plant tissues.

Translocation studies to determine residues in bee relevant matrices: Empirical data can be used to refine conservative exposure estimates and reduce uncertainties associated with the Tier I exposure assessment by providing direct pesticide concentration measurements in pollen and nectar resulting from field use. To study root uptake and translocation, three studies investigating concentrations of broflanilide and relevant transformation products in bee-relevant matrices were available to provide residue data for crops, including corn (following soil in-furrow spray), canola (following seed treatment), and oilseed rape (succeeding crop grown in a corn field previously treated with in-furrow application). Data showed essentially no translocation of broflanilide or its transformation products in bee relevant matrices including pollen, nectar or flowers. As no residues were detected, no exposure through pollen and nectar residues is expected.

Plant metabolism data: Plant metabolism studies conducted with radiolabeled broflanilide suggested very limited translocation from treated to untreated plant parts in crops. These results were also observed in a confined rotational crop study where only limited uptake of broflanilide into succeeding crops was observed after application to bare-soil (above the proposed Canadian label rates). The results from the radiolabelled studies indicating a non-systemic nature and very low translocation were confirmed in the supervised field trials. The residue levels found in corn, wheat, and barley destined for human food or animal feed were in most cases below the LOD of the method (0.0002 mg/kg). Findings of residues above LOQ (for example, potatoes) can be best explained by direct contact with treated soil rather than by actual uptake. Overall, plant metabolism studies further support the non-systemic nature of broflanilide and its transformation products.

Crop attractiveness considerations:

Seed treatments: The majority of the cereal grains proposed for seed treatment (barley, pearl millet, proso millet, oats, rye, sorghum, triticale, canary seed, and wheat) are not considered attractive to bees, and thus, the exposure through bee resources such as pollen and nectar would be negligible regardless of whether or not the product is systemic. These cereal grains do not require insect pollination and are not a major source of pollen or nectar for honey bees, bumble bees, or solitary bees. Of the (cereal grains/crops) proposed for seed treatment, the one exception is buckwheat, which is highly attractive to bees and has both pollen and nectar sources. The refined assessment considers the non-systemic nature of broflanilide and its transformation products, and the lack of detectable residues (<LOD 0.0002 mg/kg) in pollen and nectar of canola grown from treated seed. Therefore, buckwheat poses a negligible risk to bees via pollen and nectar as negligible exposure is expected.

Soil treatments: Soil applications are made in-furrow or via T-band, at planting, to corn and potato. Corn and potato have moderate pollinator exposure potential. Corn does not require insect pollination, has only pollen, and is considered a minor source of pollen for honey bees but is not attractive to bumble bees or solitary bees. Potato plants produce no nectar and very little pollen, which is not attractive to most bees. Bumble-bees and solitary bees may visit potato occasionally, whereas honey bees typically do not utilize potato pollen.

Corn and potato have only moderate pollinator exposure potential. Additionally, there is negligible risk expected through pollen and nectar based on the refined risk assessment. The refined assessment considers the non-systemic nature of broflanilide and its transformation products, and the lack of detectable residues in pollen and nectar of soil-treated corn and in canola grown in a field previously containing soil-treated corn (succeeding crop). Corn and potato pose a negligible risk to bees via pollen and nectar as negligible exposure is expected.

SUMMARY OF REFINED RISK ASSESSMENT

The proposed seed treatments include small grain cereals, which are not attractive to bees, with the exception of buckwheat. Proposed soil treatments include potato and corn, both of which have only pollen and a low/moderate potential for pollinator exposure. Residue data showed essentially no translocation of broflanilide or its transformation products in bee-relevant matrices, including pollen, nectar, and flowers. As no residues were detected, no exposure

through residues in pollen and nectar is expected from the proposed uses. Plant metabolism studies and physical-chemical properties support the non-systemic nature of broflanilide. Therefore, risk to bees from broflanilide residues in nectar and/or pollen after soil or seed treatment applications is expected to be negligible.

Based on the high toxicity of broflanilide to bees, best management practices should be followed and are required on the seed treatment product labels to mitigate risks from dust exposure during planting of treated seed.

Beneficial arthropods:

Tier I screening level assessment

Acute exposure on glass plates of the predatory mite, *Typhlodromus pyri*, and the parasitoid wasp, *Aphidius rhopalosiphi*, to the broflanilide end-use product, Cimegra, resulted in significant survival effects. The risk quotients for *Typhlodromus pyri* and *Aphidius rhopalosiphi* exceeded the level of concern for both soil and seed treatment applications (Appendix I, Table 17).

The screening level exposure estimates are highly conservative, as the seed treatment rates and soil application rates are not expected to result in plant residues comparable to those from direct residues on the plant. Foliar applications are not proposed for any of the broflanilide end-use products. The predatory mite, *Typhlodromus pyri*, and the parasitoid wasp, *Aphidius rhopalosiphi*, are not soil organisms; however, they are used as surrogates for all predatory and parasitic arthropods.

Tier II refined assessment

The risk to predatory and parasitic arthropods was further characterized using results from higher tier, extended laboratory toxicity studies. Based on exposure to spray residues of Cimegra on-field from a direct application of 25 g a.i./ha, the risk quotients for survival and reproduction of *Aphidius rhopalosiphi* and *Typhlodromus pyri* exceeded the level of concern (Appendix I, Table 19).

All higher tier toxicity studies with terrestrial arthropod species were conducted with the end-use product, Cimegra. Cimegra Insecticide is proposed as an in-furrow or T-band spray and is not to be applied directly to the soil surface. Most predatory and parasitic arthropod species will not be directly exposed through spray contact because they are not expected to be present on the surface of the soil at the time of application. The risk assessment conducted for earthworms and the soil mite, *Hypoaspis aculeifer*, is more relevant based on broflanilide's use pattern and chemical characteristics. Because broflanilide does not have systemic activity in plants, negligible exposure of non-target arthropods is expected from both soil and seed treatment applications. No mitigation is required on broflanilide end-use product labels.

Birds: Broflanilide was practically nontoxic to birds on an acute basis when exposed by dietary consumption or through oral administration. Effects on reproduction were observed in birds following 21-week exposures in chronic reproductive studies. For the screening level risk assessment (Appendix I, Table 18), the most sensitive endpoints were chosen from acute and reproductive toxicity studies. The risk quotients for birds resulting from acute oral exposure to

broflanilide did not exceed the level of concern at the screening level. The screening level risk quotients for birds resulting from reproductive exposure slightly exceeded the level of concern for small and medium sized birds (RQs of 2.8 and 2.2, respectively).

There were no treatment-related mortalities in any of the acute, dietary, or reproductive studies. The most sensitive endpoint from the reproductive toxicity studies was chosen for the screening level risk assessment, which corresponded to a NOAEL of 4.6 mg a.i./kg bw/day for the mallard duck based on slight statistically significant (5–6%) reductions in survivor weights at the two higher treatment levels. Aside from the reduction in survivor weights and reductions in egg production (19%) at the highest treatment level (35 mg a.i./kg bw/day), there were no other treatment-related effects on any other reproductive parameters measured. In the other available mallard duck study there were slight statistically significant (5–6%) reductions in mean egg shell thickness at all treatment levels resulting in a NOAEL of <32.8 mg a.i./kg bw/day. At higher treatment levels, effects on other reproductive parameters (offspring weight and number of eggs/pen) were observed. In the northern bobwhite study, the NOAEL was determined to be 22.2 mg a.i./kg bw/day based on inhibitions in survivors/hatchlings at the next treatment level.

Based on the effects observed in the reproductive studies, the use of the LOAEL from the mallard duck study (13.0 mg a.i./kg bw/day) is considered to be more representative of potential effects on birds. When using the LOAEL, all risk quotients were <1.0 (Appendix I, Table 20). In addition, there would also be no risk if considering the reproductive NOAEL from the bobwhite quail study (22.2 mg a.i./kg bw/d). Based on these results, the concern for risks of broflanilide to birds is low.

Mammals: Broflanilide and its end-use products were practically non-toxic to rats, with no observed acute toxicity at the highest dose tested. For chronic effects, the two-generation rat reproduction study resulted in a NOAEL of 26 mg a.i./kg bw/day based on decreased body weight/body weight gain in rats observed at the next higher dose. The acute and chronic risk quotients for mammals did not exceed the screening level of concern. Broflanilide is expected to pose negligible risk to mammals.

Terrestrial vascular plants: Cabbage was considered the most sensitive species tested in the seedling emergence study with an ER_{25} of 11 g a.i./ha for survival. No species tested in the vegetative vigor study exhibited significant effects for survival, length, or dry weight at the maximum application rate of 102 g a.i./ha.

The risk to terrestrial vascular plants at the screening level was assessed using the maximum application rate of Cimegra Insecticide (25 g a.i./ha). The calculated risk quotients for in-field exposure slightly exceeded the level of concern for seedling emergence (RQ = 2.3) but did not exceed the level of concern for vegetative vigour. Direct overspray is assumed in the screening level assessment, and the EEC represents a conservative (maximum) exposure to non-target terrestrial plants. Based on the proposed use pattern of broflanilide as an in-furrow soil or seed treatment, off-field exposure to non-target terrestrial plants is not expected. The use of broflanilide is not expected to pose a risk to non-target terrestrial vascular plants.

4.2.2 Risks to Aquatic Organisms

A risk assessment for broflanilide and its transformation products was conducted for freshwater and marine aquatic organisms based on available toxicity data. A summary of aquatic toxicity data is presented in Appendix I, Table 21. For acute toxicity studies, uncertainty factors of 1/2 and 1/10 of the EC_{50} (LC_{50}) are typically used for aquatic plants, invertebrates, and fish species when calculating risk quotients. No uncertainty factors are applied to chronic NOEC endpoints. For groups where the level of concern is exceeded ($RQ \geq 1$), a refined Tier 1 assessment is conducted to determine risk resulting from spray drift and runoff separately. Risk quotients were calculated based on the highest maximum application rate for all uses. The screening-level and Tier 1 refined risk quotients for broflanilide are summarized in Appendix I, Tables 22 and 23.

Invertebrates:

Pelagic invertebrates: Broflanilide was very highly toxic to aquatic invertebrates on an acute basis, with the lowest EC_{50} = 21.5 ng a.i./L for the mysid shrimp. The mysid shrimp also had the most sensitive chronic NOEC of 6.23 ng a.i./L, with effects on survival, growth, and reproduction. The screening level risk quotients for acute and chronic exposure of *Daphnia magna* to broflanilide and its transformation products do not exceed the level of concern at the screening level. Therefore, the use of broflanilide is not expected to pose a risk to freshwater invertebrates.

For marine invertebrates, the screening level risk quotients for acute and chronic exposure of the mysid shrimp, *Americamysis bahia*, to broflanilide exceeded the level of concern (RQs of 290 and 501, respectively). Acute exposure to broflanilide's transformation products does not exceed the level of concern. The screening level risk quotient for acute exposure of the eastern oyster, *Crassostrea virginica*, to broflanilide does not exceed the level of concern. The acute and chronic risk of broflanilide to marine invertebrates was further characterized through the refined runoff assessment.

Benthic invertebrates: Toxicity tests with freshwater and marine invertebrates conducted with midges (*Chironomus* sp.) and amphipods (*Hyalella azteca* and *Leptocheirus plumulosus*) indicate that benthic invertebrate species are generally equally sensitive to acute and chronic broflanilide exposure. These tests were designed to simulate exposure to accumulated pesticide in sediment from runoff. The risk of broflanilide to freshwater and marine benthic invertebrates was characterized directly through the refined aquatic risk assessment.

Refined risk assessment (runoff)

The EEC used for the screening level assumes a direct application to a water body. In order to better characterize the risk, the risk from exposure to runoff was determined. It is noted that exposure of aquatic organisms through spray drift is negligible from in-furrow or T-band (10 to 20 cm band over the top of the open seed furrow) applications and will not occur from seed treatment applications. Spray buffer zones are not required for the proposed broflanilide end-use products.

Exposure through surface run-off was estimated using the PWC model, which simulates pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. The water body consists of a 1 ha wetland with an average depth of 80 cm and a drainage area of 10 ha. The risk quotients for exposure to broflanilide through runoff are provided in Appendix I, Table 23. Two EECs were used for each organism endpoint to represent the highest soil application (corn T-band) and highest seed treatment (spring wheat). Based on the toxicity endpoints and EECs representing the 90th percentile of concentrations for a timeframe reflecting the exposure duration of the toxicity tests, the level of concern is still exceeded for freshwater and marine invertebrates (Appendix I, Table 23).

Runoff EECs for both marine and freshwater exposures are calculated using models that assume no outflow. This is a very conservative assessment as the resulting EECs do not account for tides and dilution present in the Canadian marine environment. The primary runoff risk is for chronic exposure of pelagic marine invertebrates. Broflanilide is expected to partition to sediment; therefore, chronic exposure would be more likely for benthic (sediment-dwelling) invertebrates. Studies show that broflanilide is less toxic to benthic invertebrates than pelagic invertebrates.

Seed treatments had lower RQs than soil applications (seed treatment maximum RQ = 5.8; soil application maximum RQ = 91). The model conservatively assumes 100% removal of active ingredient from the seeds into surrounding soil, therefore the runoff risk from seed treatment uses is considered to be negligible and no mitigation measures are required for runoff for the two seed treatment products. In order to mitigate potential exposure of broflanilide to freshwater and marine invertebrates from soil applications, standard label statements to mitigate runoff into aquatic habitats are required on the Cimegra end-use product label.

Fish: Broflanilide is considered highly toxic to most freshwater and marine fish on an acute basis; however, no mortality was observed at the highest tested concentration (which was at or near the limit of solubility) for some fish species. In chronic studies, effects on fish survival and growth were observed, with the most sensitive NOEC being 11.1 µg a.i./L for sheepshead minnow. The risk quotients for freshwater and marine fish resulting from acute and early-life stage exposure to broflanilide do not exceed the level of concern at the screening level. The use of broflanilide is not expected to pose a risk to freshwater and marine fish.

Amphibians: Using the endpoints from acute and early-life stage studies with fish as a surrogate, along with an EEC for broflanilide in a 15-cm deep body of water, the risk quotients for amphibians resulting from acute and early-life stage exposure to broflanilide do not exceed the level of concern at the screening level. The use of broflanilide is not expected to pose a risk to amphibians.

Algae: The toxicity of broflanilide was tested with four different algae species. The most sensitive species was the marine diatom (*Skeletonema costatum*) with an IC_{50} of 0.31 mg/L. For all other species, the IC_{50} was higher than the highest concentration tested (at or near the limit of solubility). The risk quotients for freshwater and marine algae resulting from acute exposure to broflanilide do not exceed the level of concern at the screening level. The use of broflanilide is not expected to pose a risk to freshwater or marine algae.

Aquatic vascular plants: In a study with the aquatic vascular plant, *Lemna gibba*, there were no treatment-related effects at the highest tested concentration. The risk quotient for aquatic vascular plants resulting from exposure to broflanilide does not exceed the level of concern at the screening level. The use of broflanilide is not expected to pose a risk to aquatic vascular plants.

4.2.3 Environmental Incident Reports

Environmental incident reports are obtained from two main sources: the Canadian pesticide incident reporting system (including both mandatory reporting from the registrant and voluntary reporting from the public and other government departments) and the USEPA Ecological Incident Information System (EIIS). Specific information regarding the mandatory reporting system regulations that came into force 26 April 2007, under the *Pest Control Products Act* can be found on the Report a Pesticide Incident page on Canada.ca .

Broflanilide is a new active ingredient pending registration for use in Canada. As of 4 September 2019, no incident reports had been submitted to the PMRA. The USEPA EIIS, which was last updated on 5 October 2015, did not have any environment incidents involving broflanilide.

A number of incident reports involving the registered active ingredients (pyraclostrobin, fluxapyroxad, triticonazole and metalaxyl) in the proposed end-use product, Teraxxa F4 Insecticide and Fungicide Seed Treatment, were available. The reported incidents were mainly minor in severity or had unlikely causality. Many involved products containing multiple active ingredients thus introducing confounding elements due to the simultaneous exposure to other pesticides. Furthermore, for many of the incidents, the exposure pathways are not relevant to the proposed seed treatment product (for example, direct application exposure, drift, etc.) or are related to potential misuse, product spills, or possible direct damage to the treated crop.

The environmental precautions and directions for use statements on the Teraxxa F4 Seed Treatment label are expected to mitigate environmental risks associated with accepted use of the product. No additional mitigation measures are recommended based on the available incident reports.

5.0 Value

Value information reviewed in support of Cimegra included scientific rationales and 12 field trials on wireworm in potato, 4 field trials on wireworm in corn, and 4 trials on corn rootworm (northern and western) in corn. Wireworm species identified in the potato trials were *Conoderus* sp., *Melatonus* sp., *Limonius californicus, Hypnoides bicolor, Agriotes obscurus, and Agriotes sputator*. Wireworm species identified in the corn trials were *Limonius infuscatus* and *Melanotus cribulosus*. Trials were conducted in Canada and the United States. Applications of Cimegra in the efficacy field trials demonstrated control of wireworms in potato and wireworms and corn rootworm in corn. The trials supported a claim that Cimegra, when applied in-furrow at an application rate of 250 mL product per ha, controls wireworms in potato and wireworms and corn rootworm (northern and western) in corn. No phytotocixity was observed in any of the trials.

Value information reviewed in support of Teraxxa and Teraxxa F4 included rationales and 12 field trials conducted in Canada and the United States on wireworm in cereals (spring barley and spring wheat). Wireworm species identified in these trials were *Limonius californicus, Limonius agonis, Limonius* spp., *Agriotes obscurus, Agriotes sputator,* and *Agriotes mancus*. The field trials also assessed crop safety of both Teraxxa and Teraxxa F4. In addition to the field trials, two laboratory studies were conducted to evaluate wireworm mortality upon exposure to insecticide treatments. Six additional fungicide trials were conducted to confirm that there was no antagonism between the broflanilide and fungicides in the Teraxxa F4 premix. Applications of Teraxxa at 16.7 mL product per 100 kg seed and Teraxxa F4 at a rate of 300 mL product per 100 kg seed in the efficacy field trials demonstrated control of wireworms. Follow-up studies on wireworm populations in the year following treatment and the additional laboratory trials further supported the claim that broflanilide seed treatments provide control of wireworm. The value information supported claims that Teraxxa F4 controls or suppresses certain seed- and soil-borne diseases of specified small cereal grains and wheat. No phytotoxicity was observed in any of the trials.

Broflanilide has value as a new mode of action for use in resistance management. Alternative active ingredients registered for control of wireworms and/or corn rootworms in the labelled crops include IRAC mode of action Group 1B (chlorpyrifos), Group 3A (bifenthrin, tefluthrin), Group 4A (clothianidin, thiamethoxam, imidacloprid) and Group 28 (cyantraniliprole, chlorantraniliprole) insecticides. There are no reported cases of cross-resistance of broflanilide to currently registered insecticide modes of action.

The reviewed efficacy trials demonstrated that broflanilide can provide control of wireworms and corn rootworms. In addition, broflanilide was demonstrated to reduce wireworm populations in treated fields. Broflanilide has value in providing control of corn rootworms and wireworms, which are major pests of the labelled crops, and wireworms are difficult to kill with currently registered pest control products. Details of the supported uses can be found in Appendix I, Table 24.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The *Toxic Substances Management Policy* (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, in other words, those that meet all four criteria outlined in the policy: persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*. The *Pest Control Products Act* requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, broflanilide and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that broflanilide and its transformation products do not meet all of the TSMP Track 1 criteria (Appendix I, Table 25).

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.*[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations, including the *Toxic Substance Management Policy* and *Formulants Policy*,[8] and taking into consideration the *Ozone-Depleting Substance Regulations*, 1998, of the *Canadian Environmental Protection Act* (substances designated under the *Montreal Protocol*).

The PMRA has reached the conclusion that broflanilide and its end-use products, Cimegra Insecticide, Teraxxa Insecticide Seed Treatment, and Teraxxa F4 Insecticide and Fungicide Seed Treatment, do not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.*

The use of formulants in registered pest control products is assessed on an ongoing basis through the PMRA formulant initiatives and Regulatory Directive DIR2006-02.

7.0 Summary

7.1 Human Health and Safety

The toxicology database is adequate to characterize the potential health hazards associated with broflanilide. There was evidence of treatment-related tumours in rats after long-term dosing, with increased incidences of Leydig cell adenomas in males, and ovarian luteomas, ovarian tumours of sex cord stromal origin, ovarian granulosa cell tumours, as well as adrenal cortex carcinomas and uterine adenocarcinoma in females. There was no evidence of increased sensitivity of the young in reproductive or developmental toxicity studies. There was not evidence of neurotoxicity. In short-term and chronic studies on laboratory animals, the primary targets of toxicity were the adrenal glands and the ovaries as evidenced by increased organ weight and vacuolation. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

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5 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6 SI/2005-114, last amended on June 25, 2008. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.*.

7 PMRA's Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

8 DIR2006-02, *Formulants Policy and Implementation Guidance Document.*

Mixers, loaders and applicators handling Cimegra are not expected to be exposed to levels of broflanilide that will result in unacceptable risks when used according to label directions. Workers handling Cimegra must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. Chemical-resistant gloves are not required when applying using a closed cab tractor. Postapplication exposure to workers is expected to be negligible as the end-use product is only applied to the subsurface soil as an in-furrow and/or T-band application when potato and corn are planted. As such, a restricted-entry interval is not required.

Workers in commercial seed treatment facilities, mobile treaters, on-farm workers treating and planting and workers planting and/or handling treated cereal seeds are not expected to be exposed to levels of broflanilide that will result in unacceptable risks when used according to label directions. The PPE for workers in commercial seed treatment facilities and for mobile treaters is coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, shoes, socks and a dust-mask. When cleaning seed treatment equipment, workers must wear chemical-resistant coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, chemical-resistant footwear, socks and a dust-mask. Workers completing on-farm seed treatment must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. Workers planting and handling treated seed must wear coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks and use only a closed cab tractor. A dust-mask must be worn during the on-farm transfer of treated seed to planters/seeders.

Bystander and residential exposure is not of concern.

The nature of the residues in plants and animals is adequately understood. The residue definition for enforcement is broflanilide in plant products, and broflanilide and the metabolite DM-8007 in animal matrices. The proposed use of broflanilide on potatoes, corn and small cereal grains does not constitute a risk of concern for chronic (cancer and non-cancer) dietary exposure (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend MRLs. The PMRA recommends that the following MRLs be specified.

Commodity	Recommended MRL (ppm)
CSG 1C	0.04
Eggs, fat, meat, and meat byproducts of cattle, goats, hogs, horses, sheep and poultry, milk	0.02
Cereal grains (CG 15), except rice, amaranth grain, annual canarygrass seeds, cañihua grain, chia grain, cram-cram grain, huauzontle grain, quinoa, spelt grain, teff grain	0.01[1]
Food and wild rice commodities (other than those listed in this item)	0.01[1]

[1] The uses are not on the Canadian label. Proposed MRLs are to allow importation from the United States.

7.2 Environmental Risk

When used according to the label directions, broflanilide does not present a risk of concern to wild mammals, birds, beneficial insects, earthworms, terrestrial and aquatic plants, fish, or amphibians. Exposure to broflanilide can affect freshwater and marine invertebrates if they are

exposed to high levels, therefore, precautionary label statements are required on product labels. Precautionary label statements and best management practices are also required for pollinators to minimize potential exposure to dust during planting of treated seed; however, when used according to label directions, minimal exposure or risk to bees is expected. With the proposed mitigation measures in place, the use of broflanilide and its associated end-use products poses an acceptable risk to the environment.

7.3 Value

Cimegra has value for control of wireworm in potatoes and corn rootworm (western and northern) and wireworm in corn. Corn rootworms are a major pests of corn. Wireworms are major pests of potatoes and corn, and are difficult to kill with currently registered pest control products.

Teraxxa F4 and Teraxxa have value for control of wireworms in small cereal grains (barley, buckwheat, pearl millet, proso millet, oats, rye, sorghum, triticale, canary seed, and annual canarygrass (grown for human consumption), and wheat (all types: winter, spring and durum). Wireworms are major pests of the small cereal grains and wheat, and are difficult to kill with currently registered pest control products. In addition, as Teraxxa F4 is a pre-mix formulation with pyraclostrobin, fluxapyroxad, triticonazole, and metalaxyl, it provides control or suppression of certain seed- and soil-borne diseases.

Broflanilide has value as a new mode of action for use in resistance management; there are no reported cases of cross-resistance of broflanilide to currently registered insecticide mode of actions.

8.0 Proposed Regulatory Decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of Broflanilide Technical Insecticide, Cimegra, Teraxxa and Teraxxa F4 containing the technical grade active ingredient Broflanilide, to be used as a soil treatment to control wireworm in potatoes and wireworm and corn rootworm in corn, and as a seed treatment to control wireworm in small cereal grains and wheat.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

Additional Information Being Requested

Since this technical product is manufactured only at pilot scale before registration, five-batch data representing commercial-scale production will be required as post-market information after registration.

List of Abbreviations

↑	increased
↓	decreased
♂	male
♀	female
°C	degree Celsius
µg	micrograms
a.i.	active ingredient
ADD	absorbed daily dose
ADI	acceptable daily intake
AHETF	Agriculture Handler Exposure Task Force
ALS	acetolactate synthase
ARfD	acute reference dose
atm	atmosphere
AUC	area-under-the-curve
BAF	bioaccumulation factor
BCF	bioconcentration factor
bw	body weight
C_{max}	maximum concentration
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CDPR	California Department of Pesticide Regulation
cm	centimetres
DEEM–FCID	Exposure Evaluation Model
DF	dry flowable
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
dw	dry weight
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
EEC	estimated environmental concentration
ER_{25}	effective rate for 25% of the population
FDA	Food and Drugs Act
g	gram
GABA	Gamma-aminobutyric acid
GUS	Groundwater Ubiquity Score
ha	hectare(s)
HDPE	high-density polyethylene
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
IRAC	Insecticide Resistance Action Committee
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram

K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
KE	key events
km	kilometre
KMD	kinetically-derived maximum dose
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LADD	lifetime average daily dose
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LH	luteinizing hormone
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
mg	milligram
mL	millilitre
MAS	maximum average score
MOA	mode of action
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
NOAEL	no observed adverse effect level
NOAEC	no observed adverse effect concentration
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
PBI	plantback interval
PHI	preharvest interval
pH	measure of the acidity or basicity of an aqueous solution
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	Personal protective equipment
ppm	parts per million
PWC	Pesticide in Water Calculator
q1*	cancer potency factor
RQ	risk quotient
RSD	relative standard deviation
SC	soluble concentrate
T	testosterone

$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 1 Residue Analysis

Analyte	Matrix	Method ID	Method Type	LOQ (ng/L)	Reference
Broflanilide	Soil/sediment*	D1603/01	HPLC-MS/MS	1 ppb	PMRA# 2828143
	Surface water	D1608/01	HPLC-MS/MS	5	PMRA# 2828146
	Drinking water	D1608/01	HPLC-MS/MS	5	PMRA# 2828146
DC-DM-8007	Soil/sediment*	D1603/01	HPLC-MS/MS	1 ppb	PMRA# 2828143
	Surface water	D1608/01	HPLC-MS/MS	25	PMRA# 2828146
	Drinking water	D1608/01	HPLC-MS/MS	25	PMRA# 2828146
DC-8007	Soil/sediment*	D1603/01	HPLC-MS/MS	1 ppb	PMRA# 2828143
	Surface water	D1608/01	HPLC-MS/MS	25	PMRA# 2828146
	Drinking water	D1608/01	HPLC-MS/MS	25	PMRA# 2828146
DM-8007	Soil/sediment*	D1603/01	HPLC-MS/MS	1 ppb	PMRA# 2828143
	Surface water	D1608/01	HPLC-MS/MS	25	PMRA# 2828146
	Drinking water	D1608/01	HPLC-MS/MS	25	PMRA# 2828146
S(PFP-OH)-8007	Soil/sediment*	D1603/01	HPLC-MS/MS	1 ppb	PMRA# 2828143
	Surface water	D1608/01	HPLC-MS/MS	25	PMRA# 2828146
	Drinking water	D1608/01	HPLC-MS/MS	25	PMRA# 2828146
S(Br-OH)-8007	Surface water	D1705/01	HPLC-MS/MS	25	PMRA# 2828147
	Drinking water	D1705/01	HPLC-MS/MS	25	PMRA# 2828147
AB-Oxa	Surface water	D1705/01	HPLC-MS/MS	25	PMRA# 2828147
	Drinking water	D1705/01	HPLC-MS/MS	25	PMRA# 2828147
MFBA	Surface water	D1705/01	HPLC-MS/MS	25	PMRA# 2828147
	Drinking water	D1705/01	HPLC-MS/MS	25	PMRA# 2828147
* The soil method can be extended for sediment.					

Analytical Methods	Matrix	Analyte(s)	Method ID/ Type	LOQ	Reference
Livestock Commodities					
Enforcement Method	Bovine muscle, liver, kidney, fat, egg and milk	Broflanilide and DM-8007	D1604/01/ LC-MS/MS	0.01 ppm/ analyte in all matrices, except: 0.001 ppm/ analyte in milk	PMRA# 2828140
ILV of Enforcement Method	Bovine muscle, liver, milk, fat, egg		D1604/01/ LC-MS/MS		PMRA# 2828141
Data-Gathering Method	Bovine muscle, liver, milk, fat, egg		D1710/01/ LC-MS/MS		PMRA# 2828142
Radiovalidation	No radiovalidation study was conducted. Same extraction solvents (acetonitrile/water) as those of the enforcement method were used in the livestock metabolism studies.				

Analytical Methods	Matrix	Analyte(s)	Method ID/ Type	LOQ	Reference
Plant Commodities					
Enforcement Method	Wheat grain, dry bean seed, tomato, citrus whole fruit, coffee bean and soybean seed	Broflanilide	D1417/01/ LC-MS/MS	0.001 ppm	PMRA# 2828136
ILV of Enforcement Method	Green coffee bean, kidney bean, soybean, grape, lettuce and potato	Broflanilide	D1417/01/ LC-MS/MS	0.01 ppm	PMRA# 2828139
Data-Gathering Method	Kidney bean, soybean, grape, lettuce and potato	Broflanilide	D1713/01/ LC-MS/MS	0.01 ppm	PMRA# 2828137
Radiovalidation	No radiovalidation study was conducted. Same extraction solvents (acetonitrile/water) as those of the enforcement method were used in the plant metabolism studies.				

Table 2 Identification of Select Broflanilide Metabolites

Code Name	Chemical Name (IUPAC)	Matrices[a]
DM-8007	3-benzamido-N-[2-bromo-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluorobenzamide	Rat, plants, poultry, goat
DC-DM-8007	3-amino-N-[2-bromo-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluorobenzamide	Rat, poultry, goat
S(PFP-OH)-8007	N-[2-bromo-4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluoro-3-(N-ethylbenzamido)benzamide	Rat, plants
DC-8007	N-[2-bromo-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluoro-3-(methylamino)benzamide	Environmental degradate
MFBA	2-fluoro-3-(N-methylbenzamido)benzoic acid	Environmental degradate
AB-oxa	N-{2-fluoro-3-[6-(perfluoropropan-2-yl)-4-(trifluoromethyl)-1,3-benzooxazol-2-yl]phenyl}-Nmethylbenzamide	Environmental degradate
S(Br-OH)-8007	2-fluoro-N-[2-hydroxy-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-3-(Nmethylbenzamido)benzamide	Rat, environmental degradate
DM-(C-H_2O)-8007 cysteine conjugate	Not provided	Rat
DM-(A,C-diOH)-8007	Not provided	Rat
DC-DM-(A-OH)-8007	Not provided	Rat
DM-(C34-diOH)-8007	N-[2-bromo-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-3-(3,4-dihydroxybenzamido)-2-fluorobenzamide	Rat
S(PFP-OH)-8007	N-[2-bromo-4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluoro-3-(N-methylbenzamido)benzamide	Rat, plants
DM-(C4-OH)-8007	N-[2-bromo-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluoro-3-(4-hydroxybenzamido)benzamide	Rat, goat

[a] Observed in matrices based on information provided by the applicant.

Table 3 Toxicity Profile of End-use Products Containing Broflanilide

Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons

Study Type/Animal/PMRA#	Study Results
Cimegra	
Acute oral toxicity (acute toxic class) Wistar rats (♀) PMRA# 2827889	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) No clinical signs of toxicity.
Acute dermal toxicity Wistar rats PMRA# 2827890	Low acute toxicity LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity.
Acute inhalation toxicity (nose-only) Wistar rats PMRA# 2827891	Low acute toxicity LC_{50} > 4.3 mg/L (♂/♀) No clinical signs of toxicity.
Skin irritation NZW rabbits PMRA# 2827892	Minimally irritating MAS = 0.44 MIS = 1.33 at 1 hr and 24 hrs
Eye irritation NZW rabbits PMRA# 2827893	Minimally irritating MAS = 0.22 MIS = 2 at 1 hr
Dermal sensitization (Buehler) Dunkin-Hartley guinea pigs PMRA# 2827894	Negative
Teraxxa	
Acute oral toxicity (acute toxic class) Wistar rats (♀) PMRA# 2828019	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) No clinical signs of toxicity.
Acute dermal toxicity Wistar rats PMRA# 2828020	Low acute toxicity LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity.

Acute inhalation toxicity (nose-only) Wistar rats PMRA# 2828021	Low acute toxicity LC_{50} > 4.4 mg/L (♂/♀) Clinical signs of toxicity included hunched posture, ruffled fur and ↓ activity.
Skin irritation NZW rabbits PMRA# 2828022	Minimally irritating MAS = 0.2 MIS = 1 at 1 hr
Eye irritation NZW rabbits PMRA# 2828023	Minimally irritating MAS = 1.6 MIS = 3.3 at 1 hr and 24 hrs
Dermal sensitization (Buehler) Dunkin-Hartley guinea pigs PMRA# 2828024	Negative
Teraxxa F4 (contains broflanilide as well as pyraclostrobin, triticonazole, metalaxyl, and fluxapyroxad)	
Acute oral toxicity (acute toxic class) Wistar rats (♀) PMRA# 2827945	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) No clinical signs of toxicity.
Acute dermal toxicity Wistar rats PMRA# 2827946	Low acute toxicity LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity.
Acute inhalation toxicity (nose-only) Wistar rats PMRA# 2827947	Low acute toxicity LC_{50} > 5.54 mg/L (♂/♀) Clinical signs of toxicity included irregular respiration.
Skin irritation NZW rabbits PMRA# 2827948	Slightly irritating MAS = 1.33 MIS = 2 at 1 hr and 24 hrs
Eye irritation NZW rabbits PMRA# 2827949	Minimally irritating MAS = 1.33 MIS = 5.67 at 1 hr
Dermal sensitization (Buehler) Dunkin-Hartley guinea pigs PMRA# 2827950	Positive Potential dermal sensitizer

Table 4 Toxicity Profile of Technical Broflanilide

Effects observed in both sexes are presented first followed by sex-specific effects in males, then females, each separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted. Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.

Study Type/Animal/PMRA#	Study Results
Toxicokinetic Studies	
Absorption, distribution, toxicokinetics metabolism and excretion study following single gavage or i.v. doses (low and high) Wistar rats PMRA# 2828152	Single gavage dose administered at 5 mg/kg bw ([C-ring-U-^{14}C]broflanilide or [B-ring-U-^{14}C]broflanilide) or 500 mg/kg bw ([C-ring-U-^{14}C]broflanilide); i.v. dose administered at 1.6 mg/kg bw ([B-ring-U-^{14}C]broflanilide); 4/sex/group for excretion/distribution, and 12/sex/group for plasma/blood cell kinetics. Absorption: Absorption was rapid, with T_{max} of 0.5–2 hrs for the B-ring and 4 hrs for the C-ring. The oral bioavailability following oral dosing (B-ring) was 16/13% of the AD in ♂/♀ at 5 mg/kg bw based on the ratio of plasma AUC following oral and intravenous administration (adjusted for AD). Excretion: Mainly via the faeces (77–96% of the AD). Urinary excretion at 5 mg/kg bw for the B-ring (0.3–0.5% of the AD) was lower than that observed for the C-ring at 5 mg/kg bw (8/13% of the AD in ♂/♀) and 500 mg/kg bw (1.4–1.5% of the AD). By 48 hrs, approximately 90% of the AD had been eliminated, with the exception of ♀ at 5 mg/kg bw dosed with the C-ring (81%). Radioactivity was negligible in expired air (≤0.02% of the AD). Distribution: At 168 hrs, retention of radioactivity in tissues was low and accounted for 0.7/1.5% of the AD in ♂/♀ (C-ring) and 0.3/0.5% of the AD in ♂/♀ (B-ring) at 5 mg/kg bw, and 0.10% of the AD (C-ring) at 500 mg/kg bw. The pattern of distribution was similar at both dose levels and with both radiolabel positions, with the greatest concentration of radioactivity observed in the fat. In all groups, concentrations of radioactivity in tissues were generally greater in ♀ than ♂. Toxicokinetics: Levels of radioactivity in plasma and whole blood were generally similar between sexes with the exception of the rats administered 5 mg/kg bw of the C-ring where values were higher in ♀. The terminal half-life of plasma radioactivity following oral dosing was 42–79 hrs at 5 mg/kg bw and 8-58 hrs at 500 mg/kg bw. Plasma concentrations of radioactivity and AUC values were not proportional to dose (2–16-fold increases compared to a 100-fold increase in dose). Metabolites: Unchanged broflanilide was the major component in faecal extracts, accounting for 52–75% of the AD (both radiolabel positions) at 5 mg/kg bw, and 91–94% of the AD (C-ring) at 500 mg/kg bw. Metabolites detected in faeces were DM-(C-H_2O)-8007 cysteine conjugate, which accounted for 2–6% of the AD (both radiolabel positions), and DM-8007, which accounted for 3–5% of the AD (both radiolabel positions) at 5 mg/kg bw. These metabolites were less significant at 500 mg/kg bw and accounted for ≤ 2% of the AD. In the urine the major metabolite was hippuric acid which accounted for 6-11% of the AD (C-ring) at 5 mg/kg bw and 0.7–0.8% at 500 mg/kg bw.

Absorption, and metabolism (biliary excretion) following single gavage doses (low and high) Wistar rats PMRA# 2828153	Single gavage dose administered at 5 mg/kg bw ([C-ring-U-^{14}C]broflanilide or [B-ring-U-^{14}C]broflanilide) or 500 mg/kg bw ([C-ring-U-^{14}C]broflanilide); 4/sex/group. Absorption: The total absorbed radioactivity was 14–23% of the AD at 5 mg/kg bw ([B- and C-ring]) and 2% of the AD at 500 mg/kg bw based on levels in the bile, urine, liver and remaining carcass. Metabolites: Unchanged broflanilide was the major component in faecal extracts accounting for 60–71% of the AD at 5 mg/kg bw and 89% of the AD at 500 mg/kg bw. Metabolites detected in feces were DM-(C-H_2O)-8007 cysteine conjugate, DM-(A,C-diOH)-8007, DC-DM-(A-OH)-8007 and DM-8007, each of which accounted for <5% of the AD. In urine, broflanilide was metabolised to one major metabolite following administration of [C-ring-U-^{14}C] broflanilide which accounted for a maximum of 7–9% of the AD and was confirmed in another study to be hippuric acid. In the bile, broflanilide was metabolised to at least seven identified minor metabolites following administration of both B-ring and C-ring radiolabel, each of which accounted for a maximum of 3% of the AD. Six Phase II metabolites were identified. Overall, only unchanged broflanilide and hippuric acid accounted for >5% of the AD
Distribution, metabolism (tissue depletion) following single gavage doses (low and high) Wistar rats PMRA# 2828154	Single gavage dose administered at 5 mg/kg bw of [B-ring-U-^{14}C]broflanilide or 500 mg/kg bw of [C-ring-U-^{14}C]broflanilide (12/sex/group). Groups of 4/sex were sacrificed at 4, 24 and 72 hrs post dosing with [B-ring-U-^{14}C]broflanilide at 5 mg/kg bw, and groups of 4/sex were sacrificed at 1, 8 and 24 hrs post dosing with [C-ring-U-^{14}C]broflanilide at 500 mg/kg bw. Distribution: With the (B-ring) radiolabel, peak tissue concentrations occurred at 4 hrs with greatest concentrations present in the liver, pancreas, adrenal, thyroid, epididymis and ovaries. Concentrations of radioactivity observed in tissues were generally greater than those in plasma except for whole blood, blood cells, brain, spleen (♂ only), testes, bone and bone marrow (♀ only). At 24 hrs, concentrations in fat increased approximately twofold compared to those at 4 hrs. Concentrations in liver, pancreas, adrenal, thyroid, epididymis and ovaries also increased over time but to a lesser extent. Concentrations in most other tissues remained similar to those at 4 hrs or had declined. Thereafter concentrations of radioactivity generally declined; the pattern of distribution remained similar. With the (C-ring) radiolabel, peak tissue concentrations occurred at 1 hr with greatest concentrations observed in the kidney and liver. Initially the majority of tissues had radioactivity concentrations less than those in plasma. At 8 hrs the pattern of distribution changed with concentrations in the majority of tissues exceeding those in plasma, despite the overall radioactivity levels declining. The greatest concentrations at 8 hrs were observed in liver, adrenal and fat. Levels continued to decline at 24 hrs, but the pattern of distribution was similar to that at 8 hrs. Concentrations of radioactivity in ♂ tissues were greater than those in ♀, particularly at 8 and 24 hrs. Metabolites: With the (B-ring) radiolabel, profiles of radioactivity in plasma, liver, kidney and fat indicated that DM-8007 was the main component in tissues at 4 hrs accounting for 42–58% of tissue radioactivity. DC-DM-8007 was a significant component in tissues accounting for 3–17% of tissue radioactivity. With the (C-ring) radiolabel, profiles of radioactivity at peak concentrations in plasma, liver, kidney and fat indicated that DM-8007 was the main component accounting for 8–50% of tissue radioactivity. In plasma and kidney, a polar component(s), accounted for up to 49% of tissue radioactivity. In liver, DM-

	(C34-diOH)-8007, S(PFPOH)-8007, DM-(C4-OH)-8007 and S(Br-OH)-8007 were characterised as low level components accounting for up to 15% of tissue radioactivity collectively. Unchanged broflanilide accounted for 1.2–8.5% of tissue radioactivity.
Toxicokinetics following single gavage doses (three dose levels) Wistar rats PMRA# 2828155	Single gavage dose at 20, 100, 500 mg/kg bw of [B-ring-U-^{14}C]broflanilide (4/sex/group). RBC concentration-versus-time curves were more variable and showed more multiple peak patterns than those for plasma. The increases in C_{max} and AUC values in plasma and RBC were less than dose proportional: values increased by roughly a factor 10–19 from 20 to 500 mg/kg bw, compared to a 25-fold increase in dose. Concentrations in RBC were lower than in plasma during the first part of the concentration time curves; however, after approximately 72–96 hrs, the concentrations in RBC were similar to or even higher than those in plasma. This result together with the longer t1/2 values in RBC suggests that the [^{14}C]broflanilide was significantly distributed to RBC and only slowly released.
Distribution, excretion, metabolism, and toxicokinetics following repeat gavage doses (one dose level) Wistar rats PMRA# 2828156	Repeat gavage dosing at 5 mg/kg bw/day for 14 days of [B-ring-U-^{14}C]broflanilide (4/sex (excretion/tissue distribution), 12/sex (plasma/blood cell kinetics)). Excretion: Mainly via faeces (87–89% of the AD), with only 0.3–0.8% of the AD excreted in urine. Distribution: At 168 hrs after the final dose, retention of radioactivity in tissues accounted for 5/8% of the AD in ♂/♀. Peak tissue concentrations occurred 24 hrs after the final (14th) dose with greatest concentrations in the fat and notable concentrations also present in liver, pancreas, adrenal, thyroid, epididymis and ovaries. Concentrations of radioactivity observed in tissues were generally greater than those in plasma except for whole blood, blood cells, brain, testes and bone. Thereafter, concentrations in tissues declined, with a similar pattern of distribution at 96 and 168 hrs. There was no notable sex difference in the distribution of radioactivity. At 168 hrs after the final dose, the majority of the AD was recovered in the residual carcass (2–3%) with significant levels also recovered in fat (2–3%). Radioactivity in the remaining tissues was generally <1% of the AD. Toxicokinetics: Pharmacokinetic parameters indicated that the rate and extent of exposure was similar in ♂ and ♀. Maximum plasma and whole blood concentrations occurred at 4 hrs after the final dose. Metabolites: Unchanged broflanilide was identified as the major component in faecal extracts, accounting for 53–75% of the AD during the 24 hr period after the first dose and 61–77% of the AD during the 24 hr period after the seventh dose. During 0–96 hrs after the final dose, unchanged broflanilide accounted for 57–65% of the AD.

Acute Toxicity Studies	
Acute oral toxicity (up-down method) Wistar rats (♀) PMRA# 2828159	Low acute toxicity LD_{50} > 5000 mg/kg bw (♀) No clinical signs of toxicity.
Acute dermal toxicity	Low acute toxicity

Wistar rats PMRA# 2828160	LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity.
Acute inhalation toxicity (nose-only) Wistar rats PMRA# 2828161	Low acute toxicity LC_{50} > 2.2 mg/L (♂/♀) No clinical signs of toxicity.
Skin irritation NZW rabbits PMRA# 2828162	Non-irritating MAS = 0 MIS = 0 (at 1 hr)
Eye irritation NZW rabbits PMRA# 2828163	Non-irritating MAS = 0 MIS = 3.3 (at 1 hr)
Dermal sensitization (LLNA) CBA mice PMRA# 2828164	Supplemental Negative Limitations: only one dose tested.
Dermal sensitization (LLNA) CBA mice PMRA# 2828165	Negative
Dermal sensitization (Maximization test) Hartley guinea pigs PMRA# 2828167	Negative
Short-Term Toxicity Studies	
28-day oral toxicity (diet) CD1 mice PMRA# 2828169	Supplemental NOAEL and LOAEL not established Effects at ≥ 107/119 mg/kg bw/day: ↑ abs spleen wt (♂); ↑ glucose (♀) Effects at 1068 mg/kg bw/day: ↑ total protein (♂) Limitations: limited pathology.
90-day oral toxicity (diet) CD1 mice PMRA# 2828173	Supplemental NOAEL and LOAEL not established Effects at ≥ 230 mg/kg bw/day: ↑ adrenal wt (♀) Effects at 955/1148 mg/kg bw/day: ↓ bwg (♂); ↑ adrenal cortical vacuolation (♀) Unchanged broflanilide and DM-8007 levels ↑ with increasing dose level, but not in a dose-proportional manner, and were generally similar between ♂ and ♀. DM-8007

	concentrations were much higher than those of unchanged broflanilide. Limitations: clinical chemistry not assessed.
90-day oral toxicity (diet) Wistar rats PMRA# 2828174	NOAEL not established LOAEL = 35/41 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ adrenal wt, ↑ adrenal cortex vacuolation (♂/♀); ↑ reticulocytes, ↑ adrenal cortex hypertrophy, ↑ ovarian interstitial gland vacuolation (♀) Effects at the highest dose tested (1007/1212 mg/kg bw/day in ♂/♀) that subsided after a 4-week recovery period: ↓ bw/bwg, ↑ urine volume, ↓ urine specific gravity (♂); ↓ bwg, ↑ ovary wt, ↑ reticulocytes, ↑ adrenal cortex hypertrophy, ↑ adrenal cortex vacuolation (♀) Effects at the highest dose tested that persisted after a 4-week recovery period: ↑ adrenal wt (♂/♀); ↑ adrenal cortex vacuolation (♂); ↑ ovarian interstitial gland vacuolation (♀) Unchanged broflanilide and DM-8007 levels ↑ with increasing dose level, but not in a dose-proportional manner. For broflanilide, ♀ had higher plasma levels than ♂, while DM-8007 levels were generally similar between ♂ and ♀. DM-8007 concentrations were much higher than those of unchanged broflanilide.
90-day oral toxicity (diet) Wistar rats PMRA# 2828175	Complimentary study to PMRA 2828174 to establish a NOAEL for effects identified at the lowest dose tested. NOAEL = 2.0/2.2 mg/kg bw/day (♂/♀) LOAEL not established No treatment-related findings in parameters examined. Limitations: only one dose level tested, pathology examinations limited to target organs identified at lowest dose tested in PMRA# 282174 (adrenal gland, ovary), no hematology or clinical chemistry.
14-day oral toxicity (capsule) – Dose range-finding Beagle dogs PMRA# 2828171	Supplemental No treatment-related findings at 1000 mg/kg bw/day. Limitations: one dose level tested, limited reporting, no hematology/clinical chemistry, no pathology.
28-day oral toxicity (capsule) Beagle dogs PMRA# 2828172	NOAEL = 300/1000 mg/kg bw/day (♂/♀) LOAEL = 1000 mg/kg bw/day/not established (♂/♀) Effects at LOAEL: ↑ cholesterol, ↑ liver wt, ↑ adrenal wt, ↓ prostate wt, ↓ testes wt, ↓ thyroid wt (♂) Unchanged broflanilide and DM-8007 levels were detected and quantified in all examined dog plasma samples, and were generally similar between ♂ and ♀. DM-8007 concentrations were much higher than those of unchanged broflanilide.
90-day oral toxicity (capsule) Beagle dogs PMRA# 2828182	NOAEL = 300 mg/kg bw/day (♂/♀) LOAEL = 1000 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ ALP, ↑ cholesterol, ↑ liver wt, ↑ adrenal wt (♂/♀); ↓ fc, ↑ triglycerides (♂); ↑ liver wt (♀) DM-8007 levels were higher compared to unchanged broflanilide. Broflanilide and

	DM-8007 levels ↑ with increasing dose levels, but not in a dose-proportional manner. Broflanilide and DM-8007 levels were generally similar between ♂ and ♀.
12-month oral toxicity (capsule) Beagle dogs PMRA# 2828183	NOAEL not established LOAEL = 100 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ ALP (♂/♀); ↑ adrenal wt, enlargement of the adrenal, adrenal hypertrophy (♂); ↑ ALT, ↓ bw/bwg, adrenal vacuolation (♀)
28-day dermal toxicity Wistar rats PMRA# 2828186	NOAEL = 1000 mg/kg bw/day (♂/♀) LOAEL not established No treatment-related adverse findings.
5-day inhalation toxicity (head-nose) – Dose range-finding Wistar rats PMRA# 2828184	Supplemental NOAEL and LOAEL not established Effects at ≥ 0.10 mg/L: ↑ heart wt (♀) Effects at ≥ 0.32 mg/L: ↓ bwg (♂/♀); ↑ rel eosinophil count (♂) Effects at 1.1 mg/L: ↑ inflammatory cell infiltrates in the bronchio-alveolar region, ↑ hypertrophy/hyperplasia of terminal bronchioles, ↑ epithelial alteration of the larynx (♂/♀); ↑ adrenal wt, ↑ rel brain wt, ↑ heart wt, ↑ rel kidney wt, ↑ rel liver wt, ↓ abs thymus wt (♀) Limitations: limited reporting, short duration of study.
28-day inhalation toxicity (nose-only) Wistar rats PMRA# 2828185	NOAEC = 0.031 mg/L (8.4 mg/kg bw/day) (♂/♀) LOAEC = 0.19 mg/L (52 mg/kg bw/day) (♂/♀) Effects at LOAEC: ↑ reticulocytes, ↑ adrenal vacuolation, spleen extramedullary hematopoiesis, ↑ adrenal wt, larynx epithelial alteration (♂/♀); ↑ neutrophil count, ↓ lymphocyte count (♂); ↑ heart wt, ↑ ovary wt, ↑ severity of spleen pigment storage, ovary vacuolation (♀) Effects at the highest dose tested (0.94 mg/L) that subsided after a 4-week recovery period: ↓ bwg, ↑ cholesterol, ↑ reticulocytes, ↑ lung wt, ↑ adrenal wt, spleen extramedullary hematopoiesis, larynx epithelial alteration, regenerative bronchiolar hyperplasia in the lung, alveolar histiocytosis in the lung, debris in the lung (♂/♀); ↑ neutrophil count, ↓ lymphocyte count, ↑ severity of spleen pigment storage, cribriform change in the epididymides (♂); ↑ GGT, ↑ total bilirubin, ↑ ovary wt, ↑ heart wt, ↑ adrenal vacuolation, ↑ severity of spleen pigment storage (♀) Effects at the highest dose tested that persisted after a 4-week recovery period: ↑ thyroid wt, adrenal vacuolation (♂); ↓ bwg, ↓ creatinine, ovary vacuolation (♀)
Chronic Toxicity/Oncogenicity Studies	
18-month oncogenicity (diet) CD1 mice PMRA# 2828194	NOAEL = 745/172 mg/kg bw/day (♂/♀) LOAEL = not established/820 mg/kg bw/day (♂/♀) Effects at LOAEL: pale lower teeth, abnormal teeth, ↑ adrenal wt, ↑ ovary wt, large adrenal, ovarian cysts, adrenal lesions (accessory nodules, hemopoiesis, cortical and corticomedullary vacuolation, inflammatory cell foci) (♀) Unchanged broflanilide and DM-8007 levels ↑ with increasing dose level, but not in a dose-proportional manner, and were generally similar between ♂ and ♀. DM-8007 concentrations were much higher than those of unchanged broflanilide.

	No evidence of tumourigenicity
24-month chronic toxicity/oncogenicity (diet) Wistar rats PMRA# 2828193	**24-month sacrifice** NOAEL = 4.5 mg/kg bw/day/not established (♂/♀) LOAEL = 14/5.9 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ adrenal vacuolization, ↑ adrenal wt (♂); ↑ adrenal wt, ↑ ovarian interstitial gland vacuolation (♀) **12-month sacrifice** NOAEL = 1.7/2.1 mg/kg bw/day (♂/♀) LOAEL = 5.7/7.2 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ adrenal vacuolization (♂); ↑ reticulocytes, ↑ cholesterol, ↑ adrenal wt, ↑ abs heart wt (♀) Unchanged broflanilide was not detected in plasma. DM-8007 was detected and quantified in all treated rat plasma sample and levels ↑ with increasing dose level. DM-8007 levels were generally similar between ♂ and ♀. Tumour incidences (in %) Ovarian luteomas: 0/2/0/0/6 Ovarian granulosa cells: 2/2/6/22/12 Combined ovarian tumours of sex cord stromal origin: 6/6/6/22//24 Uterine adenocarcinomas: 12/8/12/22/28 Adrenal carcinoma (♀): 0/0/0/0/4 Leydig cell adenomas: 2/4/10/8/28 Evidence of carcinogenicity
Developmental/Reproductive Toxicity Studies	
Developmental/reproductive toxicity (diet) – Screening study Wistar rats PMRA# 2828170	Supplemental Parental NOAEL and LOAEL not established Effects at ≥ 299/360 mg/kg bw/day: ↑ reticulocytes, ↑ adrenal wt (♂/♀); ↓ RBC, enlarged adrenal, splenic hematopoiesis (♀) Effects at ≥ 644/711 mg/kg bw/day: splenic hematopoiesis (♂); ↓ potassium, ↑ rel liver wt, ↑ abs heart wt (♀) Effects at 983/1067 mg/kg bw/day: ↓ potassium (♂); ↑ mean platelet volume, ↑ platelet distribution width, ↑ glucose, adrenal cortical hypertrophy (♀) Reproductive NOAEL and LOAEL not established Effects at 983/1067 mg/kg bw/day: 1 complete litter loss (5 pups PND 0-1) Offspring NOAEL and LOAEL not established Effects at 1067 mg/kg bw/day: ↑ pup deaths PND 1-4 (pup basis only) Limitation: small group sizes, limited examination of reproductive and developmental parameters, hematology and histopathology were not examined in littering females.

2-generation reproductive toxicity (diet) Wistar rats PMRA# 2828201	Parental NOAEL = 2.3/2.5 mg/kg bw/day (♂/♀) Parental LOAEL = 7.5/8.3 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ adrenal vacuolation [P, F1] (♂/♀); ↑ adrenal wt [F1] (♂); ↑ adrenal wt [P] (♀) Reproductive NOAEL = 7.5/2.5 mg/kg bw/day (♂/♀) Reproductive LOAEL = 23/8.3 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ cauda epididymis wt [F1], ↑ epididymides wt [F1], ↑ testes wt [F1] (♂); ↑ ovary vacuolation [P] (♀) Offspring NOAEL = 27 mg/kg bw/day (♂/♀) Offspring LOAEL = 126 mg/kg bw/day (♂/♀) Effects at LOAEL: ↓ bw [F1, PND 21; F2, PND 4-21], ↓ bwg [F1, PND 1-21; F2, PND 1-21], ↓ thymus wt [F1, F2], ↓ abs brain wt [F2] (♂/♀); ↓ abs brain wt [F1] (♂) No evidence of sensitivity of the young.
Developmental toxicity (gavage) – Dose range-finding Wistar rats PMRA# 2828204	Supplemental NOAEL and LOAEL not established No treatment-related findings up to 1000 mg/kg bw/day. Limitations: non-pregnant ♀ tested, limited reporting, small group sizes.
Developmental toxicity (gavage) – Dose range-finding Wistar rats PMRA# 2828206	Supplemental NOAEL and LOAEL not established No treatment-related findings up to 1000 mg/kg bw/day. Limitations: limited reporting, small group sizes, limited fetal examination.
Developmental toxicity (gavage) Wistar rats PMRA# 2828202	Maternal NOAEL = 1000 mg/kg bw/day Maternal LOAEL not established No treatment-related findings. Developmental NOAEL = 1000 mg/kg bw/day Developmental LOAEL not established No treatment-related findings. No evidence of sensitivity of the young.
Developmental toxicity (gavage) – Dose range-finding NZW rabbits PMRA# 2828211	Supplemental NOAEL and LOAEL not established No treatment-related findings up to 1000 mg/kg bw/day. Limitations: non-pregnant ♀ tested, limited reporting, small group sizes.

Developmental toxicity (gavage) – Dose range-finding NZW rabbits PMRA# 2828212	Supplemental NOAEL and LOAEL not established No treatment-related findings up to 1000 mg/kg bw/day. Limitations: limited reporting, small group sizes, limited fetal examination.
Developmental toxicity (gavage) NZW rabbits PMRA# 2828210	Maternal NOAEL = 1000 mg/kg bw/day Maternal LOAEL not established No treatment-related adverse findings. Developmental NOAEL = 1000 mg/kg bw/day Developmental LOAEL not established No treatment-related findings. No evidence of sensitivity of the young.
Genotoxicity Studies	
Bacterial reverse mutation assay S. typhimurium strains TA100, TA1535, TA98, and TA1537 and E. Coli strain WP2 uvrA PMRA# 2828187	Negative ± metabolic activation Tested up to a limit concentration.
In vitro chromosomal aberration assay Chinese hamster lung cells PMRA# 2828188	Negative ± metabolic activation Tested up to a precipitating concentration.
In vitro forward mutation assay in mammalian cells Chinese hamster ovary cells PMRA# 2828189	Negative ± metabolic activation Tested up to a precipitating concentration.
In vivo micronucleus assay (♂) NMRI mice PMRA# 2828190, 2828191	Negative No mortality or clinical signs of toxicity. Tested up to a limit concentration.
Neurotoxicity Studies	
Acute oral neurotoxicity (gavage) – Dose range-finding Wistar rats PMRA# 2828213	Supplemental NOAEL and LOAEL not established No treatment-related findings at 2000 mg/kg bw. Limitations: limited reporting, small group size, one dose level tested.

Acute oral neurotoxicity (gavage) Wistar rats PMRA# 2828214	NOAEL = 2000 mg/kg bw (♂/♀) LOAEL not established No treatment-related findings. No evidence of neurotoxicity.
90-day neurotoxicity (diet) Wistar rats PMRA# 2828215	NOAEL = 1041/1137 mg/kg bw/day (♂/♀) LOAEL not established No treatment-related findings. No evidence of neurotoxicity.
Other Studies	
28- day immunotoxicity study (diet) Wistar rats (♂) PMRA# 2828157	NOAEL = 1020 mg/kg bw/day (♂) LOAEL not established No treatment-related findings. No treatment-related effect on anti-SRBC IgM antibody response. No evidence of immune dysregulation.
90-day toxicity study (diet) to determine treatment-related effects on hormone levels Wistar rats PMRA# 2828195, 2828199	Supplemental NOAEL and LOAEL not established Effects at ≥ 32/36 mg/kg bw/day: ↑ aldosterone/creatinine ratio, ↑ corticosterone (post-challenge with ACTH), ↑ adrenal wt, ↑ enlarged and discoloured adrenal, ↑ incidence and severity of adrenal i) cortical vacuolation, ii) lipid content, iii) cholesterol content (♂/♀); ↑ prolactin, ↑ testosterone (day 10), ↓ number and overall intensity of staining of LH-positive epithelial cells, ↑ cytoplasmic vacuolation of LH cells (♂); ↓ progesterone (day 10 and 91 all ♀), ↓ prolactin (diestrus ♀), ↑ LH (45 days all and estrous ♀), ↑ ovary wt, ↑ incidence and severity adrenal hypertrophy, ↑ incidence and severity ovarian interstitial gland cell vacuolation, ↑ severity of ovary lipid content (♀) Effects at 972/1127 mg/kg bw/day: ↑ LH (day 45 and 91) (♂); ↓ bwg, ↓ progesterone (day 45 all ♀), ↑ LH (91 days all and estrous ♀), ↑ corticosterone (90 days, all and estrus ♀ without ACTH, and satellite pre-challenge), ↑ uterus wt, ↑ pituitary wt (♀) No apparent effects on FSH or estradiol. Interpretation of hormone data confounded by high variability and lack of hormone assessment prior to initiation of dosing. Limitation: non-guideline study.

Table 5 Toxicity Profile of Metabolites of Broflanilide

Effects observed in both sexes are presented first followed by sex-specific effects in males, then females, each separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted. Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.

Study Type/Animal/PMRA#	Study Results
DM-8007	
Acute oral toxicity (up-down method) Wistar rats (♀) PMRA# 2828216	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) No clinical signs of toxicity.
14-day oral toxicity (diet) – Dose range-finding Wistar rats PMRA# 2828220	Supplemental NOAEL and LOAEL not established No treatment-related findings up to 1527/1594 mg/kg bw/day (♂/♀). Limitations: small group sizes, limited pathology, short duration of study.
28-day oral toxicity (diet) Wistar rats PMRA# 2828221	NOAEL = 85/378 mg/kg bw/day (♂/♀) LOAEL = 278 mg/kg bw/day/not established (♂/♀) Effects at LOAEL: ↑ seminal vesicles wt, ↑ prostate wt, ↓ testes wt
90-day oral toxicity (diet) Wistar rats PMRA# 2828222	NOAEL = 190/215 mg/kg bw/day (♂/♀) LOAEL not established No treatment-related adverse effects.
Bacterial reverse mutation assay S. typhimurium strains TA100, TA1535, TA98, and TA1537 and E. Coli strain WP2 uvrA PMRA# 2828219	Negative ± metabolic activation Tested up to a limit concentration.
Metabolite DC-DM-8007	
Acute oral toxicity (up-down method) Wistar rats (♀) PMRA# 2828223	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) No clinical signs of toxicity.
14-day oral toxicity (diet) – Dose range-finding Wistar rats PMRA# 2828225	Supplemental NOAEL and LOAEL not established Effects at ≥ 196/274 mg/kg bw/day: piloerection, ↓ fc, ↓ wc, ↓ bw/bwg, grey-white discolouration of the adrenal cortex, enlarged liver (♂/♀); tremors, poor general health, encrusted nose, semi-closed eyelid (only at this dose) (♀) Effects at 699 mg/kg bw/day: poor general health, encrusted nose, semi-closed

	eyelids, tremors, black focus in glandular stomach (♂) All animals sacrificed on day 6 due to severe clinical signs of toxicity. Limitations: small group sizes, limited pathology, short duration of study.
14-day oral toxicity (diet) – Dose range-finding Wistar rats PMRA# 2828226	Supplemental NOAEL and LOAEL not established Effects at ≥ 11 mg/kg bw/day: ↑ rel adrenal wt, ↑ rel liver wt (♀) Effects at ≥ 32 mg/kg bw/day: ↑ abs adrenal wt, discoloured spleen (♀) Effects at 150/152 mg/kg bw/day: ↑ spleen wt, enlarged adrenal cortex, enlarged spleen (♂/♀); discoloured spleen, enlarged liver, ↓ bwg, ↑ adrenal wt (♂); ↓ wc, ↑ abs liver wt, focus in the liver (♀) Limitations: limited pathology, short duration of study.
28-day oral toxicity (diet) Wistar rats PMRA# 2828229, 2923484	NOAEL not established LOAEL = 11/12 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ reticulocyte, ↑ extramedullary hematopoiesis in the spleen (♂/♀); ↑ spleen wt (♀)
90-day oral toxicity (diet) Wistar rats PMRA# 2828230	NOAEL = 5.3/2.2 mg/kg bw/day (♂/♀) LOAEL = 54/5.7 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ thyroid wt, ↑ liver wt, ↑ adrenal wt, ↓ MCHC, ↑ MCV, ectasia vessels in the spleen, ↓ eosinophils (♂); ↓ RBC, ↓ HGB, ↓ HCT, ↑ reticulocytes, ↑ extramedullary hematopoiesis in the spleen, ↑ spleen wt (♀)
Bacterial reverse mutation assay S. typhimurium strains TA100, TA1535, TA98, and TA1537 and E. Coli strain WP2 uvrA PMRA# 2828224	Negative ± metabolic activation Tested up to a limit concentration.
S(PFP-OH)-8007	
Acute oral toxicity (up-down method) Wistar rats (♀) PMRA# 2828231	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) No clinical signs of toxicity.
14-day oral toxicity (diet) – Dose range-finding Wistar rats PMRA# 2828233	Supplemental NOAEL and LOAEL not established Effects at ≥ 472/503 mg/kg bw/day: adrenal discoloration (♂/♀) Effects at 1450 mg/kg bw/day: enlarged adrenal (♀) Limitations: small group sizes, limited pathology, short duration of study.

28-day oral toxicity (diet) Wistar rats PMRA# 2828234	NOAEL = 26 mg/kg bw/day/not established (♂/♀) LOAEL = 81/30 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ adrenal wt, ↑ adrenal vacuolation, adrenal discoloration (♂/♀)
90-day oral toxicity (diet) Wistar rats PMRA# 2828236	NOAEL not established LOAEL = 8.3/9.1 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ adrenal wt, ↑ vacuolation in the adrenal cortex (♂/♀); ↑ ovary wt, ↑ ovarian interstitial gland vacuolation (♀)
Bacterial reverse mutation assay S. typhimurium strains TA100, TA1535, TA98, and TA1537 and E. Coli strain WP2 uvrA PMRA# 2828232	Negative ± metabolic activation Tested up to a limit concentration.
DC-8007	
Acute oral toxicity (up-down method) Wistar rats (♀) PMRA# 2828238	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) No clinical signs of toxicity.
Bacterial reverse mutation assay S. typhimurium strains TA100, TA1535, TA98, and TA1537 and E. Coli strain WP2 uvrA PMRA# 2828239	Negative ± metabolic activation Tested up to a limit concentration.
MFBA	
Acute oral toxicity (up-down method) Wistar rats (♀) PMRA# 2828240	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) No clinical signs of toxicity.
In vitro chromosomal aberration assay Chinese hamster lung cells PMRA# 2828242	Negative ± metabolic activation ↑ chromosomal aberrations noted after 24 hrs of exposure in the absence of metabolic activation at precipitating concentrations Tested up to cytotoxic and precipitating concentrations.
In vivo micronucleus assay Sprague-Dawley rats (♂) PMRA# 2828243	Negative No mortalities or clinical signs of toxicity. Tested up to a limit dose.
28-day oral toxicity (gavage) Sprague-Dawley rats PMRA# 2828250	NOAEL = 330 mg/kg bw/day (♂/♀) LOAEL = 1000 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ infiltration of lymphocyte in the prostate (♂); ↑ lymphocyte count, ↑ hyperplasia in the squamous cells of the limiting ridge of the forestomach (♀)

	Effects at the highest dose tested that subsided after a 14-day recovery period: ↑ infiltration of lymphocyte in the prostate (♂); ↑ lymphocyte count, ↑ hyperplasia in the squamous cells of the limiting ridge of the forestomach (♀) There were no effects at the highest dose tested that persisted after a 14-day recovery period.
Bacterial reverse mutation assay S. typhimurium strains TA100, TA1535, TA98, and TA1537 and E. Coli strain WP2 uvrA PMRA# 2828241	Negative ± metabolic activation Tested up to a limit concentration.
AB-oxa	
Acute oral toxicity (acute toxic class) (♀) Wistar rats PMRA# 2828244	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) Clinical signs of toxicity included impaired general state and piloerection.
Bacterial reverse mutation assay S. typhimurium strains TA100, TA1535, TA98, and TA1537 and E. Coli strain WP2 uvrA PMRA# 2828247	Negative ± metabolic activation Tested up to a limit concentration.
S(Br-OH)-8007	
Acute oral toxicity (acute toxic class) Wistar rats (♀) PMRA# 2828248	Low acute toxicity LD_{50} > 2000 mg/kg bw (♀) Clinical signs of toxicity included impaired general state, piloerection and dyspnea.
Bacterial reverse mutation assay S. typhimurium strains TA100, TA1535, TA98, and TA1537 and E. Coli strain WP2 uvrA PMRA# 2828249	Negative ± metabolic activation Tested up to a limit concentration.

Table 6 Toxicological Reference Values for Use in Health Risk Assessment for Broflanilide

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary general population	Not established as no endpoint of concern attributable to a single exposure was identified.		
	ARfD not established		
Repeated dietary	12-month dietary toxicity in rats (from the 24-month oncogenicity study)	NOAEL = 1.7 mg/kg bw/day Adrenal gland vacuolization and ↑ adrenal gland wt	100
	ADI = 0.02 mg/kg bw/day		

Short-term dermal	28-day dermal toxicity in rats	NOAEL = 1000 mg/kg bw/day No adverse effects	100
Intermediate-term dermal	28-day dermal toxicity in rats	NOAEL = 1000 mg/kg bw/day No adverse effect	300
Short-term inhalation	28-day inhalation toxicity in rats	NOAEL = 8.4 mg/kg bw/day Adrenal gland vacuolation, spleen extramedullary hematopoiesis, ↑ severity of spleen pigment storage, ovary vacuolation, ↑ adrenal gland wt, ↑ ovary wt, ↑ heart wt	100
Intermediate-term inhalation	28-day inhalation toxicity in rats	NOAEL = 8.4 mg/kg bw/day Adrenal gland vacuolation, spleen extramedullary hematopoiesis, ↑ severity of spleen pigment storage, ovary vacuolation, ↑ adrenal gland wt, ↑ ovary wt, ↑ heart wt	300
Cancer	Leydig cell adenomas in male rats, and ovarian luteomas, ovarian granulosa cell tumours, and ovarian tumours of sex cord stromal origin (combined incidences of luteomas, thecomas, granulosa cell tumours, and sex cord stromal tumours), as well as adrenal cortex carcinomas and uterine adenocarcinoma in female rats. $q^1* = 2.1 \times 10^{-3}$ (mg/kg bw/day)$^{-1}$, based on the incidence of Leydig cell adenomas in male rats in the 2-year dietary study. For inhalation cancer risk assessment, $q^1* = 2.1 \times 10^{-2}$ (mg/kg bw/day)$^{-1}$, based on the incidence of Leydig cell adenomas in male rats in the 2-year dietary study and the application of a 10-fold adjustment factor to account for differences in absorption when extrapolating from an oral toxicity study to the inhalation route of exposure.	

[1] CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments; MOE refers to a target MOE for occupational assessments.

Table 7 M/L/A Non-Cancer Risk Assessment for Application of Cimegra In-furrow and/or T-Band at Planting

Crop	ATPD (ha/day)	Dermal UE (µg/kg a.i. handled)	Dermal Exposure (mg/kg bw/day) [1]	Dermal MOE [2]	Inhalation UE (µg/kg a.i. handled)	Inhalation Exposure (mg/kg bw/day) [1]	Inhalation MOE [3]
Potato	104	83.9	0.00273	367000	2.31	7.51×10^{-5}	1.12×10^5
Corn	100		0.00262	381000		7.22×10^{-5}	1.16×10^5

[1] Exposure (µg/kg a.i. handled) = (ATPD × Rate × Unit exposure)/(80 kg bw × 1000 µg/mg)
[2] MOE = Dermal NOAEL of 1000 mg/kg bw/day ÷ Dermal Exposure (mg/kg bw/day); Target MOE = 100
[3] MOE = Inhalation NOAEL of 8.4 mg/kg bw/day ÷ Inhalation Exposure (mg/kg bw/day); Target MOE = 100

Table 8 M/L/A Cancer Risk Assessment for Application of Cimegra In-furrow and/or T-Band at Planting

Crop	Dermal $q^{1*} = 0.0021$ (mg/kg bw/day)$^{-1}$			Inhalation $q^{1*} = 0.021$ (mg/kg bw/day)$^{-1}$			Total Cancer Risk [4]
	ADD [1]	LADD [2]	Cancer Risk [3]	ADD [1]	LADD [2]	Cancer Risk [3]	
Potato	2.73×10^{-3}	5.75×10^{-5}	1.2×10^{-7}	7.51×10^{-5}	1.58×10^{-6}	3.3×10^{-8}	2×10^{-7}
Corn	2.62×10^{-3}	5.53×10^{-5}	1.2×10^{-7}	7.22×10^{-5}	1.52×10^{-6}	3.2×10^{-8}	1×10^{-7}

[1] Absorbed Daily Dose (ADD) = Dermal/Inhalation Exposure (Table 1)
[2] Lifetime Average Daily Dose (LADD) = ADD × Number of Days of Exposure (15 days/year) × Duration of Exposure (40 years/lifetime) ÷ 365 days/year ÷ Life Expectancy (78 years/lifetime)
[3] Cancer Risk = LADD (mg/kg bw/day) × q^*_1 for the relevant route
[4] Total Cancer Risk = Dermal Cancer Risk + Inhalation Cancer Risk

Table 9 Exposure and non-cancer risk estimates to Teraxxa F4 and Teraxxa for workers in commercial seed treatment facilities and mobile treaters

Scenario/Task	kg a.i. handled per day[1]	Unit Exposure [2] (µg/kg a.i. handled)		Exposure [3,4] (mg/kg bw/day)		MOE	
		Dermal	Inhalation	Dermal	Inhalation	Dermal [5]	Inhalation [6]
Treating	4.6	265.7	2.47	1.53×10^{-2}	1.42×10^{-4}	65 500	59 100
Bagging		17.67	0.89	1.02×10^{-3}	5.12×10^{-5}	984 000	164 000
Cleaning	Application Rate: 5 g a.i./100 kg seed	18.46 µg/g a.i./100 kg seed	0.016 µg/g a.i./100 kg seed	1.15×10^{-3}	1.00×10^{-6}	867 000	8 400 000

[1] Estimated amount (kg) a.i. handled per day = Throughput (92 000 kg seed/day) × Application Rate (0.00005 kg a.i./kg seed)
[2] Unit exposure values from surrogate worker exposure studies on file with the PMRA.
[3] For treating and bagging:

$$\text{Exposure (mg/kg bw/day)} = \frac{\text{Unit exposure (µg/kg a.i. handled per day)} \times \text{kg a.i. handled per day}}{80 \text{ kg bw} \times 1000 \text{ µg/mg}}$$

[4] For cleaning, unit exposures are normalized for application rate therefore:

$$\text{Exposure (mg/kg bw/day)} = \frac{\text{Unit exposure (µg/g a.i./100 kg seed/day)} \times \text{application rate (g a.i./100 kg seed)}}{80 \text{ kg bw} \times 1000 \text{ µg/mg}}$$

[5] MOE = Dermal NOAEL of 1000 mg/kg bw/day ÷ Dermal Exposure (mg/kg bw/day); Target MOE = 300 or 100
[6] MOE = Inhalation NOAEL of 8.4 mg/kg bw/day ÷ Inhalation Exposure (mg/kg bw/day); Target MOE = 300 or 100

Table 10 Exposure and Non-Cancer Risk Estimates to Teraxxa F4 and Teraxxa from On-farm Treatment and Planting

Scenario/Task	kg a.i. handled per day [1]	Unit Exposure (µg/kg a.i. handled) [2]		Exposure (mg/kg bw/day) [3]		MOE	
		Dermal	Inhalation	Dermal	Inhalation	Dermal [4]	Inhalation [5]
Planting	1.34	1166.14	360.64	1.95×10^{-2}	6.04×10^{-3}	51 200	1390
On-farm Treating and Planting		145.22	7.61	2.43×10^{-3}	1.27×10^{-4}	411 000	65 900

[1] Estimated amount (kg) a.i. handled per day by a planter = Application Rate (kg a.i./kg seed) × Area planted per day (200 ha/day) × Wheat Seeding Rate (134 kg seed/ha) (PMRA# 2828009)
[2] Unit exposure values from surrogate worker exposure studies on file with the PMRA.
[3] Exposure (mg/kg bw/day) = $\frac{\text{Unit exposure (µg/kg a.i. handled per day)} \times \text{kg a.i. handled per day}}{80 \text{ kg bw} \times 1000 \text{ µg/mg}}$
[4] MOE = Dermal NOAEL of 1000 mg/kg bw/day ÷ Dermal Exposure (mg/kg bw/day); Target MOE = 100
[5] MOE = Inhalation NOAEL of 8.4 mg/kg bw/day ÷ Inhalation Exposure (mg/kg bw/day); Target MOE = 100

Table 11 Cancer Risk Assessment to Teraxxa F4 and Teraxxa from On-farm Treatment and Planting

Scenario/Task	Dermal q^1*=0.0021			Inhalation q^1* = 0.021			Total Cancer Risk [3]
	ADD	LADD [1]	Cancer Risk [2]	ADD	LADD [1]	Cancer Risk [2]	
Treating	7.97×10^{-3}	3.36×10^{-4}	7.06×10^{-7}	7.41×10^{-5}	3.12×10^{-6}	6.56×10^{-8}	3×10^{-6}
Bagging	5.30×10^{-4}	2.23×10^{-5}	4.69×10^{-8}	2.67×10^{-5}	1.13×10^{-6}	2.36×10^{-8}	1×10^{-6}
Cleaning	1.15×10^{-3}	4.86×10^{-5}	1.02×10^{-7}	1.00×10^{-6}	4.21×10^{-8}	8.85×10^{-10}	4×10^{-8}
Planting	1.95×10^{-2}	4.12×10^{-4}	8.64×10^{-7}	6.04×10^{-3}	1.27×10^{-4}	2.67×10^{-6}	4×10^{-6}
On-farm Treating and Planting	2.43×10^{-3}	5.13×10^{-5}	1.08×10^{-7}	1.27×10^{-4}	2.69×10^{-6}	5.64×10^{-8}	2×10^{-7}

[1] Lifetime Average Daily Dose (LADD) = ADD × Number of Days of Exposure (30 days/year for treating/bagging/cleaning and 15 days/year for Planting and On-Farm Treating and Planting) × Duration of Exposure (40 years/lifetime) ÷ 365 days/year ÷ Life Expectancy (78 years/lifetime)
[2] Cancer Risk = LADD (mg/kg bw/day) × q^1* for the relevant route
[3] Total Cancer Risk = Dermal Cancer Risk + Inhalation Cancer Risk

Table 12 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN LAYING HEN	PMRA# 2828264
Species and Numbers	24 laying hens (*Gallus gallus domesticus*)
Radiolabel position	[^{14}C-B-ring] (specific activity: 4.44 GBq/mmol) and [^{14}C-C-ring] (specific activity: 4.0 GBq/mmol)
Average dose	[^{14}C-B-ring]-label: 14.10 mg/kg feed (corresponding to 0.86 mg/kg bw/day) [^{14}C-C-ring]-label: 14.72 mg/kg feed (corresponding to 0.84 mg/kg bw/day)
Treatment Regimen	Once daily/Oral in gelatin capsule, in the morning after collection of eggs and excreta

Study period	14 consecutive days
Collection time	Eggs: 2/day (morning and evening); Excreta: 2/day
Tissues collected	Muscle (breast, thigh), fat (abdominal and subcutaneous), liver and eggs
Interval from last dose to sacrifice	6 hours
Plateau of residues in eggs	Not determined
Extraction solvent(s)	acetonitrile/water (1:1, v/v), acetone/hexane (1:4, v/v) and acetonitrile for fat

Matrices	**[^{14}C-B-ring]**		**[^{14}C-C-ring]**	
	TRRs (ppm)	**% of Administered Dose**	**TRRs (ppm)**	**% of Administered Dose**
Liver	0.5	*2.631*	0.4	*1.843*
Thigh (Leg) Muscle	0.8	*2.140*	0.5	*1.397*
Breast Muscle	0.1	*0.330*	0.1	*0.240*
Abdominal Fat	3.9	*19.132*	3.4	*15.770*
Subcutaneous Fat	1.5	*18.549*	1.0	*14.579*
Egg White (average of Day 1–14)	0.0	*0.014*	0.0	*0.012*
Egg Yolk (average of Day 1–14)	4.1	*3.605*	2.8	*3.365*
Excreta	56.0	*4.782*	65.0	*5.490*
GI Tract	6.1	*6.581*	6.0	*6.715*
Cagewash	0.1	*0.139*	0.1	*0.152*

Summary of Major Identified Metabolites in Hen Matrices	
Radiolabel Position	[^{14}C-B-ring], [^{14}C-C-ring]
Metabolites Identified	Major Metabolite
Breast muscle	DM-8007
Thigh muscle	
Abdominal fat	
Subcutaneous fat	
Egg yolk	
Egg white	
Liver	

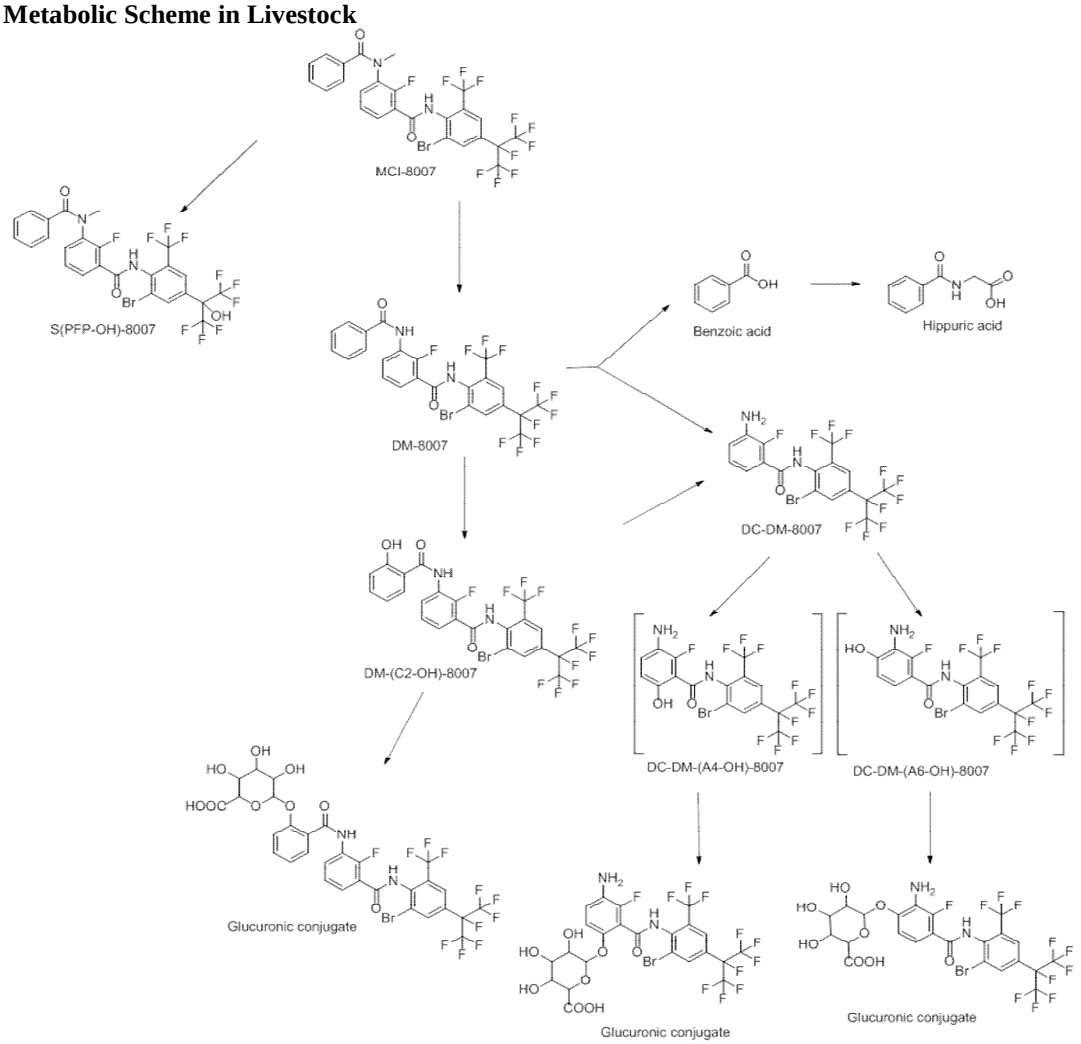
NATURE OF THE RESIDUE IN LACTATING GOAT	**PMRA# 2828265**
Species and Numbers	2 goats (*Capra hircus*)
Radiolabel position	[^{14}C-B-ring] (specific activity: 4.44 GBq/mmol) and [^{14}C-C-ring] (specific activity: 4.0 GBq/mmol)
Average dose	[^{14}C-B-ring]-label: 19.49 mg/kg feed (corresponding to 0.62 mg/kg bw/day) [^{14}C-C-ring]-label: 20.19 mg/kg feed (corresponding to 0.73 mg/kg bw/day)
Treatment Regimen	Once daily/Oral in gelatin capsule, in the morning after milking
Study period	10 consecutive days
Collection time	Milk: 2/day (morning and evening); Excreta: 2/day
Tissues collected	Muscle (flank, loin), fat (subcutaneous, omental, renal), kidney, liver and milk
Interval from last dose to sacrifice	8-12 hours
Plateau of residues in milk	Not determined
Extraction solvent(s)	acetonitrile/water (1:1, v/v), acetone/hexane (1:4, v/v) and acetonitrile for fat

Matrices	[^{14}C-B-ring]		[^{14}C-C-ring]	
	TRRs (ppm)	**% of Administered Dose**	**TRRs (ppm)**	**% of Administered Dose**
Flank Muscle	0.0	0.300	0.0	0.370
Loin Muscle	0.0	0.216	0.0	0.228
Skim Milk [1)]	0.0	0.017	0.0	0.028
Milk Fat [1)]	0.7	2.967	0.7	1.628
Whole Milk [2)]	0.7	0.254	0.7	0.269
Omental Fat	0.9	3.411	0.8	3.422
Subcutaneous Fat	0.1	2.598	0.1	2.830
Renal Fat	0.2	3.065	0.3	3.290
Liver	0.7	2.197	0.1	0.457
Kidney	0.0	0.250	0.0	0.265
Blood	0.0	0.095	0.0	0.071
Urine	0.7	0.068	23.6	4.187
Bile	0.0	6.511	0.0	1.122
Faeces	75.4	19.154	51.0	9.057
Cagewash	0.0	0.045	0.8	0.513
Gastrointestinal Tract	13.0	3.181	9.6	2.795
Muscle				

[1)] TRR for skim milk and milk fat was calculated based on the average dpm/g of Day 1 pm to Day 10 pm samples.
[2)] TRR (ppm) in whole milk = (TRR in skim milk+TRR in milk fat)/sample weight of whole milk.

Summary of Major Identified Metabolites in Goat Matrices	
Radiolabel Position	[^{14}C-B-ring], [^{14}C-C-ring]
Metabolites Identified	Major Metabolites
Subcutaneous fat	DM-8007, DC-DM-8007
Omental fat	DM-8007, DC-DM-8007
Renal fat	DM-8007, DC-DM-8007
Flank muscle	DM-8007, DC-DM-8007
Loin muscle	DM-8007, DC-DM-8007
Liver	DM-8007, DC-DM-8007, DC-DM-(A4-OH)-8007, DC-DM-(A6-OH)-8007, DM-(C2-OH)-8007, Hippuric acid
Kidney	DM-8007, DC-DM-8007, Hippuric acid
Skim milk	DM-8007, DC-DM-8007, Hippuric acid
Milk fat	DM-8007, DC-DM-8007

Proposed Metabolic Scheme in Livestock



FREEZER STORAGE STABILITY IN ANIMAL MATRICES		
Tested Matrices	**Analyte(s)**	**Tested Intervals (months)**
Whole milk, fat, liver, kidney and muscle	Broflanilide and DM-8007	60 days (2 months)

Concurrent freezer storage stability study was conducted as part of the cattle feeding study and the analytes were confirmed stable during the freezer storage period of 60 days.

All laying hen samples in the feeding study were stored frozen and analyzed within 15 days of storage. No freezer storage stability test is required.

LIVESTOCK FEEDING – Dairy cattle	**PMRA# 2828271**

Lactating dairy cows were administered broflanilide at dose levels of 0.015 ppm, 0.152 ppm, 1.5 ppm and 10.1 ppm in the feeds for 41 consecutive days. The dose levels represent 2.1-fold, 22-fold , 214-fold , and 1443-fold , respectively, the estimated more balanced diet (MBD) for beef cattle (0.007 ppm) and 2.5-fold , 25-fold , 250-fold , and 1683-fold , respectively, for dairy cattle (0.006 ppm). Animals were sacrificed within 24 hours after the last dose. A depuration study was conducted using the 10.1 ppm feeding level and selected animals were sacrificed at 44, 48 and 55 days after the last dose. Clearance of residues of broflanilide and its metabolites from milk and tissues during the depuration period was observed.

Commodity/Collection Day	Actual Feeding Level (ppm)	Highest Residues (ppm)		Combined Residues * (ppm)
		Broflanilide	DM-8007	
Milk	0.015	<0.001	<0.001	0.0020
	0.152	<0.001	0.0025	0.0036
	1.5	<0.001	0.016	0.0174
	10.1	0.0018	0.120	0.1244
Skimmed milk	0.015	<0.001	<0.001	0.0020
	0.152	<0.001	<0.001	0.0020
	1.5	<0.001	0.0016	0.0026
	10.1	<0.001	0.0140	0.0153
Cream	0.015	<0.001	0.0044	0.0055
	0.152	<0.001	0.022	0.0235
	1.5	0.0051	0.18	0.1891
	10.1	0.016	1.3	1.3446
Muscle	0.015	<0.001	<0.01	0.020
	0.152	<0.01	<0.01	0.020
	1.5	<0.01	<0.01	0.020
	10.1	<0.01	0.038	0.049
Liver	0.015	<0.01	<0.01	0.020
	0.152	<0.01	<0.01	0.020
	1.5	<0.01	0.013	0.023
	10.1	<0.01	0.078	0.090
Kidney	0.015	<0.01	0.01	0.020
	0.152	<0.01	<0.01	0.020
	1.5	<0.01	<0.01	0.020
	10.1	<0.01	0.080	0.092
Fat Perirenal	0.015	<0.01	<0.01	0.020
	0.152	<0.01	0.013	0.023
	1.5	<0.01	0.11	0.122
	10.1	<0.01	0.61	0.633
Fat Mesenterial	0.015	<0.01	<0.01	0.020
	0.152	<0.01	0.016	0.026
	1.5	<0.01	0.16	0.174
	10.1	<0.01	0.79	0.817
Fat Subcutaneous	0.015	<0.01	<0.01	0.020
	0.152	<0.01	0.01	0.020
	1.5	<0.01	0.11	0.122
	10.1	<0.01	0.55	0.572

* Sum of broflanilide and DM-8007, expressed as parent equivalents based on the conversion factor of 1.02 for DM-8007. The calculations were performed using LOQ values when the DM-8007 residues were <LOQ.

Anticipated Residues in Animal Matrices

Matrices	Residue Definition	Dietary Burden (ppm)	Anticipated Combined Residues (ppm)
Beef/Dairy Cattle			
Cattle Milk	Parent+DM-8007	0.006	0
Cattle Milk fat	Parent+DM-8007	0.006	0.001
Cattle Skim milk	Parent+DM-8007	0.006	0
Beef Muscle	Parent+DM-8007	0.007	< LOQ (0.02)
Beef Liver	Parent+DM-8007	0.007	< LOQ (0.02)
Beef Kidney	Parent+DM-8007	0.007	< LOQ (0.02)
Beef Perirenal fat	Parent+DM-8007	0.007	0.001
Beef Mesenterial fat	Parent+DM-8007	0.007	0.001
Beef Subcutaneous fat	Parent+DM-8007	0.007	< LOQ (0.02)

LIVESTOCK FEEDING – Laying hens	**PMRA# 2828270**

Laying hens were administered broflanilide at dose levels of 0.021 ppm, 0.102 ppm and 0.509 ppm in the feeds for 29 (Low dose), 36 (Mid dose) and 50 (High dose) consecutive days. The dose levels represent 3x, 15x, and 73x, respectively, the estimated MBD to poultry (0.007 ppm). Animals were sacrificed approximately 6 hours after the last dose. A depuration study was conducted using the 0.509 ppm feeding level and selected animals were sacrificed at 52, 56, 59 and 63 days after the last dose. Residues of broflanilide were <LOQ (0.01 ppm) throughout depuration period. Residues of DM-8007 decreased from 0.0218 ppm on Day 52 to <LOQ (0.01 ppm) on Day 62.

Commodity/Collection Day	**Actual Feeding Level (ppm)**	**Highest Residues (ppm)**		**Combined Residues (ppm)**
		Broflanilide	DM-8007	
Whole eggs	0.021	<0.01	<0.01	0.020
	0.102	<0.01	<0.01	0.020
	0.509	<0.01	0.0226	0.033
Muscle (Thigh and Breast)	0.021	<0.01	<0.01	0.020
	0.102	<0.01	<0.01	0.020
	0.509	<0.01	<0.01	0.020
Liver	0.021	<0.01	<0.01	0.020
	0.102	<0.01	<0.01	0.020
	0.509	<0.01	0.0211	0.032
Fat (Abdominal + Subcutaneous)	0.021	<0.01	0.0108	0.021
	0.102	<0.01	0.0392	0.050
Sum of broflanilide and DM-8007 expressed as parent equivalents based on the conversion factor of 1.02 for DM-8007. The calculations were performed using LOQ values when the DM-8007 residues were <LOQ.	0.509	<0.01	0.1522	0.166

Anticipated Residues in Poultry Matrices

Matrices	**Residue Definition**	**Dietary Burden (ppm)**	**Anticipated Combined Residues (ppm)**
Poultry Whole eggs	Parent+DM-8007	0.007	< LOQ (0.02)
Poultry Muscle	Parent+DM-8007	0.007	< LOQ (0.02)
Poultry Liver	Parent+DM-8007	0.007	< LOQ (0.02)
Poultry Fat	Parent+DM-8007	0.007	0.004

NATURE OF THE RESIDUE IN Cabbage	**PMRA# 2828258**
Radiolabel Position	[^{14}C-B-ring] (specific activity: 4.33 GBq/mmol) and [^{14}C-C-ring] (specific activity: 4.44 GBq/mmol)
Treatment	
Test Site	In individual pots maintained in a outdoor
Treatment	Two post-emergence foliar treatment at BBCH 45-46
Total Rate	Both radio-labels: 2 × 25 g a.i./ha; Total rate of 52.3–54.4 g a.i./ha
Formulation	Suspension concentrate (SC) formulation
Harvest	Immature cabbage: 6 days after 1st application (6DAT1) Mature cabbage: 21 days after 2nd application (21DAT2)
Extraction solvent(s)	acetonitrile:water (1:1, v/v)

Matrices	**PHI (days)**	**[^{14}C-B-ring] TRR (ppm)**	**[^{14}C-C-ring] TRR (ppm)**
Wrapper leaves	6 (6DAT1)	0.288	0.199
Head without wrapper leaves		0.064	0.105
Wrapper leaves	21 (21DAT2)	0.181	0.300
Head without wrapper leaves		0.000	0.005

Summary of Major Identified Metabolites in Cabbage Matrices			
Radiolabel Position	[^{14}C-B-ring], [^{14}C-C-ring]		
Matrices	Major Residue		
Immature cabbage Mature cabbage	Broflanilide		
NATURE OF THE RESIDUE IN Japanese Radish			**PMRA# 2828261**
Radiolabel Position	[^{14}C-B-ring] (specific activity: 4.19 GBq/mmol) and [^{14}C-C-ring] (specific activity: 4.44 GBq/mmol)		
Treatment			
Test Site	In individual pots maintained in a greenhouse		
Treatment	Soil drench first at BBCH 00, followed by post-emergence foliar treatment		
Total Rate	Both radio-labels: 1st at 390–394 g a.i./ha; 2nd at 220–227 g a.i./ha; total of 610–621 g a.i./ha		
Formulation	Suspension concentrate (SC) formulation		
Harvest	Leaves and roots: 40 days after 1st treatment (40DAT1), 14 days after 2nd treatment (14DAT2) and 29 days after 2nd treatment (29DAT2)		
Extraction solvent(s)	acetonitrile:water (8:2, v/v)		
Matrices	**PHI (days)**	**[^{14}C-B-ring] TRR (ppm)**	**[^{14}C-C-ring] TRR (ppm)**
Radish leaves (40DAT1)	40	0.0059	0.0069
Radish leaves (14DAT2)	14	3.8682	4.4428
Radish leaves (29DAT2)	29	4.1775	3.6079
Radish roots (40DAT1)	40	0.0038	0.0076
Radish roots (14DAT2)	14	0.0113	0.0112
Radish roots (29DAT2)	29	0.0036	0.0119
Summary of Major Identified Metabolites in Japanese Radish Matrices			
Radiolabel Position	[^{14}C-B-ring], [^{14}C-C-ring]		
Matrices	Major Residue		
Radish leaves	Broflanilide		
NATURE OF THE RESIDUE IN Rice			**PMRA# 2828263**
Radiolabel Position	[^{14}C-B-ring] (specific activity: 2.788 GBq/mmol) and [^{14}C-C-ring] (specific activity: 2.093 GBq/mmol)		
Treatment			
Test Site	In individual pots maintained greenhouse		
Treatment	Applied to flooding water on paddy soil, first at transplanting, followed by post-emergence foliar treatment		
Total Rate	Both radio-labels: 1st at 295–299 g a.i./ha; 2nd at 147-148 g a.i./ha; total of 442–447 g a.i./ha		
Formulation	Suspension concentrate (SC) formulation		
Harvest	Foliage at a PHI of 13 days, Brown rice, hull, straw and root at a PHI of 32 days		
Extraction solvent(s)	acetonitrile:water, 8:2, v/v		
Matrices	**PHI (days)**	**[^{14}C-B-ring] TRR (ppm)**	**[^{14}C-C-ring] TRR (ppm)**
Foliage	13	1.1491	1.9096
Brown rice	32	0.0207	0.1114
Hull		5.5093	6.7494
Straw		4.8864	4.1665
Root		1.6821	0.7560
Summary of Major Identified Metabolites in Rice Matrices			
Radiolabel Position	[^{14}C-B-ring], [^{14}C-C-ring]		
Matrices	Major Residue		
Foliage, brown rice, hull and straw	Broflanilide		

NATURE OF THE RESIDUE IN Soybean			**PMRA# 2828259**
Radiolabel Position	[^{14}C-B-ring] (specific activity: 4.33 GBq/mmol) and [^{14}C-C-ring] (specific activity: 4.44 GBq/mmol)		
Treatment			
Test Site	Grown outdoor		
Treatment	2 post-emergence foliar treatments at BBCH 49-51 and BBCH 79-81		
Total Rate	Both radio-labels: 2 × 25 g a.i./ha; Total rate of 50.4-53.6 g a.i./ha		
Formulation	Suspension concentrate (SC) formulation		
Harvest	Forage: 21 days after 1st application (21DAT1), Hay: 35 days after 1st application (35DAT1) Soybean seed: 12 days after 2nd application (12DAT2)		
Extraction solvent(s)	acetonitrile:water (1:1, v/v)		
Matrices	**PHI (days)**	**[^{14}C-B-ring] TRR (ppm)**	**[^{14}C-C-ring] TRR (ppm)**
Forage (21DAT1)	21	0.460	0.433
Hay (35DAT1)	35	0.261	0.287
Soybean seed (12DAT2)	12	0.008	0.008
Summary of Major Identified Metabolites in Soybean Matrices			
Radiolabel Position	[^{14}C-B-ring], [^{14}C-C-ring]		
Matrices	Major Residue		
Soybean forage and hay	Broflanilide		
NATURE OF THE RESIDUE IN TEA			**PMRA# 2828260**
Radiolabel Position	[^{14}C-B-ring] (specific activity: 4.33 GBq/mmol) and [^{14}C-C-ring] (specific activity: 4.44 GBq/mmol)		
Treatment			
Test Site	Grown outdoor		
Treatment	2 post-emergence foliar treatments (growth stage was not provided in the study report)		
Total Rate	Both radio-labels: 2 × 100 g a.i./ha; Total rate of 224–225 g a.i./ha		
Formulation	Suspension concentrate (SC) formulation		
Harvest	Tea leaves: 7 and 14 days after the 2nd application		
Extraction solvent(s)	acetonitrile:water (1:1, v/v)		
Matrices	**PHI (days)**	**[^{14}C-B-ring] TRR (ppm)**	**[^{14}C-C-ring] TRR (ppm)**
Tea leaves	7	19.359	20.289
Tea leaves	14	17.016	15.000
Summary of Major Identified Metabolites in Tea Leaves			
Radiolabel Position	[^{14}C-B-ring], [^{14}C-C-ring]		
Matrices	Major Residue		
Tea leaves	Broflanilide		
NATURE OF THE RESIDUE IN TOMATO			**PMRA# 2828257**
Radiolabel Position	[^{14}C-B-ring] (specific activity: 4.33 GMBq/mmol) and [^{14}C-C-ring] (specific activity: 4.44 GMBq/mmol)		
Treatment			
Test Site	In individual pots maintained in a greenhouse		
Treatment	2 post-emergence foliar treatments at BBCH 49-50 and BBCH 79-81		
Total Rate	Both radio-labels: 2 × 25 g a.i./ha; Total rate of 50.3–52.7 g a.i./ha		
Formulation	Suspension concentrate (SC) formulation		
Harvest	Tomato leaves and fruits: 71 days after 1st application (71DAT1) and 10 days after 2nd application (10DAT2)		
Extraction solvent(s)	acetonitrile:water (1:1, v/v)		

Matrices	PHI (days)	[^{14}C-B-ring] TRR (ppm)	[^{14}C-C-ring] TRR (ppm)
Leaves	71 (71DAT1)	≤0.001	1.596
Leaves Surface Rinse		0.000	1.057
Rinsed Leaves		0.001	0.539
Fruits		≤0.001	0.01
Fruit Surface Rinse		Not detectable	0.007
Rinsed Fruits		Not detectable	0.003
Leaves	10 (10DAT2)	≤0.001	0.904
Leaves Surface Rinse		0.000	0.678
Rinsed Leaves		0.000	0.226
Fruits		≤0.001	0.01
Fruit Surface Rinse		Not detectable	0.008
Rinsed Fruits		Not detectable	0.002

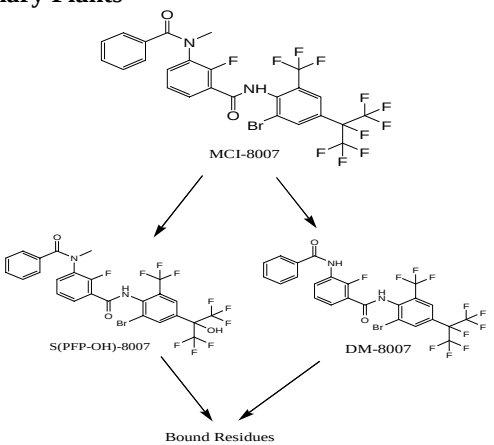
Summary of Major Identified Metabolites in Tomato Matrices	
Radiolabel Position	[^{14}C-B-ring], [^{14}C-C-ring]
Metabolites Identified	Major Residue
Tomato leaves	Broflanilide
Tomato fruits	

NATURE OF THE RESIDUE IN WHEAT		**PMRA# 2828257**
Radiolabel Position	[^{14}C-B-ring] (specific activity: 6.71 MBq/mg) only	
Treatment		
Test Site	In individual pots maintained in a greenhouse	
Treatment	Seed treatment	
Total Rate	10 g a.i./100 kg seed	
Formulation	Suspension concentrate (SC) formulation	
Harvest	Forage and hay: 77 days after planting Straw and grain: 154 days after planting	
Extraction solvent(s)	acetonitrile:water, 1:1, v/v	

Matrices	PHI (days)	[^{14}C-B-ring] TRR (ppm)	[^{14}C-C-ring] TRR (ppm)
Wheat forage	77	0.002	Not applicable
Wheat hay		0.006	
Wheat straw	154	0.029	
Wheat grain		0.011	

Summary of Major Identified Metabolites in Wheat Matrices	
Radiolabel Position	[^{14}C-B-ring]
Matrices	Major Residue
Wheat forage, hay, straw and grain	None identified

Proposed Metabolic Scheme in Primary Plants



FREEZER STORAGE STABILITY IN PLANT MATRICES				PMRA# 2828254, 3004631, 3004632
Tested Matrices	**Analyte(s)**	**Tested Intervals (months)**	**Temperature (°C)**	**Category**
Lettuce	Broflanilide	0, 3, 5, 9, 12, 15 and 24	-20	High-water
Kidney bean				High-protein
Potato				High-starch
Soybean seed				High-oil
Grape				High-acid

CROP FIELD TRIALS AND RESIDUE DECLINE ON POTATO — **PMRA# 2828266**

Twenty independent field trials on potatoes were conducted in 2015–2016 in Canada and the United States encompassing North American growing regions 1 (3 trials in New York and 1 trial in Pennsylvania), 2 (1 trial in Georgia), 3 (1 trial in Florida), 5 (1 trial each in Iowa, North Dakota and Nebraska), 5A (1 trial in Wisconsin), 7 (1 trial in Saskatchewan), 8 (1 trial in Kansas), 9 (2 trials in Utah), 10 (1 trial in California), 11 (2 trials in Idaho and 1 trial in Washington), 12 (1 trial in California), 14 (1 trial in Alberta).

At each test location, one untreated (Plot 1) and two treated plots (Plots 2 and 3) were established. Treated Plot 2 (in 19 of 20 trials) received two foliar broadcast applications of BAS 450 00 I (SC formulation containing 100 g/L of active substance), the first of which was 20–22 days prior to potato harvest at 23.9–28.2 g a.i./ha, and the last application was 13–14 days prior to potato harvest at 23.1–26.1 g a.i./ha, with total rates of 47.8–53.9 g a.i./ha/season. An adjuvant (non-ionic spreader/sticker/surfactant) was included in the spray mixture. Treated Plot 3 (in 19 of 20 trials) received one in-furrow application, at planting, of BAS 450 00 I (containing 100 g/L of active substance) at 47.7–53.8 g a.i./ha. Potato RAC samples were harvested 146 days after the in-furrow application. The locations of the field trials conducted did not meet the requirements of DIR2010-05. Given the total number and the geographic representation of the trials, the locations of the potato trials are considered adequate. At two field trial sites (Plot 2 only), samples were collected at different time intervals (0, 7, 18, and 21 days after last application) to monitor residue decline. Broflanilide residues were not quantifiable in all potato samples except for one sample at 0.0013 ppm with a PHI of 0 day. Therefore, no trend was observed.

Adequate storage stability data for broflanilide are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	**Total Application Rate (g a.i./ha)**	**PHI (days)**	**Analyte**	**Residue Levels (ppm)**					
				n	**LAFT**	**HAFT**	**Median**	**Mean**	**SDEV**
Potato tuber (foliar)	47.8–53.9	13–14	Broflanilide	19	<0.001	0.0068	0.001	0.0019	0.002
Potato tuber (in-furrow)	47.7–53.8	80–146		19	<0.001	0.0335	0.0017	0.0044	0.008

n = number of independent trials.

CROP FIELD TRIALS AND RESIDUE DECLINE ON CORN (FIELD AND SWEET)	PMRA# 2828267

Nineteen independent trials (in seven of these trials, field corn was sampled at milking stage to simulate sweet corn RAC samples (K+CWHR and forage)) were conducted on field corn in the United States encompassing the North America Growing Regions 1 (1 trial each in New York and New Jersey), 5 (3 trials in Iowa, 1 trial in Minnesota, 1 trial in Indiana, 3 trials in Illinois, 1 trial in Missouri, 3 trials in Nebraska and 1 trial in Kansas), 5A (1 trial in Michigan and 2 trials in Wisconsin), 6 (1 trial in Oklahoma). Five independent trials were conducted on sweet corn in Canada and the United States encompassing NAFTA Growing Regions 3 (1 trial in Florida), 7A (1 trial in Alberta), 10 (1 trial in California), 11 (1 trial in Washington), and 12 (1 trial in Oregon).

At each location, one untreated control plot (treatment 1) and one treated plot (treatment 2) were established for field corn and sweet corn. The treated plots received one in-furrow application of broflanilide (SC formulation, nominal concentration 100 g a.i./L) at 48.8-51.2 g a.i./ha. No adjuvant was included in the spraying mixtures. Sweet corn kernel + cob with husk removed (K+CWHR) and forage RAC samples were collected 62–94 days after application (DAA). Sweet corn stover RAC samples were collected 99–146 DAA. Field corn forage RAC samples were collected 73–110 DAA. Field corn grain and stover RAC samples were collected 112–164 DAA. No residue decline trial was conducted.

Adequate storage stability data for broflanilide are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method. The locations of the field trials conducted meet the requirements of DIR2010-05 for field corn, but do not meet the requirements for sweet corn. Given the total number and geographic representation of the trials, the sweet corn trials are considered adequate.

Crop	Total Application Rate (g a.i./ha)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
K+CWHR	49.7–51.2	62–94	Broflanilide	12	<0.001	<0.001	<0.001	<0.001	0
Forage (field and sweet)	48.8–51.2	62–110		25	<0.001	<0.001	<0.001	<0.001	0
Stover (field and sweet)		99–164		25	<0.001	<0.001	<0.001	<0.001	0
Grain	48.8–51.2	112–164		20	<0.001	<0.001	<0.001	<0.001	0

n = number of independent trials.

CROP FIELD TRIALS AND RESIDUE DECLINE ON WHEAT	PMRA# 2828268

A total of 23 independent trials were conducted on wheat during the 2015–2016 growing seasons, including 10 independent winter wheat trials in the United States encompassing the North America Growing Regions 2 (1 trial in North Carolina), 4 (1 trial in Arkansas), 5 (1 trial each in Iowa, Illinois and Kansas), 6 (1 trial each in Texas and 1 Oklahoma) and 8 (2 trials in Texas and 1 trial in Kansas) and 13 independent trials on spring wheat in Canada and the United States encompassing Growing Regions 5 (1 trial in Nebraska), 7 (2 trials each in North Dakota and Nebraska), 7A (1 trial in Alberta), 11 (1 trial in Indiana), 14 (3 trials in Manitoba, 2 trials in Saskatchewan and 1 trial in Alberta).

At each location, one untreated control plot (Treatment 1) and one treated plot (Treatment 2) were established in wheat (winter and spring wheat). The treated plot was planted with wheat seed treated with broflanilide at 9.52–10.7 g a.i./100 kg of seed. No adjuvant was used in the seed treatment. RAC samples (wheat forage, hay, grain and straw) were harvested at maturity.

Adequate storage stability data for broflanilide are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method. The locations of the field trials conducted did not meet the requirements of DIR2010-05. Given the total number and the geographic representation of the trials, the locations of the potato trials are considered adequate.

Crop	Total Application Rate (g a.i./100 kg seed)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Wheat forage	9.52–10.7	25–190	Broflanilide	23	<0.001	0.0011	<0.001	<0.001	0.000020
Wheat hay		46–220		23	<0.001	0.0012	<0.001	<0.001	0.000035
Wheat grain		83–274		23	<0.001	<0.001	<0.001	<0.001	0
Wheat straw		83–274		23	<0.001	0.0011	<0.001	<0.001	0.00002

n = number of independent trials.

CROP FIELD TRIALS AND RESIDUE DECLINE ON BARLEY **PMRA# 2828269**

A total of 16 independent trials were conducted on barley during the 2015–2016 growing seasons in Canada and the United States encompassing North America Growing Regions 1 (1 trial in New York), 5 (1 trial in North Dakota), 5A (1 trial in Wisconsin), 7 (2 trials in Nebraska and 1 trial in North Dakota), 7A (1 trial in Alberta), 9 (1 trial in Utah), 10 (1 trial in California), 11 (1 trial in Idaho), 14 (2 trials in Manitoba, 3 trials in Saskatchewan and 1 trial in Alberta).

At each location, one untreated control plot (Treatment 1) and one treated plot (Treatment 2) were established. The treated plot was planted with barley seed treated with broflanilide at 9.48–10.44 g a.i./100 kg of seed. No adjuvant was used in the seed treatment. RAC samples (barley forage, hay, grain and straw) were harvested at maturity.

Adequate storage stability data are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method. The locations of the field trials conducted did not meet the requirements of DIR2010-05. Given the total number and the geographic representation of the trials, the locations of the potato trials are considered adequate.

Crop	Total Application Rate (g a.i./ha)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Barley hay	9.48–10.44	57–420	Broflanilide	16	<0.001	0.0032	0.0010	0.0012	0.0006
Barley grain		72–448		16	<0.001	<0.001	0.0010	0.0010	0
Barley straw		72–448		16	<0.001	<0.001	0.0010	0.0010	0

n = number of independent trials.

PROCESSED FOOD AND FEED – Potato, field corn and wheat **PMRA# 2828274,2828275 and 2828276**

Processing studies were conducted in 2 distinctive North American growing regions using SC formulation of broflanilide at 8–36-fold of maximum single seasonal use rates in/on potato, field corn and wheat. Adequate storage stability data are available on diverse crop types to support the storage intervals of the processed food and feed. Samples were analyzed using a validated analytical method.

RAC	Processed Fractions	$HAFT_{[RAC]}$ at GAP (ppm)	Median Processing Factor of Broflanilide	Anticipated Residues of Broflanilide (ppm)
Potato	Peeled potato	0.0335	<0.1	<0.0034
	Peel, wet		2.4	0.0804
	Boiled potatoes		<0.1	<0.0034
	Microwave/boiled potatoes (unpeeled)		0.22	0.0074
	Baked potato		0.18	0.0060
	Fried potato		<0.1	<0.0034
	Crisps		<0.1	<0.0034
	Chips		0.16	0.0054
	Granules/Flakes		<0.1	<0.0034
	Process waste		<0.19	<0.0064
	Ensiled		0.35	0.0117
	Starch		<0.19	<0.0064
	Dried pulp		1.2	0.0402
	Potato protein		1.4	0.0469
Field corn	Bran	<0.001	1.7	<0.0017
	Dry Milling Grits		0.23	<0.0002
	Dry Milling Meal		1.4	<0.0014

	Dry Milling Flour		2.1	<0.0021
	Flour - Wet Process		0.16	<0.0002
	Germ		0.74	<0.0007
	Germ (Wet Milling)		1.2	<0.0012
	Gluten		1.5	<0.0015
	Gluten Feed Meal		5.2	<0.0052
	Milled Byproducts		6.3	<0.0063
	Wet Milling RBD Oil		0.35	<0.00035
	Dry Milling RBD Oil		0.81	<0.0008
	Wet Milling Starch		0.16	<0.00016
Wheat	Bran	<0.001	0.92	<0.00092
	Flour		0.44	<0.00044
	Middlings		0.38	<0.00038
	Shorts		0.47	<0.00047
	Gluten		4.1	<0.0041
	Gluten Feed Meal		1.8	<0.0018
	Milled Byproducts		8.3	<0.0083
	Starch		0.02	<0.00002
	Germ		1.8	<0.0018
	Whole Meal Flour		0.63	<0.00063
	Whole Grain Bread		0.63	<0.00063

CONFINED ACCUMULATION IN ROTATIONAL CROPS – Lettuce, radish and wheat	**PMRA# 2828277**
Radiolabel Position	[^{14}C-A-ring] (specific activity: 6.53 MBq/mg) and [^{14}C-B-ring] (specific activity: 6.69 MBq/mg)

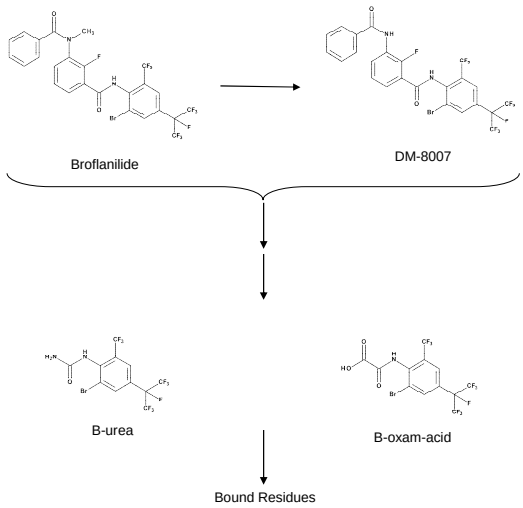
Treatment

Test Site	Field plots outdoors
Soil Type	Sandy loam
Treatment	Bare soil was treated at 143–158 g a.i./ha, and aged for 30, 120 and 270 days.
Formulation	Suspension concentrate (SC) formulation of Broflanilide
Extraction solvent(s)	Acetonitrile:water (8:2, v/v)

Matrices	**PBI (days)**	**[^{14}C-A-ring] TRR (ppm)**	**[^{14}C-B-ring] TRR (ppm)**
Lettuce (Immature)	30	0.002	0.007
Lettuce (Mature)		0.005	0.008
Radish (Top)		0.003	0.006
Radish (Root)		0.002	0.002
Wheat (Forage)		0.003	0.006
Wheat (Hay)		0.014	0.030
Wheat (Straw)		0.026	0.052
Wheat (Grain)		0.004	0.007
Lettuce (Immature)	120	0.008	0.013
Lettuce (Mature)		0.009	0.020
Radish (Top)		0.006	0.008
Radish (Root)		0.003	0.006
Wheat (Forage)		0.004	0.016
Wheat (Hay)		0.016	0.045
Wheat (Straw)		0.022	0.038
Wheat (Grain)		0.005	0.004
Lettuce (Immature)	270	0.012	0.016
Lettuce (Mature)		0.002	0.011
Radish (Top)		0.015	0.014
Radish (Root)		0.003	0.003
Wheat (Forage)		0.009	0.016
Wheat (Hay)		0.029	0.067
Wheat (Straw)		0.028	0.075
Wheat (Grain)		0.009	0.013

Summary of Major Identified Metabolites in Rotated Crops (>10% TRRs)			
Plant-back Intervals (PBI)	1st Rotation (30-day PBI)	2nd Rotation (120-day PBI)	3rd Rotation (270-day PBI)
Radiolabel Position	[^{14}C-A-ring], [^{14}C-B-ring]		
Matrices	Major Residues		
Wheat forage	-	B-urea	B-oxam-acid, B-urea, broflanilide
Wheat hay	B-oxam-acid, B-urea	B-oxam-acid, B-urea	B-oxam-acid, B-urea
Wheat straw	B-oxam-acid, broflanilide	B-oxam-acid, B-urea, broflanilide	B-oxam-acid, B-urea
Radish foliage	-	-	Broflanilide, B-oxam-acid, B-urea
Immature lettuce	-	Broflanilide, B-urea	Broflanilide, B-urea
Mature lettuce	-	Broflanilide	Broflanilide, B-urea

Proposed Metabolic Scheme in Rotational Crops



RESIDUE DATA IN ROTATIONAL CROPS | **PMRA# 2828278, 3004633**

Eighteen trials (two each for radish, lettuce and winter wheat) were conducted during the 2016 growing season in North American growing regions 5 and 10. One broadcast application was made to bare soil with broflanilide in SC formulation at a rate of 48-52 g a.i./ha. No adjuvants were used at all trial sites. Adequate storage stability data are available on diverse commodity categories to support the storage intervals of the rotational crop field trials. Samples were analyzed using a validated analytical method.

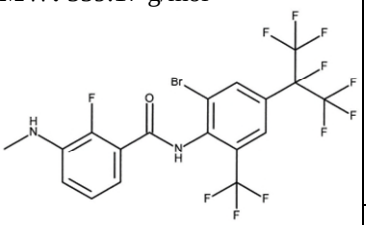
Commodity	Total Application Rate (g a.i./ha)	PBI (days)	Residue Levels (ppm)	
			n	Broflanilide
Wheat forage	49.9	30	2	<0.01, <0.01
Wheat hay				<0.01, <0.01
Wheat grain				<0.01, <0.01
Wheat straw				<0.01, <0.01
Wheat forage	49.9-51.9	60	2	<0.01, <0.01
Wheat hay				<0.01, <0.01
Wheat grain				<0.01, <0.01
Wheat straw				<0.01, <0.01
Wheat forage	49.7-51.9	91	2	<0.01, <0.01
Wheat hay				<0.01, <0.01
Wheat grain				<0.01, <0.01
Wheat straw				<0.01, <0.01
Lettuce	47.7–49.9	30	2	<0.01, 0.015
	48.6–51.9	58–60	2	<0.01, <0.01
	50.2–51.9	91–92	2	<0.01, <0.01
Radish tops	49.5–49.9	30	2	<0.01, <0.01

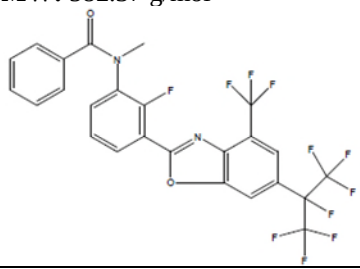
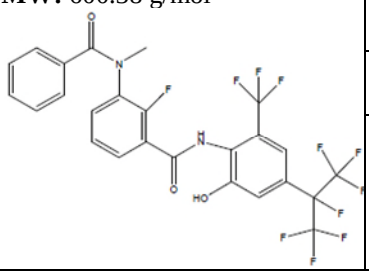
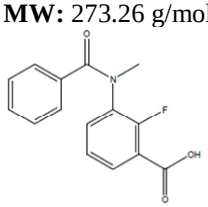
Radish roots				<0.01, <0.01
Radish tops	48.3–51.9	58–60	2	<0.01, <0.01
Radish roots				<0.01, <0.01
Radish tops	49.8–51.9	91–92	2	<0.01, <0.01
Radish roots				<0.01, <0.01
n = number of independent field trials.				
Based on the results of the field accumulation study, immediate plant-back is permitted for labelled crops. A plant-back interval of 30 days is recommended for all other crops.				

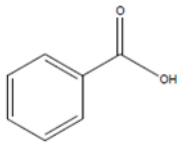
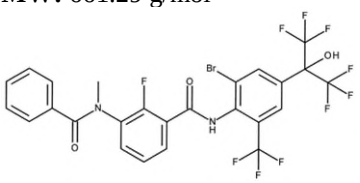
Table 13 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

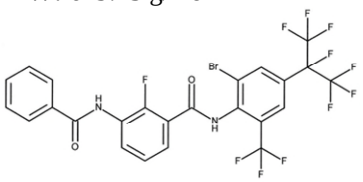
PLANT STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops (cabbage, radish, rice, soybean, tea, tomato and wheat)** **Rotational crops (wheat, lettuce and radish)**		Broflanilide	
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops** **Rotational crops**		Broflanilide	
METABOLIC PROFILE IN DIVERSE CROPS		Similar in cabbage, radish, rice, soybean, tea, tomato and wheat.	
ANIMAL STUDIES			
ANIMALS		**Ruminant and Poultry**	
RESIDUE DEFINITION FOR ENFORCEMENT		Broflanilide and DM-8007	
RESIDUE DEFINITION FOR RISK ASSESSMENT		Broflanilide and DM-8007	
METABOLIC PROFILE IN ANIMALS **(goat, hen, rat)**		Similar in lactating goat, hen and rat	
FAT SOLUBLE RESIDUE		Yes	
DIETARY RISK FROM FOOD AND DRINKING WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Alone	**Food and Drinking Water**
Basic chronic [non-cancer] dietary exposure analysis **ADI = 0.02 mg/kg bw/day** **Estimated chronic drinking water concentration (Level I) = 0.00072 ppm**	Total population	1.2	1.3
	All infants <1 year	1.8	2.1
	Children 1–2 years	5.6	5.7
	Children 3–5 years	3.5	3.6
	Children 6–12 years	2.0	2.1
	Youth 13–19 years	1.1	1.1
	Adults 20–49 years	0.8	0.9
	Adults 50–99 years	0.7	0.8
	Females 13–49 years	0.8	0.9
Basic cancer dietary exposure analysis	**POPULATION**	**ESTIMATED LIFETIME CANCER RISK**	
		Food Alone	**Food and Drinking Water**
q_1^* = 2.1 × 10^{-3} (mg/kg bw/day)$^{-1}$ **Estimated chronic drinking water concentration (Level I) = 0.00072 ppm**	Total population	$5x10^{-7}$	$5x10^{-7}$

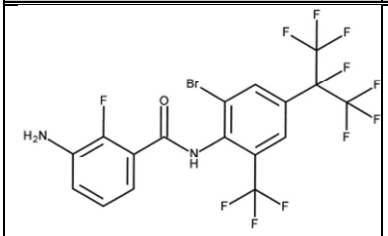
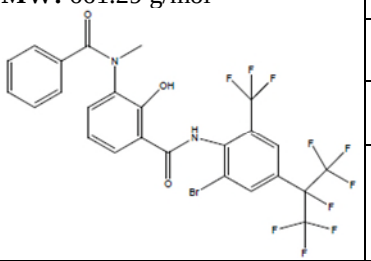
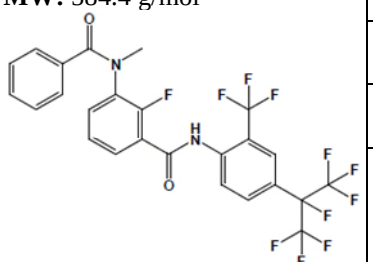
Table 14 Transformation Products of Broflanilide Detected in Laboratory and Field Dissipation Studies

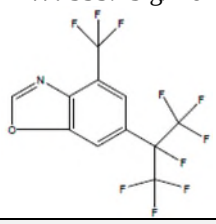
Compound	Study				Max %AR (day)	%AR at study end (study length)[1]
MAJOR TRANSFORMATION PRODUCTS						
DC-8007 *N*-[2-bromo-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluoro-3-(methylamino)benzamide **Formula:** $C_{18}H_{10}BrF_{11}N_2O$ **MW:** 559.17 g/mol 	Hydrolysis				NA	
	Aqueous photolysis	PMRA# 2828126 (pH 7)			NA	
		PMRA# 2828128	pH 5: B-ring-labelled		1.0 (1)	ND (16)
			pH 5: C-ring-labelled		ND (0-16)	
			pH 9: B-ring-labelled		1.3 (0)	ND (16)
			pH 9: C-ring-labelled		ND (0-16)	
	Soil photolysis				ND (0-14)	
	Aerobic aquatic	PMRA# 2828303	Brandywine	B-ring-labelled	**11.8 (273)**	9.9 (365)
				C-ring-labelled	ND (0-365)	
			Choptank	B-ring-labelled	7.1 (365)	7.1 (365)
				C-ring-labelled	ND (0-365)	
	Anaerobic aquatic	PMRA# 2828305	Brandywine	B-ring-labelled	**18.2 (365)**	**18.2 (365)**
				C-ring-labelled	ND (0-365)	
			Choptank	B-ring-labelled	**13.3 (365)**	**13.3 (365)**
				C-ring-labelled	ND (0-365)	
	Aerobic soil	PMRA# 2828280			<3%	
		PMRA# 2828290	Illinois	Processed soil	<LOQ (0-365)	
				Intact core	ND (0-365)	
			North Carolina	Processed soil	<LOQ (0-365)	
				Intact core	0.5 (30)	<LOQ (365)
			Tennessee	Processed soil	ND (0-365)	
				Intact core	ND (0-365)	
	Anaerobic soil	PMRA# 2828282	California (A-ring-labelled)		**18.7 (300)**	6.0 (363)
			California (B-ring-labelled)		**23.8 (300)**	5.4 (363)
			California (C-ring-labelled)		ND (0-363)	
			Illinois (A-ring-labelled)		**71.7 (363)**	**71.7 (363)**
			North Carolina (A-ring-labelled)		6.5 (363)	6.5 (363)
			Tennessee (A-ring-labelled)		**13.9 (300)**	**11.0 (363)**

Compound	Study			Max %AR (day)	%AR at study end (study length)[1]
AB-oxa *N*-{2-fluoro-3-[6-(perfluoropropan-2-yl)-4-(trifluoromethyl)-1,3-benzooxazol-2-yl]phenyl}-*N*-methylbenzamide **Formula:** $C_{25}H_{13}F_{11}N_2O_2$ **MW:** 582.37 g/mol 	Hydrolysis			NA	
	Aqueous photolysis	PMRA# 2828126	pH 7: B-ring-labelled	6.1 (12)	4.7 (16)
			pH 7: C-ring-labelled	1.6 (12)	1.5 (16)
		PMRA# 2828128	pH 5: B-ring-labelled	6.9 (6)	2.1 (16)
			pH 5: C-ring-labelled	4.7 (3)	0.6 (16)
			pH 9: B-ring-labelled	**37.6 (3)**	1.3 (16)
			pH 9: C-ring-labelled	**27.8 (2)**	ND (16)
	Soil photolysis			ND (0-14)	
	Aerobic aquatic	PMRA# 2828303		ND (0-365)	
	Anaerobic aquatic	PMRA# 2828305		ND (0-365)	
	Aerobic soil	PMRA# 2828280		ND (0-365)	
		PMRA# 2828290		ND (0-365)	
	Anaerobic soil	PMRA# 2828282		ND (0-363)	
S(Br-OH)-8007 2-fluoro-*N*-[4-(1,1,1,2,3,3,3-heptafluoropropan-2-yl)-2-hydroxy-6-(trifluoromethyl)phenyl]-3-(*N*-methylbenzamido) benzamide **Formula:** $C_{25}H_{15}F_{11}N_2O_3$ **MW:** 600.38 g/mol 	Hydrolysis			NA	
	Aqueous photolysis	PMRA# 2828126 (pH 7)		ND (0-16)	
		PMRA# 2828128	pH 5: B-ring-labelled	**14.3 (9)**	**11.4 (16)**
			pH 5: C-ring-labelled	7.0 (6)	4.6 (16)
			pH 9: B-ring-labelled	5.5 (9)	1.0 (16)
			pH 9: C-ring-labelled	3.6 (6)	ND (16)
	Soil photolysis			ND (0-14)	
	Aerobic aquatic	PMRA# 2828303		ND (0-365)	
	Anaerobic aquatic	PMRA# 2828305		ND (0-365)	
	Aerobic soil	PMRA# 2828280		ND (0-365)	
		PMRA# 2828290		ND (0-365)	
	Anaerobic soil	PMRA# 2828282		ND (0-363)	
MFBA 2-fluoro-3-(N-methylbenzamido)benzoic acid **Formula:** $C_{15}H_{12}FNO_3$ **MW:** 273.26 g/mol 	Hydrolysis			NA	
	Aqueous photolysis	PMRA# 2828126 (pH 7)		NA	
		PMRA# 2828128	pH 5: B-ring-labelled	ND (0-16)	
			pH 5: C-ring-labelled	**19.7 (16)**	**19.7 (16)**
			pH 9: B-ring-labelled	ND (0-16)	
			pH 9: C-ring-labelled	**25.6 (16)**	**25.6 (16)**
	Soil photolysis			NA	
	Aerobic aquatic	PMRA# 2828303		NA	
	Anaerobic aquatic	PMRA# 2828305		NA	
	Aerobic soil	PMRA# 2828280		NA	
		PMRA# 2828290		NA	
	Anaerobic soil	PMRA# 2828282		NA	

Compound	Study				Max %AR (day)	%AR at study end (study length)[1]
Benzoic acid **Formula:** $C_7H_6O_2$ **MW:** 122.1 g/mol 	Hydrolysis				NA	
	Aqueous photolysis	PMRA# 2828126 (pH 7)			NA	
		PMRA# 2828128	pH 5: B-ring-labelled		ND (0-16)	
			pH 5: C-ring-labelled		**25.7 (13)**	**25.6 (16)**
			pH 9: B-ring-labelled		ND (0-16)	
			pH 9: C-ring-labelled		**43.5 (9)**	**42.9 (16)**
	Soil photolysis				NA	
	Aerobic aquatic	PMRA# 2828303			NA	
	Anaerobic aquatic	PMRA# 2828305			NA	
	Aerobic soil	PMRA# 2828280			ND (0-365)	
		PMRA# 2828290			NA	
	Anaerobic soil	PMRA# 2828282			ND (0-363)	
MINOR TRANSFORMATION PRODUCTS						
S(PFP-OH)-8007 *N*-[2-bromo-4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluoro-3-(*N*-methylbenzamido)benzamide **Formula:** $C_{25}H_{15}BrF_{10}N_2O_3$ **MW:** 661.29 g/mol 	Hydrolysis				NA	
	Aqueous photolysis	PMRA# 2828126	pH 7: B-ring-labelled		5.0 (16)	5.0 (16)
			pH 7: C-ring-labelled		3.4 (12)	2.5 (16)
		PMRA# 2828128	pH 5: B-ring-labelled		6.4 (16)	6.4 (16)
			pH 5: C-ring-labelled		3.5 (16)	3.5 (16)
			pH 9: B-ring-labelled		8.3 (6)	5.5 (16)
			pH 9: C-ring-labelled		3.2 (6)	ND (16)
	Soil photolysis				ND (0-14)	
	Aerobic aquatic	PMRA# 2828303			ND (0-365)	
	Anaerobic aquatic	PMRA# 2828305			ND (0-365)	
	Aerobic soil	PMRA# 2828280	California (A-ring-labelled)		1.1 (0)	ND (365)
			California (B-ring-labelled)		1.0 (120)	ND (365)
			California (C-ring-labelled)		1.0 (30)	ND (365)
		PMRA# 2828290	Illinois	Processed soil	0.9 (58)	<LOQ (365)
				Intact core	1.1 (30)	<LOQ (365)
			North Carolina	Processed soil	1.0 (15)	0.5 (365)
				Intact core	1.2 (0)	0.5 (365)
			Tennessee	Processed soil	1.1 (30)	<LOQ (365)
				Intact core	0.7 (15)	<LOQ (365)
	Anaerobic soil	PMRA# 2828282	California (A-ring-labelled)		3.9 (14)	<LOQ (363)
			California (B-ring-labelled)		1.9 (37)	<LOQ (363)
			California (C-ring-		1.8 (7)	<LOQ

Compound	Study				Max %AR (day)	%AR at study end (study length)[1]
			labelled)			(363)
			Illinois (A-ring-labelled)		1.5 (30)	<LOQ (363)
			North Carolina (A-ring-labelled)		1.8 (14)	<LOQ (363)
			Tennessee (A-ring-labelled)		2.4 (0)	<LOQ (363)
DM-8007 3-benzamido-*N*-[2-bromo-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluorobenzamide **Formula:** $C_{24}H_{12}BrF_{11}N_2O_2$ **MW:** 649.25 g/mol 	Hydrolysis				NA	
	Aqueous photolysis				NA	
	Soil photolysis	PMRA# 2828284	A-ring-labelled		2.3 (14)	2.3 (14)
			B-ring-labelled		ND (0-14)	
			C-ring-labelled		4.2 (6)	2.6 (14)
	Aerobic aquatic	PMRA# 2828303			ND (0-365)	
	Anaerobic aquatic	PMRA# 2828305			ND (0-365)	
	Aerobic soil	PMRA# 2828280	California (A-ring-labelled)		1.0 (269)	0.9 (365)
			California (B-ring-labelled)		1.3 (91)	1.1 (365)
			California (C-ring-labelled)		1.6 (91)	<0.6 (365)
		PMRA# 2828290	Illinois	Processed soil	1.4 (0)	<LOQ (365)
				Intact core	2.3 (15)	1.6 (365)
			North Carolina	Processed soil	1.7 (15)	<LOQ (365)
				Intact core	2.9 (365)	2.9 (365)
			Tennessee	Processed soil	1.1 (120)	<LOQ (365)
				Intact core	4.9 (177)	3.0 (365)
	Anaerobic soil	PMRA# 2828282	California (A-ring-labelled)		ND (0-363)	
			California (B-ring-labelled)		0.9 (30)	ND (363)
			California (C-ring-labelled)		1.1 (300)	ND (363)
			Illinois (A-ring-labelled)		1.5 (30)	ND (363)
			North Carolina (A-ring-labelled)		ND (0-363)	
			Tennessee (A-ring-labelled)		ND (0-363)	
DC-DM-8007 3-amino-*N*-[2-bromo-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-2-fluorobenzamide **Formula:** $C_{17}H_8BrF_{11}N_2O$ **MW:** 545.15 g/mol	Hydrolysis				NA	
	Aqueous photolysis	PMRA# 2828126			NA	
		PMRA# 2828128			NA	
	Soil photolysis				ND (0-14)	
	Aerobic aquatic	PMRA# 2828303			ND (0-365)	
	Anaerobic aquatic	PMRA# 2828305			ND (0-365)	

Compound	Study				Max %AR (day)	%AR at study end (study length)[1]
	Aerobic soil	PMRA# 2828280			<3%	
		PMRA# 2828290	Illinois	Processed soil	0.7 (58)	<LOQ (365)
				Intact core	0.7 (365)	0.7 (365)
			North Carolina	Processed soil	0.9 (259)	<LOQ (365)
				Intact core	1.7 (86)	0.5 (365)
			Tennessee	Processed soil	ND (0-365)	
				Intact core	2.3 (58)	<LOQ (365)
	Anaerobic soil	PMRA# 2828282			ND (0-363)	
S(F-OH)-8007 *N*-[2-bromo-4-(perfluoropropan-2-yl)-6-(trifluoromethyl)phenyl]-2-hydroxy-3-(*N*-methylbenzamido)benzamide **Formula:** $C_{25}H_{15}BrF_{10}N_2O_3$ **MW:** 661.29 g/mol 	Hydrolysis				NA	
	Aqueous photolysis	PMRA# 2828126 (pH 7)			ND (0-16)	
		PMRA# 2828128	pH 5: B-ring-labelled		ND (0-16)	
			pH 5: C-ring-labelled		ND (0-16)	
			pH 9: B-ring-labelled		3.8 (6)	0.7 (16)
			pH 9: C-ring-labelled		ND (0-16)	
	Soil photolysis				ND (0-14)	
	Aerobic aquatic	PMRA# 2828303			ND (0-365)	
	Anaerobic aquatic	PMRA# 2828305			ND (0-365)	
	Aerobic soil	PMRA# 2828280			ND (0-365)	
		PMRA# 2828290			ND (0-365)	
	Anaerobic soil	PMRA# 2828282			ND (0-365)	
DBr-8007 2-fluoro-3-(N-methylbenzamido)-N-[4-(perfluoropropan-2-yl)-2-(trifluoromethyl)phenyl]benzamide **Formula:** $C_{25}H_{15}F_{11}N_2O_2$ **MW:** 584.4 g/mol 	Hydrolysis				NA	
	Aqueous photolysis	PMRA# 2828126 (pH 7)			NA	
		PMRA# 2828128	pH 5: B-ring-labelled		3.8 (2)	0.2 (16)
			pH 5: C-ring-labelled		0.6 (3)	ND (16)
			pH 9: B-ring-labelled		3.8 (6)	1.7 (16)
			pH 9: C-ring-labelled		0.3 (6)	ND (16)
	Soil photolysis				ND (0-14)	
	Aerobic aquatic	PMRA# 2828303			ND (0-365)	
	Anaerobic aquatic	PMRA# 2828305			ND (0-365)	
	Aerobic soil	PMRA# 2828280			NA	
		PMRA# 2828290			NA	
	Anaerobic soil	PMRA# 2828282			NA	
B-oxa 6-(1,1,1,2,3,3,3-	Hydrolysis				NA	
	Aqueous photolysis	PMRA# 2828126			ND (0-16)	
		PMRA# 2828128			ND (0-16)	

Compound	Study				Max %AR (day)	%AR at study end (study length)[1]
heptafluoropropan-2-yl)-4-(trifluoromethyl)-1,3-Benzoxazole **Formula:** $C_{11}H_3F_{10}NO$ **MW:** 355.13 g/mol 	Soil photolysis				ND (0-14)	
	Aerobic aquatic	PMRA# 2828303			ND (0-365)	
	Anaerobic aquatic	PMRA# 2828305			ND (0-365)	
	Aerobic soil	PMRA# 2828280			ND (0-365)	
		PMRA# 2828290			ND (0-365)	
	Anaerobic soil	PMRA# 2828282			ND (0-363)	
OTHER						
Carbon dioxide **Formula**: CO_2 **MW:** 44.0 g/mol	Hydrolysis				N/A	
	Aqueous photolysis	PMRA# 2828126			<5 (16)	
		PMRA# 2828128			<10 (16)	
	Soil photolysis	PMRA# 2828284			<5 (14)	
	Aerobic aquatic	PMRA# 2828303	Brandywine	B-ring-labelled	0.15 (365)	
				C-ring-labelled	**13.5 (365)**	
			Choptank	B-ring-labelled	0.25 (365)	
				C-ring-labelled	**15.4 (365)**	
	Anaerobic aquatic	PMRA# 2828305			<1 (365)	
	Aerobic soil	PMRA# 2828280			<5 (365)	
		PMRA# 2828290	Illinois	Processed soil	<LOQ (365)	
				Intact core	1.6 (365)	
			North Carolina	Processed soil	0.5 (365)	
				Intact core	4.0 (365)	
			Tennessee	Processed soil	1.1 (365)	
				Intact core	2.7 (365)	
	Anaerobic soil	PMRA# 2828282			<2.0 (363)	
Non-extracted Residues (NER)	Hydrolysis				N/A	
	Aqueous photolysis				N/A	
	Soil photolysis	PMRA# 2828284			<5 (14)	
	Aerobic aquatic	PMRA# 2828303	Brandywine	B-ring-labelled	**12.2 (365)**	
				C-ring-labelled	7.8 (365)	
			Choptank	B-ring-labelled	**14.2 (365)**	

Compound	Study				Max %AR (day)	%AR at study end (study length)[1]
				C-ring-labelled	6.0 (365)	
	Anaerobic aquatic	PMRA# 2828305			<10 (365)	
	Aerobic soil	PMRA# 2828280			<10 (365)	
		PMRA# 2828290	Illinois	Processed soil	8.0 (365)	
				Intact core	**12.1 (365)**	
			North Carolina	Processed soil	**12.9 (365)**	
				Intact core	**40.6 (365)**	
			Tennessee	Processed soil	**10.3 (365)**	
				Intact core	**26.2 (365)**	
	Anaerobic soil	PMRA# 2828282			<10 (363)	
Total Unidentified Extracted Residues (UER)	Hydroly-sis	PMRA# 2828123			<10 (0-5)	
	Aqueous photolysis	PMRA# 2828126 (pH 7)			**<15 (0-16)**	
		PMRA# 2828128	pH 5: B-ring-labelled		**45.4 (16)**	**45.4 (16)**
			pH 5: C-ring-labelled		5.0 (16)	5.0 (16)
			pH 9: B-ring-labelled		**64.8 (16)**	**64.8 (16)**
			pH 9: C-ring-labelled		**18.4 (16)**	**18.4 (16)**
	Soil photolysis	PMRA# 2828284			<5 (0-14)	
	Aerobic aquatic	PMRA# 2828303			<10 (0-365)	
	Anaerobic aquatic	PMRA# 2828305			<5 (0-365)	
	Aerobic soil	PMRA# 2828280			<10 (0-365)	
		PMRA# 2828290	Illinois	Processed soil	1.0 (365)	1.0 (365)
				Intact core	3.4 (58)	0.9 (365)
			North Carolina	Processed soil	1.9 (259)	0.7 (365)
				Intact core	6.9 (259)	5.5 (365)
			Tennessee	Processed soil	1.9 (365)	1.9 (365)
				Intact core	9.1 (259)	1.8 (365)
	Anaerobic soil	PMRA# 2828282			<5 (0-363)	

[1] In DAT (days after treatment)
N/A = Not Applicable
NA = Not Analysed (either no reference standard used or minor non-volatile compounds that were not identified)
ND = Not Detected
Bolded when appearing at >10%

Table 15 Fate and Behaviour of Broflanilide and its Transformation Products in the Environment

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
Abiotic transformation					
Hydrolysis	Broflanilide [B-ring-^{14}C]-labelled pH 4, 7 and 9 at 50°C	Stable to hydrolysis at pH 4, 7 and 9 at 50°C.	None identified. Total unknown peaks remained <10% AR, and no individual peak exceeded 6.2% AR.	Hydrolysis is not expected to be an important route of dissipation for broflanilide in the environment.	2828123
Phototrans-formation on soil	Broflanilide [A-ring-^{14}C], [B-ring-^{14}C], and [C-ring-^{14}C]-labelled	Stable to phototransformation on soil.	**Major:** none **Minor:** DM-8007 Soil bound residues and CO_2 <5% AR.	Phototransforma-tion on soil is not expected to be an important route of dissipation for broflanilide in the environment.	2828284
Phototrans-formation in water	Broflanilide [B-ring-^{14}C], and [C-ring-^{14}C]-labelled Phosphate buffered solutions at pH 7 and 25ºC	DT_{50} = 80 days (SFO, combined labels) Environmental phototransformation half-lives are reported here (12-hour/day photoperiod under summer sunlight at 40°N latitude).	**Major:** none **Minor:** AB-oxa, S(PFP-OH)-8007, CO_2 Unidentified minor transformation products were observed at maximum individual concentrations <6% AR, with total concentrations remaining <15% AR.	Phototransforma-tion in water is not expected to be an important route of dissipation for broflanilide in the environment; however, there is a potential for phototransforma-tion in more basic or acidic aquatic environments.	2828126
	Broflanilide [B-ring-^{14}C], and [C-ring-^{14}C]-labelled Phosphate buffered solutions at pH 5 and pH 9 and 25ºC	**pH 5 buffer:** DT_{50} = 17 days (SFO, combined labels) **pH 9 buffer:** DT_{50} = 4 days (SFO, combined labels) Environmental phototransformation half-lives are reported here (12-hour/day photoperiod under summer sunlight at 40°N latitude).	**Major:** AB-oxa, S(Br-OH)-8007, MFBA, benzoic acid **Minor:** S(PFP-OH)-8007, DC-8007, S(F-OH)-8007, DBr-8007, CO_2 Unidentified minor transformation products were observed at maximum individual		2828128

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
			concentrations <5% AR, with total concentrations reaching 65%.		
Phototrans-formation in air	Broflanilide is not expected to be volatile under field conditions based on its vapour pressure and Henry's law constant. Transformation products of broflanilide are not expected to be volatile under field conditions based on low detection of volatile organics in soil biotransformation studies.				
Biotransformation					
Biotransfor-mation in aerobic soil	Broflanilide [A-ring-^{14}C], [B-ring-^{14}C], and [C-ring-^{14}C]-labelled 1 soil: California Study duration: 365 days	DT_{50} = 1173 days (SFO)	**Major:** none **Minor:** S(PFP-OH)-8007, DM-8007, DC-8007, DC-DM-8007, CO_2 NER and UER <10% AR	Broflanilide is persistent. Biotransformation in aerobic soil is not an important route of dissipation for broflanilide.	2828280
	Broflanilide [A-ring-^{14}C]-labelled 3 soils: Illinois (IL), North Carolina (NC), and Tennessee (TN) Study duration: 120 days (The study was conducted for 365 days; however, microbial biomass was determined to be unacceptably low at 365 days, and only the 120 day values are appropriate for use in risk assessment.)	IL: DT_{50} = 5742 days (SFO) NC: DT_{50} = 804 days (SFO) TN: DT_{50} = 1546 days (SFO) Note: Testing with intact soil cores was also conducted; however the results for intact soil cores are considered supplemental to the main study, which was conducted with processed soil samples. The half-life values in the intact soil cores (438, 288 and 282 days for IL, NC and TN soils, respectively) are considered supplemental information that could be used during refinement in the risk assessment.	**Major:** none **Minor:** S(PFP-OH)-8007, DM-8007, DC-8007, DC-DM-8007, CO_2 NER and UER <15% AR	Broflanilide is persistent. Biotransformation in aerobic soil is not an important route of dissipation for broflanilide.	2828290

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
Biotransformation in anaerobic soil	Broflanilide [A-ring-^{14}C], [B-ring-^{14}C], and [C-ring-^{14}C]-labelled 4 soils: California (CA), Illinois (IL), North Carolina (NC), and Tennessee (TN) Study duration: 365 days	IL: DT_{50} = 157 days (SFO) NC: DT_{50} = 2354 days (SFO) TN: DT_{50} = 1113 days (SFO) CA: DT_{50} = 1117 days (SFO)	**Major:** DC-8007 **Minor:** S(PFP-OH)-8007, DM-8007, CO_2 NER and UER <10% AR	With the exception of the IL soil (where the DT_{50} was just under 180 days, in other words, moderately persistent), the results of this study indicate that broflanilide is persistent. Biotransformation in anaerobic soil is not an important route of dissipation for broflanilide.	2828282
Biotransformation in aerobic water systems	Broflanilide [B-ring-^{14}C], and [C-ring-^{14}C]-labelled 2 test systems: Brandywine Creek and Choptank River Study duration: 365 days	Brandywine Creek: DT_{50} = 1294 days (DFOP) t_R = 1430 days Choptank River: DT_{50} = 945 days (SFO) Note: All values are for the whole system	**Major:** DC-8007, CO_2 **Minor:** None identified as all <5% NER and UER <15%	Broflanilide is persistent. Biotransformation in aerobic water systems is not an important route of dissipation for broflanilide.	2828303
Biotransformation in anaerobic water systems	Broflanilide [B-ring-^{14}C], and [C-ring-^{14}C]-labelled. Note: DT_{50} is based on B-ring only. 2 test systems: Brandywine Creek and Choptank River Study duration: 365 days	Brandywine Creek: DT_{50} = 871 days (SFO) Choptank River: DT_{50} = 1411 days (SFO) Note: All values are for the whole system	**Major:** DC-8007, CO_2 **Minor:** CO_2, None identified as all <5% NER and UER <10%	Broflanilide is persistent. Biotransformation in anaerobic water systems is not an important route of dissipation for broflanilide.	2828305

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
Mobility					
Adsorption/desorption	Broflanilide [B-ring-^{14}C]-labelled Values obtained in 6 soils and 1 sediment.	K_{oc} = 3261–23 342	N/A	Broflanilide is classified as immobile to having a slight potential for mobility in soil.	2828297
	DC-8007 [A-ring-^{14}C]-labelled Values obtained in 5 soils.	K_{oc} = 1773–5263	N/A	DC-8007 is classified as immobile to having a low potential for mobility in soil.	2828302
	DC-DM-8007 [B-ring-^{14}C]-labelled Values obtained in 5 soils.	K_{oc} = 724–2514	N/A	DC-DM-8007 is classified as having a slight to low potential for mobility in soil.	2828301
	S(PFP-OH)-8007 Modelled results using EPI Suite.	Program estimated K_{oc} = 442–1815	N/A	S(PFP-OH)-8007 is classified as having a medium to low potential for mobility in soil.	2828300
	DM-8007 Modelled results using EPI Suite.	Program estimated K_{oc} = 2412–4015	N/A	DM-8007 is classified as having a slight potential for mobility in soil.	2828299
Soil leaching	No soil leaching study with broflanilide was submitted and none is required.				
Volatilization	A supplemental study containing AOPWIN results was submitted by the applicant indicating that broflanilide could potentially be persistent in air and has the potential to be subject to long-range transport, due to its predicted half-life in air (2.5 days) being greater than 2 days. However, broflanilide is not expected to be volatile under field conditions based on its vapour pressure (<8.9×10^{-9} Pa at 25 °C), Henry's law constant (4.1×10^{-11} atm·m^3/mol at 20 °C), and low detection of volatile organics in laboratory biotransformation studies.				2828286
Field studies					
Terrestrial field dissipation	BAS 450 00 I, SC formulation 100 g a.i./L Five bare ground sites in	NC: DT_{50} = 5.1 days , t_R = 37.8 days (IORE) FL: DT_{50} = 6.0 days , t_R = 57 days (IORE) CA: DT_{50} = 18.2 days ,	**Major:** None **Minor:** S(PFP-OH)-8007, DC-8007, DC-DM-8007	Broflanilide is unlikely to accumulate in soil and carry over to the next growing season.	2828292

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
	North Carolina (NC), Florida (FL), California (CA), Washington (WA), and North Dakota (ND). Study duration: 450 days Note: Only the WA and ND sites are in ecoregions representing Canadian field use conditions.	t_R = 118 days (IORE) WA: DT_{50} = 5.5 days , t_R = 12.8 days (IORE) ND: DT_{50} = 3.3 days , t_R = 188 days (DFOP) Mean residues of broflanilide and its transformation products were not detected in soil below 15 cm soil depth at any of the five locations.		At the sites tested, neither broflanilide nor it residues appeared to be inherently susceptible to leaching.	
	Broflanilide [A-ring-^{14}C] and [B-ring-^{14}C]-labelled Two bare ground sites in California and Georgia. Study duration: 181 days Note: CA and GA do not represent Canadian field use conditions; however, these results support binding of broflanilide to soil under field conditions.	CA: DT_{50} = 16.2 days , t_R = 56.8 days (IORE) GA: DT_{50} = 182 days (SFO) Mean residues of broflanilide and its transformation products were not detected in soil below 10 cm soil depth at both locations.	**Major:** None **Minor:** DM-8007, S(Br-OH)-8007, DC-8007, DC-DM-8007, AB-oxa, S(PFP-OH)-8007	Broflanilide is unlikely to accumulate in soil and carry over to the next growing season. At the sites tested, neither broflanilide nor it residues appeared to be inherently susceptible to leaching.	2828295
Aquatic field dissipation	No aquatic field dissipation study with broflanilide was submitted and none is required.				
Field leaching	No field leaching study with broflanilide was submitted and none is required.				

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
Bioconcentration/bioaccumulation					
Bioconcentra-tion in fish	Broflanilide Flow-through screening study – to be used qualitatively Rainbow trout were exposed to [^{14}C]-broflanilide at a nominal concentration of 200 ng/L for an uptake period of 28 days, followed by a depuration period of 14 days.	BCF_K = 181 (kinetic bioconcentration factor)	Transformation products were not measured.	This screening test was designed using a modified version of a guideline bioconcentration study; therefore, this study provides supplementary information and the results are not appropriate for risk assessment purposes. The results can be used qualitatively as they suggest that broflanilide does not readily bioconcentrate in fish tissue under the conditions of the study.	2828359
	Broflanilide Flow-through study Rainbow trout were exposed to [^{14}C]-broflanilide at a nominal concentrations of 1.0 and 10 µg/L for an uptake period of 28 days, followed by a depuration period of 10 days.	BCF_K = 97 and 96 (kinetic bioconcentration factor for whole fish, low does and high dose, respectively) BCF_{SS} = 119 and 104 (steady state bioconcentration factor for whole fish, low does and high dose, respectively)	DM-8007	Broflanilide does not readily bioconcentrate in fish tissue under the conditions of the study.	2828362

[1] DT_{50} and DT_{90} values for each fit are the times the fitted curve reaches 50% and 90%, respectively, of the fitted initial concentration. These values are used for descriptive characterization and persistence classification for soil (Goring *et al*, 1975) and natural waters (McEwen and Stephenson, 1979). The representative half-life (t_R), is the half-life of an exponential curve that is considered to be a conservative approximation of the measured concentration decline, and is used for exposure modelling. The DT_{50} for the SFO (single first-order) model is t_R if the SFO model is deemed acceptable. The t_R value from DFOP (double first-order in parallel) is a half-life determined from the slow degradation rate from the DFOP model. The t_R value from IORE (indeterminate order rate equation) is the half-life of an exponential curve passing through the DT_{90} of the IORE model fit.

UER – Unidentified Extracted Residues
NER – Non-extracted Residues
AR – Applied Radioactivity

Table 16 Toxicity of Broflanilide, its Transformation Products and End-use Products to Non-target Terrestrial Species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Invertebrates					
Earthworm, *Eisenia fetida*	14d-Acute	Broflanilide (technical grade active ingredient, purity 98.67%)	LC/EC_{50} > 987 mg a.i./kg dw soil NOAEC ≥ 987 mg a.i./kg dw soil No statistically significant effects on mortality or body weight for any of the treatment levels tested.	N/A	2828440
	14d-Acute	DC-8007 (broflanilide transformation product), purity 99.60%	LC/EC_{50} > 996 mg a.i./kg dw soil NOAEC ≥ 996 mg a.i./kg dw soil No statistically significant effects on mortality or body weight for any of the treatment levels tested.	N/A	2828442
	14d-Acute	DC-DM-8007 (broflanilide transformation product), purity 99.67%	LC/EC_{50} > 997 mg a.i./kg dw soil NOAEC ≥ 997 mg a.i./kg dw soil No statistically significant effects on mortality or body weight for any of the treatment levels tested.	N/A	2828444
	14d-Acute	End-use product, Cimegra (SC, 100 g a.i./L)	LC/EC_{50} > 94.7 mg a.i./kg dw soil (or >1000 mg end-use product/kg dw soil) NOAEC ≥ 94.7 mg a.i./kg dw soil (or ≥1000 mg end-use product/kg dw soil) No statistically significant effects on mortality or body weight for any of the treatment levels tested.	N/A	2827864
	14d-Acute	End-use product, Teraxxa (FS, 300 g a.i./L)	LC/EC_{50} > 260 mg a.i./kg dw soil (or >1000 mg end-use product/kg dw soil) NOAEC ≥ 260 mg a.i./kg dw soil (or ≥1000 mg end-use product/kg dw soil) No statistically significant effects on mortality or body weight for any of the treatment levels tested.	N/A	2827994
	56d-Chronic	Broflanilide (technical grade active ingredient, purity 98.67%)	NOAEC = 30.86 mg a.i./kg dw soil (reproduction) No statistically significant effects on survival or body weight for any of the treatment levels tested. The reproduction rate was significantly	N/A	2828447

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			lower than the control at the two highest test concentrations (55.56 and 100 mg a.i./kg dw soil).		
	56d-Chronic	End-use product, Teraxxa (FS, 300 g a.i./L)	NOAEC = 65 mg a.i./kg dw soil (or 250 mg end-use product/kg dw soil) based on effects on biomass and reproduction. No statistically significant effects on survival for any of the treatment levels tested. Biomass change and reproduction rate were significantly lower than the control at the highest test concentration (500 mg end-use product/kg dw soil).	N/A	2827996
Soil mite, *Hypoaspis aculeifer*	14d-Chronic	End-use product, Teraxxa (FS, 300 g a.i./L)	Reproduction: NOAEC = 0.24 mg a.i./kg dw soil (or 0.92 mg end-use product/kg dw soil) There were treatment-related effects on mite survival (at the highest treatment concentration) and number of offspring (at the four highest treatment concentrations).	N/A	2827998
Honey bee, *Apis mellifera*	**ACUTE LABORATORY STUDIES**				
	96h-Oral, adults	Broflanilide (technical grade active ingredient, purity 98.67%)	LD_{50} = 14.9 ng a.i./bee	Highly toxic	2828408
	96h-Contact, adults		LD_{50} = 8.8 ng a.i./bee	Highly toxic	
	96h-Oral, adults	DM-8007 (broflanilide transformation product), purity 98.84%	LD_{50} = 1.92 µg a.i./bee	Highly toxic	2828414
	96h-Contact, adults		LD_{50} = 0.19 µg a.i./bee	Highly toxic	
	48h-Oral, adults	S(PFP-OH)-8007 (broflanilide transformation product), purity 98.84%	LD_{50} > 5.6 µg a.i./bee	Non-toxic up to the approximate solubility limit	2828417
	48h-Contact, adults		LD_{50} > 5.0 µg a.i./bee		
	96h-Oral, adults	DC-8007 (broflanilide transformation product), purity 99.6%	LD_{50} > 100 µg a.i./bee	Practically nontoxic	2828420
	96h-Contact, adults		LD_{50} = 33.2 µg a.i./bee	Practically nontoxic	
	48h-Oral, adults	B-urea (broflanilide transformation product),	LD_{50} > 100 µg a.i./bee	Practically nontoxic	2828423
	48h-Contact, adults		LD_{50} > 20 µg a.i./bee	Practically nontoxic	

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
		purity 99.19%			
	48h-Oral, adults	DC-DM-8007 (broflanilide transformation product), purity 99.67%	LD_{50} > 20.27 µg a.i./bee	Practically nontoxic	2828426
	48h-Contact, adults		LD_{50} > 100 µg a.i./bee	Practically nontoxic	
	48h-Oral, adults	B-oxam-acid (broflanilide transformation product), purity 99.86%	LD_{50} > 23.55 µg a.i./bee	Practically nontoxic	2828429
	48h-Contact, adults		LD_{50} > 100 µg a.i./bee	Practically nontoxic	
	96h-Oral, adults	End-use product, Cimegra (SC, 100 g a.i./L)	LD_{50} = 45 ng a.i./bee (or 466.1 ng end-use product/bee)	Highly toxic	2827855
	96h-Contact, adults		LD_{50} = 17 ng a.i./bee (or 175 ng end-use product/bee)	Highly toxic	
	96h-Oral, adults	End-use product, Teraxxa (FS, 300 g a.i./L)	LD_{50} = 69.3 ng a.i./bee (or 261 ng end-use product/bee)	Highly toxic	2827992
	96h-Contact, adults		LD_{50} = 12.4 ng a.i./bee (or 46.8 ng end-use product/bee)	Highly toxic	
	96-h Oral, larva	Broflanilide (technical grade active ingredient, purity 98.67%)	96-h LD_{50} > 29 ng a.i./larva Maximum mortality was 36% in the highest test level.	Highly toxic	2828436
	RT_{25} Study – Cimegra applied to alfalfa at a rate of 250 mL/ha (25 g a.i./ha), 24 hour study duration	End-use product, Cimegra (SC, 100 g a.i./L)	RT_{25} < 3 hours Broflanilide residues did not cause unacceptable adverse effects on honeybee survival after 3 hours of weathering. 24-hour mortality was less than 25% in 3, 8, and 24 hours weathering intervals post application.	N/A	2828434
	CHRONIC LABORATORY STUDIES				
	10-d Chronic, adults	Broflanilide (technical grade active ingredient, purity 98.67%)	10-d LD_{50} = 1.29 ng a.i./bee/day [10-d LC_{50} = 0.037 mg a.i./kg diet] 10-d NOAEL = 0.62 ng a.i./bee [10-d NOAEC = 0.018 mg a.i./kg diet] Endpoints are based on mortality.	N/A	2828432
	22-d Chronic, larva	Broflanilide (technical grade active ingredient, purity 98.67%)	22-d NOAEL = 0.088 ng a.i./larva/day [22-d NOAEC = 2.289 µg a.i./kg diet] NOAEC/NOAEL is based on larval mortality. Effects on pupal mortality and adult emergence were observed at higher test item concentrations.	N/A	2828438

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
ACUTE NON-APIS LABORATORY STUDIES					
Bumblebee, *Bombus terrestris* L.	96h-Oral, adults	Broflanilide (technical grade active ingredient, purity 98.67%)	LD_{50} = 19.5 ng a.i./bee	Highly toxic	2828411
	96h-Contact, adults		LD_{50} > 120 ng a.i./bee	Highly toxic	
	96h-Oral, adults	End-use product, Cimegra (SC, 100 g a.i./L)	LD_{50} = 13.2 ng a.i./bee (or 137 ng end-use product/bee)	Highly toxic	2827852
	96h-Contact, adults		LD_{50} = 122 ng a.i./bee (or 1270 ng end-use product/bee)	Highly toxic	
	RESIDUE STUDIES				
	77 day field study to determine residues in pollen from corn treated once at seeding as a soil in-furrow application with 500 mL Cimegra/ha (50 g a.i./ha). Study conducted in one field trial in Germany.	End-use product, Cimegra (SC, 100 g a.i./L)	No residues of broflanilide and its transformation products, S(PFP-OH)-8007 and DM-8007 were detected in pollen samples at or above the LOD (0.0002 mg/kg) in any treated samples, at any sampling interval. Due to a number of limitations with this study, the data can only be used qualitatively to demonstrate that broflanilide is unlikely to be present in pollen under the conditions of this study. Considering this active is non-systemic, residues are not expected to translocate into pollen/nectar.	N/A	2828398
	Determination of residues in pollen and nectar from oilseed rape grown as a succeeding crop in a former corn field previously treated once as a soil in-furrow application with 500 mL Cimegra/ha (50 g a.i./ha) (study summarized above)	End-use product, Cimegra (SC, 100 g a.i./L)	No residues of broflanilide and its transformation products were detected in pollen or nectar samples of the successive oilseed rape crop at or above the LOD (0.0002 mg/kg) up to 343 DAA, except for one replicate above the LOQ for an unidentified transformation product, Reg. No. 6066332, in pollen (0.0015 mg/kg at 326 DAA). Soil samples collected 100 DAA yielded broflanilide residues of 0.0011 to 0.0061 mg/kg in the treatment plots; while no transformation product residues were detected. Due to a number of limitations with this study, the data can only be used qualitatively to demonstrate that broflanilide is unlikely to be present in pollen or nectar under the conditions of this	N/A	2828400

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			study. Considering this active is non-systemic, residues are not expected to translocate into pollen/nectar.		
	53 day greenhouse study to determine residues in leaves and flowers of canola after one seed treatment with Teraxxa at 25 g a.i./ha.	End-use product, Teraxxa (FS, 300 g a.i./L)	No residues of broflanilide and its transformation products were detected in leaf and flower samples at or above the LOD (0.0002 mg/kg) up to 53 DAA. Due to a number of limitations with this study, the data can only be used qualitatively to demonstrate that broflanilide is unlikely to be present in leaves and flowers under the conditions of this study. Considering this active is non-systemic, residues are not expected to translocate into pollen/nectar.	N/A	2828406
Predatory arthropod (mite), *Typhlodromus pyri*	7d-Contact, glass plates	End-use product, Cimegra (SC, 100 g a.i./L)	LR_{50} = 0.0573 g a.i./ha or 0.573 mL end-use product/ha (mortality) In all treatment levels, there were a large number of drowned/stuck/missing mites that contributed to the mortality count.	N/A	2827856
	14d-Contact, spray residue leaf discs	End-use product, Cimegra (SC, 100 g a.i./L)	LR_{50} = 0.1141 g a.i./ha or 1.141 mL end-use product/ha (mortality) NOAER = 0.0625 g a.i./ha or 0.625 mL end-use product/ha (based on number of eggs/female)	N/A	2827860
Parasitic arthropod (wasp), *Aphidius rhopalosiphi*	48h-Contact, glass plates	End-use product, Cimegra (SC, 100 g a.i./L)	LR_{50} = 0.17 g a.i./ha or 1.7 mL end-use product/ha (mortality)	N/A	2827858
	13d-Contact, spray residue on barley seedlings	End-use product, Cimegra (SC, 100 g a.i./L)	LR_{50} = 0.88 g a.i./ha or 8.8 mL end-use product/ha (mortality) NOAER < 0.3 g a.i./ha or < 3.0 mL end-use product/ha (based on effects on reproduction (number of mummies/female) in all treatment groups)	N/A	2827862
Birds					
Bobwhite quail, *Colinus virginianus*	14d-Acute Oral	Broflanilide (technical grade active ingredient, purity 98.67%)	LD_{50} > 2000 mg a.i./kg bw	Practically nontoxic	2828307
	5d-Dietary	Broflanilide (technical	LC_{50} > 5075 mg a.i./kg diet LD_{50} > 1364 mg a.i./kg bw/day	Practically nontoxic	2828317

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
		grade active ingredient, purity 98.67%)			
	22-w Reproduction	Broflanilide (technical grade active ingredient, purity 98.67%)	NOAEC = 254 mg a.i./kg diet NOAEL = 22.2 mg a.i./kg bw/day LOAEC = 506 mg a.i./kg diet LOAEC = 42.1 mg a.i./kg bw/day NOAEC/NOAEL is based on effects on most sensitive reproductive endpoints.	N/A	2828321
Mallard duck, *Anas platyrhynchos*	14d-Acute Oral	Broflanilide (technical grade active ingredient, purity 98.67%)	LD_{50} > 2000 mg a.i./kg bw	Practically nontoxic	2828309
	5d-Dietary	Broflanilide (technical grade active ingredient, purity 98.67%)	LC_{50} > 5073 mg a.i./kg diet LD_{50} > 2081 mg a.i./kg bw/day	Practically nontoxic	2828314
	21-w Reproduction	Broflanilide (technical grade active ingredient, purity 98.67%)	NOAEC = 29.7 mg a.i./kg diet NOAEL = 4.6 mg a.i./kg bw/day LOAEC = 87.4 mg a.i./kg diet LOAEC = 13.0 mg a.i./kg bw/day NOAEC/NOAEL is based on effects on most sensitive reproductive endpoints.	N/A	2828323
	21-w Reproduction	Broflanilide (technical grade active ingredient, purity 98.67%)	NOAEC < 258 mg a.i./kg diet NOAEL < 32.8 mg a.i./kg bw/day NOAEC/NOAEL is based on effects on most sensitive reproductive endpoints.	N/A	2828319
Canary, *Serinus canaria*	14d-Acute Oral	Broflanilide (technical grade active ingredient, purity 98.67%)	LD_{50} > 2000 mg a.i./kg bw	Practically nontoxic	2828311
Mammals					
Rat (Wistar)	Acute oral	Broflanilide (technical grade active ingredient, purity 99.67%)	LD_{50} > 5000 mg a.i./kg bw No clinical signs of toxicity at highest tested concentration.	Practically nontoxic	2828159

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
		End-use product, Cimegra (SC, 100 g a.i./L, 9.51%)	LD_{50} > 2000 mg/kg bw (> 190 mg a.i./kg bw) No clinical signs of toxicity at highest tested concentration.	Practically nontoxic	2827889
		End-use product, Teraxxa (FS, 300 g a.i./L, 25.97%)	LD_{50} > 2000 mg/kg bw (> 519 mg a.i./kg bw) No clinical signs of toxicity at highest tested concentration.	Practically nontoxic	2828019
		End-use product, Teraxxa F4 (FS, 16.7 g a.i./L, 1.552%)	LD_{50} > 2000 mg/kg bw (> 31 mg a.i./kg bw) No clinical signs of toxicity at highest tested concentration.	Practically nontoxic	2827945
	2-Generation Reproduction	Broflanilide (technical grade active ingredient, purity 98.67%)	NOAEC = 300 ppm NOAEL = 26 mg a.i./kg bw/day Based on toxicity in the F0, F1 and F2 rats (decreased body weight/body weight gain) at the next higher dose.	N/A	2828201
Vascular plants					
Monocot and dicot crop species (onion, ryegrass, wheat, corn, sugarbeet, oilseed rape, cabbage, soybean, lettuce and tomato)	21-d Seedling emergence	End-use product, Cimegra (SC, 100 g a.i./L)	Tier I: NOAEC for lettuce and cabbage (dry weight) < 0.091 lbs a.i./A (< 102 g a.i./ha) NOAEC for all other species ≥ 0.091 lbs a.i./A (≥ 102 g a.i./ha) Tier II: NOAEC for lettuce and tomato ≥ 0.091 lbs a.i./A (≥ 102 g a.i./ha) NOAEC and EC_{25} for cabbage = 0.014 and 0.0101 lbs a.i./A (16 and 11 g a.i./ha), respectively (not dose-dependent) NOAEC for sugarbeet < 0.0023 lbs a.i./A (< 2.6 g a.i./ha) (not dose-dependent)	N/A	2827872
Monocot and dicot crop species (onion, ryegrass, wheat, corn, sugarbeet, oilseed rape, cabbage, soybean, lettuce and tomato)	21-d Vegetative vigour	End-use product, Cimegra (SC, 100 g a.i./L)	Tier I: NOAEC for tomato < 0.088 lbs a.i./A (< 99 g a.i./ha) NOAEC for oilseed rape, onion, ryegrass, wheat ≥ 0.088 lbs a.i./A (≥ 99 g a.i./ha) NOAEC for cabbage, corn, lettuce, soybean, sugarbeet ≥ 0.091 lbs a.i./A (≥ 102 g a.i./ha) Tier II: NOAEC for all species ≥ 0.091 lbs a.i./A (≥ 102 g a.i./ha)	N/A	2827870

[1] Atkins *et al.*(1981) for bees and USEPA classification for others, where applicable

Table 17 Screening Level Risk Assessment of Broflanilide, its Transformation Products and End-use Products for Non-target Terrestrial Species Other than Birds and Mammals

Organism	Exposure[1]	Endpoint value (endpoint/UF)	EEC	RQ	Level of Concern[2]
Invertebrates					
Earthworm	Acute – a.i.	LC_{50}/2: >493.5 mg a.i./kg soil	0.0111 mg a.i./kg soil	<0.1	Not exceeded
	Acute – DC-8007	LC_{50}/2: >498.0 mg a.i./kg soil	0.0111 mg a.i./kg soil	<0.1	Not exceeded
	Acute – DC-DM-8007	LC_{50}/2: >498.5 mg a.i./kg soil	0.0111 mg a.i./kg soil	<0.1	Not exceeded
	Acute – Cimegra	LC_{50}/2: >47.3 mg a.i./kg soil	0.0111 mg a.i./kg soil	<0.1	Not exceeded
	Acute – Teraxxa	LC_{50}/2: >130.0 mg a.i./kg soil	0.0111 mg a.i./kg soil	<0.1	Not exceeded
	Reproduction – a.i.	NOEC: 30.86 mg a.i./kg soil	0.0111 mg a.i./kg soil	<0.1	Not exceeded
	Reproduction – Teraxxa	NOEC: 65 mg a.i./kg soil	0.0111 mg a.i./kg soil	<0.1	Not exceeded
Soil mite, *Hypoaspis aculeifer*	Reproduction – Teraxxa	NOEC: 0.24 mg a.i./kg soil	0.0111 mg a.i./kg soil	<0.1	Not exceeded
Honey bee, *Apis mellifera*	Acute oral, adults – a.i.	LD_{50}: 0.0149 µg a.i./bee	Soil application: 0.003 µg a.i./bee	0.2	Not exceeded
			Seed treatment: 0.292 µg a.i./bee	**19.6**	**Exceeded**
	Acute oral, adults – DM-8007	LD_{50}: 1.92 µg a.i./bee	Soil application: 0.003 µg a.i./bee	<0.1	Not exceeded
			Seed treatment: 0.292 µg a.i./bee	0.15	Not exceeded
	Acute oral, adults – S(PFP-OH)-8007	LD_{50}: >5.6 µg a.i./bee	Soil application: 0.003 µg a.i./bee	<0.1	Not exceeded
			Seed treatment: 0.292 µg a.i./bee	<0.1	Not exceeded
	Acute oral, adults – DC-8007	LD_{50}: >100 µg a.i./bee	Soil application: 0.003 µg a.i./bee	<0.1	Not exceeded
			Seed treatment: 0.292 µg a.i./bee	<0.1	Not exceeded
	Acute oral, adults – B-urea	LD_{50}: >100 µg a.i./bee	Soil application: 0.003 µg a.i./bee	<0.1	Not exceeded
			Seed treatment: 0.292 µg a.i./bee	<0.1	Not exceeded
	Acute oral, adults – DC-DM-8007	LD_{50}: >20.27 µg a.i./bee	Soil application: 0.003 µg a.i./bee	<0.1	Not exceeded
			Seed treatment: 0.292 µg a.i./bee	<0.1	Not exceeded
	Acute oral, adults – B-oxam-acid	LD_{50}: >23.55 µg a.i./bee	Soil application: 0.003 µg a.i./bee	<0.1	Not exceeded
			Seed treatment: 0.292 µg a.i./bee	<0.1	Not exceeded

Organism	Exposure[1]	Endpoint value (endpoint/UF)	EEC	RQ	Level of Concern[2]
	Acute oral, adults – Cimegra	LD_{50}: 0.045 µg a.i./bee	Soil application: 0.003 µg a.i./bee	<0.1	Not exceeded
	Acute oral, adults – Teraxxa	LD_{50}: 0.0693 µg a.i./bee	Seed treatment: 0.292 µg a.i./bee	**4.2**	**Exceeded**
	Chronic oral, adults – a.i.	NOAEL: 0.00062 µg a.i./bee	Soil application: 0.003 µg a.i./bee	**5.1**	**Exceeded**
			Seed treatment: 0.292 µg a.i./bee	**471.0**	**Exceeded**
	Acute oral, larvae – a.i.	LD_{50}: >0.029 µg a.i./larva	Soil application: 0.001 µg a.i./bee	<0.1	Not exceeded
			Seed treatment: 0.124 µg a.i./bee	**<4.3**	**Exceeded**
	Chronic oral, larvae – a.i.	NOAEL: 0.000088 µg a.i./bee	Soil application: 0.001 µg a.i./bee	**15.2**	**Exceeded**
			Seed treatment: 0.124 µg a.i./bee	**1404.5**	**Exceeded**
Predatory mite, *Typhlodromus pyri*	Contact, glass plates – Cimegra	LR_{50}: 0.0573 g a.i./ha	Soil application: 25 g a.i./ha	**436.3**	**Exceeded**
			Seed treatment: 12.5 g a.i./ha	**218.2**	**Exceeded**
Parasitoid wasp, *Aphidius rhopalosiphi*	Contact, glass plates – Cimegra	LR_{50}: 0.17 g a.i./ha	Soil application: 25 g a.i./ha	**147.1**	**Exceeded**
			Seed treatment: 12.5 g a.i./ha	**73.5**	**Exceeded**
Vascular plants					
Vascular plant	Seedling emergence	ER_{25}: 11 g a.i./ha	25 g a.i./ha	**2.3**	**Exceeded**
	Vegetative vigour	ER_{25}: >102 g a.i./ha	25 g a.i./ha	0.2	Not exceeded

[1] Cimegra is a soil applied product only, while Teraxxa is a seed treatment product. At the screening level, EECs for soil and seed treatment applications were divided by the effects endpoint from studies conducted with the corresponding Cimegra or Teraxxa end-use product. Where only one study was available for an organism, the endpoint was used indiscriminately in the RQ calculation for both soil and seed treatments.

[2] Level of concern = 1 for most species; 0.4 for acute risk to pollinators; 1 for chronic risk to pollinators; and 2 for glass plate studies using the standard beneficial arthropod test species, *Typhlodromus pyri* and *Aphidius rhopalosiphi.*

NOTE for pollinators:

Soil EEC: (10^(0.95*LogK_{ow}-2.05)+0.82)*(-0.0648*(LogK_{ow}^2)+0.2431*LogK_{ow}+0.5822)* (1.5/(0.2+1.5*K_{oc}*0.01))* (0.5*Srate/1.12) × consumption rate for adults and larvae (29 µg a.i./bee per kg a.i./ha for adult oral and 12 µg a.i./larva per kg/ha for larvae).

As a highly conservative assumption at the screening level that broflanilide is systemic, the Briggs model was used to estimate residue levels that may be translocated into the plant tissues, such as pollen and nectar. For the soil EEC calculation, a LogK_{ow} of 5 (the maximum value permitted by the Briggs' model), average K_{oc} of 9,274 for broflanilide, and a soil application rate of 25 g a.i./ha was used.

Seed treatment EEC: For seed treatments, the Tier I exposure method uses 1 mg a.i./kg concentration as an upper-bound for pesticides in nectar and pollen through translocation through the plant. The oral exposure estimate for adult bees is calculated by multiplying 1 µg a.i./g by the consumption value for adults (0.292 g/day) or larvae (0.124 g/day).

NOTE for predatory and parasitic arthropods:

The screening level exposure estimates are highly conservative, as seed treatment and soil applications are not expected to result in plant residues comparable to those from direct application to the plant. Foliar applications are not proposed for any of the broflanilide end-use products.

Soil EEC: The EEC for a direct application on soil was calculated using the maximum application rate of Cimegra Insecticide, which is proposed as an in-furrow or T-band spray at a rate of 25 g a.i./ha.

Seed treatment EEC: An exposure estimate on a per hectare basis is determined by applying the loading rate to the sowing rate (for example, kg active/ha = kg active/100 kg seed × kg seed/ha). The default sowing rate is 250 kg seed/ha for determination of the in-field exposure estimate. Both of the proposed broflanilide seed treatment products are for application to small cereal grains at a rate of 5 g broflanilide per 100 kg seed, therefore the EEC for seed treatments is 12.5 g a.i./ha.

Table 18 Screening Level Risk Assessment of Broflanilide for Birds and Mammals

	Study Endpoint (mg a.i./kg bw/day/UF)	EDE (mg a.i./kg bw/day)[1]	RQ	Level of Concern[2]
Small Sized Bird (0.02 kg)				
Acute	>200	12.7	<0.1	Not exceeded
Reproduction	4.6	12.7	**2.8**	**Exceeded**
Medium Sized Bird (0.10 kg)				
Acute	>200	10.0	<0.1	Not exceeded
Reproduction	4.6	10.0	**2.2**	**Exceeded**
Large Sized Bird (1.00 kg)				
Acute	>200	2.9	<0.1	Not exceeded
Reproduction	4.6	2.9	0.6	Not exceeded
Small Sized Mammal (0.015 kg)				
Acute	>500[3]	7.2	<0.1	Not exceeded
Reproduction	26	7.2	0.3	Not exceeded
Medium Sized Mammal (0.035 kg)				
Acute	>500	6.2	<0.1	Not exceeded
Reproduction	26	6.2	0.2	Not exceeded
Large Sized Mammal (1.00 kg)				
Acute	>500	3.4	<0.1	Not exceeded
Reproduction	26	3.4	0.1	Not exceeded

[1] EDE (Estimated daily exposure; expressed in mg a.i./kg bw/day) = EEC (mg a.i./kg seeds) × FIR (in kg seed/day) × BW (1/kg bw). The proposed maximum application rate for broflanilide for use as seed treatment is 5 g a.i./100 kg seed. The number of seeds that are expected to be consumed by a generic-sized group of birds and mammals is calculated using a food ingestion rate (FIR) of 5.1, 19.9 and 58.1 g diet/day for 20, 100 and 1000 g birds, respectively, and 2.2, 4.4 and 68.7 g diet/day for 15, 35 and 1000 g mammals, respectively.

[2] Level of concern = 1 for birds and mammals

[3] The acute LD_{50} value of >5000 mg a.i./kg bw obtained from the study with the technical grade active ingredient was used in the screening level risk assessment. Technical grade broflanilide and its end-use products, Cimegra, Teraxxa, and Teraxxa F4, were all practically nontoxic to rats on an acute oral basis, with oral LD_{50} values of >2000 mg product/kg bw. There were no clinical signs of toxicity at the highest tested concentration for any of the acute oral studies. When accounting for the active ingredient content of the test substances, the endpoints from the acute oral studies done with the end-use products are more conservative than the one from the study with technical broflanilide; however, this difference in endpoints is more a result of the test compound being a formulated product than an indication of higher toxicity.

Table 19 Further characterization of the risk to non-target beneficial arthropods using results from extended laboratory studies

Organism	Exposure	Endpoint Value	EEC[1]	RQ	Level of Concern[2]
Predatory arthropod, *Typhlodromus pyri*	Extended laboratory (14d-contact; spray residue on leaf discs), Cimegra Insecticide	LR_{50}: 0.1141 g a.i./ha	25 g a.i./ha	**219**	**Exceeded**
		NOER: 0.0625 g a.i./ha	25 g a.i./ha	**400**	**Exceeded**
Parasitoid arthropod, *Aphidius rhopalosiphi*	Extended laboratory (13d-contact; spray residue on barley seedlings), Cimegra Insecticide	LR_{50}: 0.88 g a.i./ha	25 g a.i./ha	**28.4**	**Exceeded**
		NOER: <0.3 g a.i./ha	25 g a.i./ha	**83.3**	**Exceeded**

[1] The EEC is based on exposure to spray residues of Cimegra on-field from a direct application of 25 g a.i./ha; however, most predatory and parasitic arthropod species will not be directly exposed through spray contact because they are not expected to be present on the soil at the time of application. Because broflanilide does not have systemic activity in plants, negligible exposure of non-target arthropods is expected from both soil and seed treatment applications.

[2] Level of concern = 1

Table 20 Refined risk assessment of broflanilide for birds using LOAEL from reproductive studies

	Study Endpoint (mg a.i./kg bw/day/UF)	EDE (mg a.i./kg bw/day)[1]	RQ	Level of Concern[2]
Small Sized Bird (0.02 kg)				
Acute	>200	12.7	<0.1	Not exceeded
Dietary	136.4	12.7	<0.1	Not exceeded
Reproduction	13.0	12.7	0.98	Not exceeded
Medium Sized Bird (0.10 kg)				
Acute	>200	10.0	<0.1	Not exceeded
Dietary	136.4	10.0	<0.1	Not exceeded
Reproduction	13.0	10.0	0.77	Not exceeded
Large Sized Bird (1.00 kg)				
Acute	>200	2.9	<0.1	Not exceeded
Dietary	136.4	2.9	<0.1	Not exceeded
Reproduction	13.0	2.9	0.22	Not exceeded

[1] EDE (Estimated daily exposure; expressed in mg a.i./kg bw/day) = EEC (mg a.i./kg seeds) × FIR (in kg seed/day) × BW (1/kg bw). The proposed maximum application rate for broflanilide for use as seed treatment is 5 g a.i./100 kg seed. The number of seeds that are expected to be consumed by a generic-sized group of birds and mammals is calculated using a food ingestion rate (FIR) of 5.1, 19.9 and 58.1 g diet/day for 20, 100 and 1000 g birds, respectively, and 2.2, 4.4 and 68.7 g diet/day for 15, 35 and 1000 g mammals, respectively.
[2] Level of concern = 1 for birds

Table 21 Toxicity of Broflanilide, its Transformation Products and End-use Products to Non-target Aquatic Species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Freshwater species					
Daphnia magna	48h-Acute, static-renewal	Broflanilide (technical grade active ingredient, purity 98.67%)	EC_{50} > 332 µg a.i./L (immobilization)	Non-toxic up to the highest concentration tested.	2828364
	48h-Acute, static	MFBA (broflanilide transformation product), purity 99.3%	EC_{50} > 100 mg a.i./L (immobilization)	Non-toxic up to the highest concentration tested.	2828366
	21d-Chronic, static-renewal	Broflanilide (technical grade active ingredient, purity 98.67%)	NOAEC = 5.93 µg a.i./L LOAEC = 11.6 µg a.i./L (length, total offspring, successful birth rate and time to first brood)	N/A	2828368
	21d-Chronic, static-renewal	MFBA (broflanilide transformation product), purity 99.3%	NOAEC ≥ 98.0 mg a.i./L LOAEC > 98.0 mg a.i./L (no treatment-related effects at highest concentration tested)	N/A	2828370
Amphipod, *Hyalella azteca*	10d-Acute, spiked sediment, static-renewal	Broflanilide (technical grade active ingredient, purity 98.67%)	Dry sediment: NOAEC = 4.9 µg/kg LOAEC = 9.5 µg a.i./kg LC_{50} = 13.5 µg a.i./kg	N/A	2828384

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			Pore water: NOAEC = 0.16 µg a.i./L LOAEC = 0.30 µg a.i./L LC_{50} = 0.461 µg a.i./L Overlying water: Not estimated as measured concentrations were, for the most part, all below the LOQ. Endpoints based on treatment-related effects on survival.		
	42d-Chronic, spiked sediment, static-renewal	Broflanilide (technical grade active ingredient, purity 98.67%)	Dry sediment: NOAEC = 1.7 µg/kg LOAEC = 3.3 µg a.i./kg Pore water: NOAEC = 0.039 µg a.i./L LOAEC = 0.099 µg a.i./L Overlying water: Not estimated as measured concentrations were all below the LOQ. Endpoints based on treatment-related effects on survival.	N/A	2828392
Midge, *Chironomus dilutus*	10d-Acute, spiked sediment, static-renewal	Broflanilide (technical grade active ingredient, purity 99.9%)	Dry sediment: NOAEC = 1.5 µg/kg LOAEC = 4.8 µg a.i./kg LC_{50} = 9.99 µg a.i./kg Pore water: NOAEC = 0.032 µg a.i./L LOAEC = 0.098 µg a.i./L LC_{50} = 0.211 µg a.i./L Overlying water: NOAEC = 0.0011 µg a.i./L LOAEC = 0.0029 µg a.i./L LC_{50} = Not estimated as no test material was detected in the overlying water of the two lowest treatment groups. Endpoints based on treatment-related effects on survival.	N/A	2828382
	10d-Acute, spiked sediment, static-renewal	DC-8007 (broflanilide transformation product), purity 99.6%	Dry sediment: NOAEC ≥ 3500 µg/kg LOAEC and LC_{50} > 3500 µg a.i./kg Pore water: NOAEC ≥ 120 µg a.i./L	N/A	2828388

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			LOAEC and LC_{50} > 120 µg a.i./L Overlying water: NOAEC ≥ 4.1 µg a.i./L LOAEC and LC_{50} > 4.1 µg a.i./L No treatment-related effects on survival or growth at highest concentration tested.		
	60d-Chronic, spiked sediment, static-renewal	Broflanilide (technical grade active ingredient, purity 99.9%)	Dry sediment: NOAEC = 1.5 µg/kg LOAEC = 4.7 µg a.i./kg Pore water: NOAEC = 0.024 µg a.i./L LOAEC = 0.079 µg a.i./L Overlying water: NOAEC = 0.00074 µg a.i./L LOAEC = 0.0016 µg a.i./L Endpoints based on treatment-related effects on survival and emergence.	N/A	2828390
Rainbow trout, *Oncorhynchus mykiss*	96h-Acute, static-renewal	Broflanilide (technical grade active ingredient, purity 98.67%)	LC_{50} = 365 µg a.i./L (mortality)	Highly toxic	2828347
Bluegill, *Lepomis macrochirus*	96h-Acute, static-renewal	Broflanilide (technical grade active ingredient, purity 98.67%)	LC_{50} = 251 µg a.i./L (mortality)	Highly toxic	2828349
Fathead minnow, *Pimephales promelas*	96h-Acute, static-renewal	Broflanilide (technical grade active ingredient, purity 98.67%)	LC_{50} > 508 µg a.i./L (no treatment-related effects at highest concentration tested)	Non-toxic up to the highest concentration tested.	2828351
	33d-ELS, flow-through	Broflanilide (technical grade active ingredient, purity 98.67%)	NOAEC = 51 µg a.i./L LOAEC = 147 µg a.i./L (larval survival)	N/A	2828355
Carp, *Cyprinus carpio*	96h-Acute, static-renewal	Broflanilide (technical grade active ingredient, purity 98.67%)	LC_{50} > 498 µg a.i./L (no mortality at highest concentration tested) At the highest test concentration, 100% of fish were observed surfacing.	Non-toxic up to the highest concentration tested.	2828353
Diatom,	96h-Acute,	Broflanilide	IC_{50} > 0.40 mg a.i./L	N/A	2828378

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Navicula pelliculosa	static	(technical grade active ingredient, purity 98.67%)	NOEC = 0.080 mg a.i./L (for most sensitive endpoints of yield and area under the growth curve)		
Green algae, *Pseudokirch-neriella subcapitata*	72h-Acute, static	Broflanilide (technical grade active ingredient, purity 98.67%)	IC_{50} > 0.60 mg a.i./L NOEC ≥ 0.60 mg a.i./L (no treatment-related effects at highest concentration tested)	N/A	2828372
	72h-Acute, static	MFBA (broflanilide transformation product), purity 99.3%	IC_{50} > 96.1 mg a.i./L NOEC ≥ 96.1 mg a.i./L (no treatment-related effects at highest concentration tested)	N/A	2828380
Green algae, *Raphidocelis subcapitata*	96h-Acute, static	Broflanilide (technical grade active ingredient, purity 98.67%)	IC_{50} > 0.71 mg a.i./L NOEC = 0.12 mg a.i./L (for most sensitive endpoint of yield)	N/A	2828374
	96h-Acute, static	DC-8007 (broflanilide transformation product), purity 99.6%	IC_{50} = 1.08 mg a.i./L NOEC < 0.0197 mg a.i./L (for most sensitive endpoint of area under the growth curve)	N/A	3027824
Blue-green algae, *Anabaena flos-aquae*	96h-Acute, static	Broflanilide (technical grade active ingredient, purity 98.67%)	IC_{50} > 0.66 mg a.i./L NOEC ≥ 0.66 mg a.i./L (no treatment-related effects at highest concentration tested)	N/A	2828376
Vascular plant, duckweed, *Lemna gibba*	7d-Static renewal	Broflanilide (technical grade active ingredient, purity 98.67%)	IC_{50} > 0.634 mg a.i./L NOEC ≥ 0.634 mg a.i./L (no treatment-related effects at highest concentration tested)	N/A	2828396
Marine species					
Amphipod, *Leptocheirus plumulosus*	10d-Acute, spiked sediment, static	Broflanilide (technical grade active ingredient, purity 98.67%)	Dry sediment: NOAEC = 9.6 µg/kg LOAEC = 20 µg a.i./kg LC_{50} = 14 µg a.i./kg Pore water: Not estimated as no test material was detected at the three lowest treatment levels. The mean-measured concentrations in the two highest treatment levels were 0.099 (corresponding to the LOAEC) and 0.21 µg a.i./L, respectively, suggesting the LC_{50} would be <0.099 µg a.i./L. Overlying water: Not estimated as no test material	N/A	2828386

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			was detected at any point. Endpoints based on treatment-related effects on survival.		
	28d-Chronic, spiked sediment, static	Broflanilide (technical grade active ingredient, purity 98.67%)	Dry sediment: NOAEC = 3.8 µg/kg LOAEC = 8.4 µg a.i./kg Pore water: Not estimated as no test material was detected at the three lowest treatment levels. The mean-measured concentrations in the two highest treatment levels were 0.034 (corresponding to the LOAEC) and 0.082 µg a.i./L, respectively. Overlying water: Not estimated as no test material was detected at any point. Endpoints based on treatment-related effects on survival.	N/A	2828394
Crustacean, mysid shrimp, *Americamysis bahia*	96h-Acute, flow-through	Broflanilide (technical grade active ingredient, purity 98.67%)	LC_{50} = 0.0215 µg a.i./L (mortality)	Very highly toxic	2828332
	96h-Acute, flow-through	S(Br-OH)-8007 (broflanilide transformation product), purity 98.86%	LC_{50} = 40.6 µg a.i./L (mortality)	Very highly toxic	2828340
	96h-Acute, flow-through	AB-oxa (broflanilide transformation product), purity 98.64%	LC_{50} = 30.2 µg a.i./L (mortality)	Very highly toxic	2828342
	96h-Acute, flow-through	MFBA (broflanilide transformation product), purity 99.87%	LC_{50} > 112 µg a.i./L (mortality)	Non-toxic up to the highest concentration tested.	3050587
	28d-Chronic, flow-through	Broflanilide (technical grade active ingredient, purity 98.67%)	NOAEC = 6.23 ng a.i./L LOAEC = 10.3 ng a.i./L (effects on survival, growth, and number of offspring per female)	N/A	2828336
Mollusk, Eastern oyster, *Crassostrea virginica*	96h-Acute, flow-through	Broflanilide (technical grade active ingredient, purity 98.67%)	IC_{50} > 0.44 mg a.i./L (no treatment-related effects at highest concentration tested)	Non-toxic up to the highest concentration tested.	2828334

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Marine diatom, *Skeletonema costatum*	96h-Acute, static	Broflanilide (technical grade active ingredient, purity 98.67%)	IC_{50} = 0.31 mg a.i./L NOEC = 0.13 mg a.i./L (for most sensitive endpoint of area under the growth curve)	N/A	2828330
Sheepshead minnow, *Cyprinodon variegatus*	96h-Acute, flow-through	Broflanilide (technical grade active ingredient, purity 98.67%)	LC_{50} > 1.3 mg a.i./L (10% mortality at highest concentration tested) At the three highest test concentrations, sublethal effects were observed in up to 30% of fish (surfacing and lethargy).	Non-toxic up to the highest concentration tested.	2828338
	34d-ELS, flow-through	Broflanilide (technical grade active ingredient, purity 98.67%)	NOAEC = 11.1 µg a.i./L LOAEC = 25.2 µg a.i./L (growth)	N/A	2828357

[1] USEPA classification, where applicable

Table 22 Screening level risk assessment of broflanilide for aquatic organisms

Organism	Exposure	Endpoint value (mg a.i./L/UF)	EEC[1] (mg a.i./L)	RQ	Level of Concern[2]
Freshwater species					
Invertebrate, *Daphnia magna*	Acute – a.i.	EC_{50}/2: >0.166	0.00312	<0.1	Not exceeded
	Acute – MFBA	EC_{50}/2: >50	0.00312	<0.1	Not exceeded
	Chronic – a.i.	NOEC: 0.00593	0.00312	0.5	Not exceeded
	Chronic – MFBA	NOEC: ≥98.0	0.00312	<0.1	Not exceeded
Rainbow trout, *Oncorhynchus mykiss*	Acute – a.i.	LC_{50}/10: 0.0365	0.00312	<0.1	Not exceeded
Bluegill, *Lepomis macrochirus*	Acute – a.i.	LC_{50}/10: 0.0251	0.00312	0.1	Not exceeded
Carp, *Cyprinus carpio*	Acute – a.i.	LC_{50}/10: >0.0498	0.00312	<0.1	Not exceeded
Fathead minnow, *Pimephales promelas*	Acute – a.i.	LC_{50}/10: >0.0508	0.00312	<0.1	Not exceeded
	ELS – a.i.	NOEC: 0.051	0.00312	<0.1	Not exceeded
Amphibians (using fish data as a surrogate)	Acute – a.i.	LC_{50}/10: 0.0251	0.0167	0.7	Not exceeded
	ELS – a.i.	NOEC: 0.051	0.0167	0.3	Not exceeded
Aquatic vascular plant, *Lemna gibba*	Acute – a.i.	IC_{50}/2: >0.317	0.00312	<0.1	Not exceeded
Diatom, *Navicula pelliculosa*	Acute – a.i.	IC_{50}/2: >0.20	0.00312	<0.1	Not exceeded
Green algae, *Pseudokirchneriella subcapitata*	Acute – a.i.	IC_{50}/2: >0.30	0.00312	<0.1	Not exceeded
	Acute – MFBA	IC_{50}/2: >48.0	0.00312	<0.1	Not exceeded
Green algae, *Raphidocelis subcapitata*	Acute – a.i.	IC_{50}/2: >0.36	0.00312	<0.1	Not exceeded
	Acute – DC-8007	IC_{50}/2: 0.54	0.00312	<0.1	Not exceeded
Blue-green algae, *Anabaena flos-aquae*	Acute – a.i.	IC_{50}/2: >0.33	0.00312	<0.1	Not exceeded

Organism	Exposure	Endpoint value (mg a.i./L/UF)	EEC[1] (mg a.i./L)	RQ	Level of Concern[2]
Marine species					
Crustacean, mysid shrimp, *Americamysis bahia*	Acute – a.i.	LC_{50}/2: 0.00001075	0.00312	**290**	**Exceeded**
	Acute – S(Br-OH)-8007	LC_{50}/2: 0.0203	0.00312	0.2	Not exceeded
	Acute – AB-oxa	LC_{50}/2: 0.0151	0.00312	0.2	Not exceeded
	Acute – MFBA	LC_{50}/2: >0.056	0.00312	<0.1	Not exceeded
	Chronic – a.i.	NOEC: 0.00000623	0.00312	**501**	**Exceeded**
Mollusk, Eastern oyster, *Crassostrea virginica*	Acute – a.i.	LC_{50}/2: >0.22	0.00312	<0.1	Not exceeded
Sheepshead minnow, *Cyprinodon variegatus*	Acute – a.i.	LC_{50}/10: >0.13	0.00312	<0.1	Not exceeded
	ELS – a.i.	NOEC: 0.0111	0.00312	0.3	Not exceeded
Marine diatom, *Skeletonema costatum*	Acute – a.i.	IC_{50}/2: 0.155	0.00312	<0.1	Not exceeded

[1] The screening level EECs in water are based on direct application of a pesticide to a body of water, and is intended to be a simple, conservative, and reasonable worst-case estimate of pesticide concentrations in water. The maximum cumulative application rate for broflanilide on water is 25 g a.i./ha, based on the proposed use of Cimegra Insecticide. Based on this application rate, the EEC in water bodies 80 cm and 15 cm deep are 0.00312 mg a.i./L and 0.0167 mg a.i./L, respectively.
[2] Level of concern = 1

Table 23 Risk quotients for aquatic organisms determined for runoff of broflanilide

Organism (exposure)	Endpoint (mg a.i./L/UF)	EEC (mg a.i./L)	RQ	Level of Concern
Freshwater species				
Hyalella azteca (acute; 10 days; technical broflanilide)	pore water IC_{50}/2: 0.0002305	Corn T-band (pore water peak): 0.00049	**2.1**	**Exceeded**
		Spring wheat seed treatment (pore water peak): 0.000033	<1.0	Not exceeded
Hyalella azteca (chronic; 42 days; technical broflanilide)	pore water NOEC: 0.000039	Corn T-band (pore water 21d): 0.00049	**12.6**	**Exceeded**
		Spring wheat seed treatment (pore water 21d): 0.000033	<1.0	Not exceeded
Chironomus dilutus (acute; 10 days; technical broflanilide)	pore water IC_{50}/2: 0.0001055	Corn T-band (pore water peak): 0.00049	**4.6**	**Exceeded**
		Spring wheat seed treatment (pore water peak): 0.000033	<1.0	Not exceeded
Chironomus dilutus (acute; 10 days; DC-8007)	pore water IC_{50}/2: >0.06	Corn T-band (pore water peak): 0.00049	<1.0	Not exceeded
		Spring wheat seed treatment (pore water peak): 0.000033	<1.0	Not exceeded
Chironomus dilutus (chronic; 60 days, technical broflanilide)	pore water NOEC: 0.000024	Corn T-band (pore water 21d): 0.00049	**20.4**	**Exceeded**
		Spring wheat seed treatment (pore water 21d): 0.000033	**1.4**	**Exceeded**
Marine species				
Leptocheirus plumulosus (acute; 10 days; technical broflanilide)[1]	pore water LC_{50}/2: <0.0000495	Corn T-band (pore water peak): 0.00049	**>9.9**	**Exceeded**
		Spring wheat seed treatment (pore water peak): 0.000033	>0.7	Not exceeded
Leptocheirus plumulosus (chronic; 28 days; technical broflanilide)[2]	pore water NOEC: 0.000034	Corn T-band (pore water 21d): 0.00049	**14.4**	**Exceeded**
		Spring wheat seed treatment (pore water 21d): 0.000033	<0.1	Not exceeded

Organism (exposure)	Endpoint (mg a.i./L/UF)	EEC (mg a.i./L)	RQ	Level of Concern
Americamysis bahia (acute; 96 hours; technical broflanilide)	LC_{50}/2: 0.00001075	Corn T-band (water column 96h, 80cm): 0.00067	**62.3**	**Exceeded**
		Spring wheat seed treatment (water column 96h, 80cm): 0.000046	**4.3**	**Exceeded**
Americamysis bahia (chronic; 28 days; technical broflanilide)	NOEC: 0.00000623	Corn T-band (water column 21d, 80cm): 0.00057	**91**	**Exceeded**
		Spring wheat seed treatment (water column 21d, 80cm): 0.000036	**5.8**	**Exceeded**

[1] The LC_{50} in pore water was not estimated as no test material was detected at the three lowest treatment levels (no significant effects on amphipod survival). The mean-measured concentrations in the two highest treatment levels were 0.099 µg a.i./L (corresponding to the LOAEC where 100% mortality was observed) and 0.21 µg a.i./L (100% mortality), respectively, suggesting the LC_{50} would be <0.099 µg a.i./L.
[2] The NOAEC in pore water was not estimated as no test material was detected at the three lowest treatment levels (no significant effects on amphipod survival or reproduction). The mean-measured concentrations in the two highest treatment levels were 0.034 µg a.i./L (corresponding to the LOAEC where 12% reduction in survival was observed) and 0.082 µg a.i./L, respectively.

Table 24 List of Supported Uses

Product	Supported Uses
Cimegra	Potatoes: • for control of wireworm, apply in furrow at planting at an application rate of 250 mL product (25 g a.i.) per hectare. Corn: • for control of wireworm and corn rootworm (western and northern), apply at a rate of 250 mL product (25 g a.i.) per hectare in furrow or as a 10 to 20 cm t-band spray over the top of the open seed furrow at planting. Cimegra is applied in a minimum application volume of 50 L per hectare.
Teraxxa	Small cereal grains (barley, buckwheat, pearl millet, proso millet, oats, rye, sorghum, triticale, canary seed, annual canarygrass (grown for human consumption)) and wheat (all types: winter, spring and durum): • for control of wireworm, apply at a rate of 16.7 mL product per 100 kg seed (5 g a.i./100 kg seed)
Teraxxa F4	Small cereal grains (barley, buckwheat, pearl millet, proso millet, oats, rye, sorghum, triticale, canary seed, annual canarygrass (grown for human consumption)) and wheat (all types: winter, spring and durum): • for control of wireworm, apply at a rate of 300 mL product per 100 kg seed (20.5 g a.i./100 kg seed). Control of following diseases on barley, canary seed, annual canarygrass (grown for human consumption), oats, rye, triticale, and wheat (all types: winter, spring and durum) at 300 mL/100 kg seed (20.5 g a.i./100 kg seed): • Seed Rot/Pre-emergent Damping-off caused by *Fusarium* spp., *Rhizoctonia solani*, *Cochliobolus sativus*, and *Pythium* spp. • Post-emergent Damping-off caused by *Fusarium spp.*, *Rhizoctonia solani*, and *Pythium* spp.

	• Seedling Blight caused by *Fusarium* spp., *Rhizoctonia solani*, and *Pythium* spp. • Root Rot caused by *Fusarium* spp., *Rhizoctonia solani*, and *Pythium* spp. Suppression of following diseases on barley, canary seed, annual canarygrass (grown for human consumption), oats, rye, triticale, and wheat (all types: winter, spring and durum) at 300 mL/100 kg seed (20.5 g a.i./100 kg seed): • Fusarium crown and root rot caused by *Fusarium* spp. • Seedling blight caused by *Cochliobolus sativus* • Root rot caused by *Cochliobolus sativus* Control of following diseases on rye, triticale, and wheat (all types: winter, spring and durum) at 300 mL/100 kg seed (20.5 g a.i./100 kg seed): • Loose Smut (*Ustilago tritici*) • Common Bunt (*Tilletia tritici, T. lavies*) Control of following diseases on barley at 300 mL/100 kg seed (20.5 g a.i./100 kg seed): • True Loose Smut (*Ustilago nuda*) • Covered Smut (*Ustilago hordei*) • False Loose Smut (*Ustilago nigra*) Control of following diseases on oat at 300 mL/100 kg seed (20.5 g a.i./100 kg seed): • Loose Smut (*Ustilago avenae*) • Covered Smut (*Ustilago kolleri*)

Table 25 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints
Toxic or toxic equivalent as defined by the *Canadian Environmental Protection Act*[1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	Yes: 804–5742 days (laboratory)
	Water	Half-life ≥ 182 days	Yes: 871–1430 days (laboratory, total system, aerobic and anaerobic systems)
	Sediment	Half-life ≥ 365 days	
	Air	Half-life ≥ 2 days or evidence of long range transport	Yes: 2.5 days (AOPWIN predicted; however, volatilisation is not an important route of dissipation for broflanilide and long-range atmospheric transport is unlikely to occur based on the vapour pressure (<8.9×10^{-9} Pa at 25°C) and Henry's law constant (4.1×10^{-11} atm·m^3/mol at 20°C).

Bioaccumulation[4]	Log $K_{ow} \geq 5$	Yes: 4.34–5.91
	BCF $\geq$ 5000	No: 96–119
	BAF $\geq$ 5000	Not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?		No, does not meet TSMP Track 1 criteria.

[1] All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (in other words, all other TSMP criteria are met).
[2] The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4] Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, logK_{ow}).

Appendix II Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

Broflanilide is an active ingredient that is concurrently being registered in Canada and the United States for use on potato, corn (all types) and small grains. The MRLs proposed for broflanilide in Canada are the same as corresponding tolerances to be promulgated in the United States.

Once established, the American tolerances for broflanilide will be listed in the Electronic Code of Federal Regulations, 40 CFR Part 180, by pesticide.

Currently, there are no Codex MRLs[9] listed for broflannilide in or on any commodity on the Codex Alimentarius Pesticide Index website.

[9] The Codex Alimentarius Commission is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

References

A. List of Studies/Information Submitted by Registrant

PMRA Document Number	Reference
	1.0 Chemistry
2828107	2017, DACO 2.3 - 2.4: Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient (TGAI), DACO: 2.3,2.3.1,2.4,IIA 1.3,IIA 1.5.1,IIA 1.5.2
2828108	2017, MCI-8007 (BAS 450 I) (pure grade) - Physico-chemical properties, DACO: 2.13.2,2.14.1,2.14.10,2.14.11,2.14.12,2.14.13,2.14.2,2.14.3,2.14.4,2.14.5,2.14.6,2.14.8,2.14.9,2.16,8.2.3.2,8.2.3.3.3,IIA 2.1.1,IIA 2.1.2,IIA 2.1.3,IIA 2.10,IIA 2.2,IIA 2.3.1,IIA 2.3.2,IIA 2.4.1,IIA 2.4.2,IIA 2.5.1.1,IIA 2.5.1.2,IIA 2.5.1.3,IIA 2.5.1.4,IIA 2.7,IIA 2.8.1,IIA 2.9.5
2828109	2017, MCI-8007 (BAS 450 I) (technical grade) - Physico-chemical properties, DACO: 2.16,IIA 2.11.1,IIA 2.11.2,IIA 2.13,IIA 2.14,IIA 2.15,IIA 2.16
2828111	2017, MCI-8007 (BAS 450 I) (technical grade) - Stability to elevated temperature and metal/metal ions, DACO: 2.14.13,IIA 2.17.2
2828112	2017, MCI-8007 (BAS 450 I) (technical grade) - Accelerated storage stability, DACO: 2.14.13,IIA 2.17.2
2828113	2017, MCl-8007 (BAS 450 I) - Water solubility, DACO: 2.14.7,IIA 2.6
2828135	2017, Sample(s) of Analytical Standards and ROC, DACO: 2.15,IIA 4.1.1
2828957	2017, Content Analysis of MCI-8007, DACO: 2.13.3,2.13.4 CBI
2828958	2017, Content Analysis of MCI-8007, DACO: 2.13.3,2.13.4 CBI
2828963	2017, Characterization of BBPA, DACO: 2.13.3,2.13.4 CBI
2828964	2017, Characterization of MDFP, DACO: 2.13.3,2.13.4 CBI
2828965	2017, Characterization of MFDBA, DACO: 2.13.3,2.13.4 CBI
2828966	2017, Characterization of [CBI removed], DACO: 2.13.3,2.13.4 CBI
2828967	2017, [CBI removed]: Confirmation of Identity by MS, DACO: 2.13.3,2.13.4 CBI
2828968	2016, METHODOLOGY/VALIDATION, DACO: 2.13.1 CBI
2828143	2017, Validation of method D1603/01: Method for the determination of residues of BAS 450 I (Reg. No. 5672774) and its metabolites DM-8007 (Reg. No. 5856361), DC-DM-8007 (Reg. No. 5936906), DC-8007 (Reg. No. 5936907) and S(PFP-OH)-8007 (Reg. No. 5959598) in soil by LC-MS/MS (at LOQ of 1ppb), DACO: 8.2.2.1,IIA 4.4
2828144	2017, Evaluation of the limit of detection (LOD) for method D1603/01, method for the determination of residue of BAS 450 I (Reg. No. 5672774) and its metabolites DM-8007 (Reg. No.5856361), DC-DM-8007 (Reg. No. 5936906), DC-8007 (Reg. No. 5936907) and S(PFP-OH)-8007 (Reg. No. 5959598) in soil by LC-MS/MS (at LOQ of 1ppb), DACO: 8.2.2.1,IIA 4.4

2828145 2017, Independent laboratory validation of the following method entitled: BASF analytical method D1603/01: Method for the determination of residues of BAS 450 I (Reg. No. 5672774) and its metabolites DM-8007 (Reg. No. 5856361), DC-DM-8007 (Reg. No. 5936906), DC-8007 (Reg. No. 5936907) and S(PFP-OH)-8007 (Reg. No. 5959598) in soil by LC-MS/MS (at LOQ of 1ppb), DACO: 8.2.2.1,IIA 4.4

2828146 2017, Validation of method D1608/01: Method for the determination of BAS 450 I (Reg. No. 5672774) and Its metabolites DM-8007 (Reg. No. 5856361), DC-DM-8007 (Reg. No. 5936906), DC-8007 (Reg. No. 5936907) and S(PFP-OH)-8007 (Reg. No. 5959598) in surface and drinking water by LC-MS/MS, DACO: 8.2.2.3,IIA 4.5

2828147 2017, Validation of method D1705/01: Method for the determination of S(Br-OH)-8007 (Reg. No. 5959595) and AB-Oxa (Reg. No. 5959600) and MFBA (Reg. No. 6088668) in surface and drinking water by LC MS/MS, DACO: 8.2.2.3,IIA 4.5

2828148 2017, Evaluation of the limit of detection (LOD) for method D1608/01: Method for the determination of BAS 450 I (Reg. No. 5672774) and its metabolites DM-8007 (Reg. No. 5856361), DC-DM-8007 (Reg. No. 5936906), DC-8007 (Reg. No. 5936907) and S(PFP-OH)-8007 (Reg. No. 5959598) in surface and drinking water by LC-MS/MS, DACO: 8.2.2.3,IIA 4.5

2828149 2017, Independent laboratory validation of method D1608/01: Method for the determination of BAS 450 I (Reg. No. 5672774) and its metabolites DM-8007 (Reg. No. 5856361), DC-DM-8007 (Reg. No. 5936906), DC-8007 (Reg. No. 5936907) and S(PFP-OH)-8007 (Reg. No. 5959598) in surface and drinking water by LC-MS/MS, DACO: 8.2.2.3,IIA 4.5

2828150 2017, Evaluation of the limit of detection (LOD) for method D1705/01, method for the determination of S(Br-OH)-8007 (Reg. No. 5959595), AB-Oxa (Reg. No.5959600), and MFBA (Reg. No. 6088668) in surface and drinking water by LC-MS/MS, DACO: 8.2.2.3,IIA 4.5

2828151 2017, Independent laboratory validation of method for the determination of S(Br-OH)-8007 (Reg. No. 5959595), AB-Oxa (Reg. No. 5959600), and MFBA (Reg. No. 6088668) in surface and drinking water by LC MS/MS (BASF method number D1705/01), DACO: 8.2.2.3,IIA 4.5

2827848 2017, DACO 3.1 - Product Identification, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,IIIA 1.1,IIIA 1.2.1,IIIA 1.3

2827849 2017, DESCRIPTION OF STARTING MATERIALS, DACO: 3.2.1,3.2.2,3.2.3,3.3.1,3.3.2,IIIA 1.4.1,IIIA 1.4.2,IIIA 1.4.3.1,IIIA 1.4.3.2,IIIA 1.4.3.3,IIIA 1.4.4,IIIA 1.4.5.1,IIIA 1.4.5.2 CBI

2827850 2017, Formulation Type of Cimegra, DACO: 3.5.4,IIIA 1.5

2827874 2017, Determination of physical / chemical properties of BAS 450 06 I: Accelerated storage stability and corrosion characteristics, 2 weeks @ 54 C in commercial containers, DACO: 3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.5,3.5.7, 3.5.9,IIIA 2.1,IIIA 2.13,IIIA 2.14,IIIA 2.4.2,IIIA 2.5.1,IIIA 2.5.2,IIIA 2.7.1

2827875 2017, Miscibility of Cimegra, DACO: 3.5.13,IIIA 2.11

2827876 2017, Dielectric Breakdown Voltage - Cimegra, DACO: 3.5.15,IIIA 2.12

2827877 2017, Container Material and Description, DACO: 3.5.5,IIIA 2.14

2827878 2017, Explodability of Cimegra, DACO: 3.5.12,IIIA 2.2.1

2827879 2014, Determination of physico-chemical properties according to Directive 94/37/EC (regulation (EC) No. 440/2008) - BAS 450 00 I, DACO: 3.5.11,3.5.12,IIIA 2.2.1,IIIA 2.3.1,IIIA 2.3.2,IIIA 2.3.3

2827880 2015, BAS 450 00 I, BAS 450 01 I: Determination of oxidation/reduction, DACO: 3.5.8,IIIA 2.2.2

2827881 2017, Physical and chemical properties of BAS 450 00 I: Storage stability and corrosion characteristics in commercial type containers, DACO: 3.5.10,3.5.6,3.7,8.2.2.1,8.2.3.6,IIIA 2.5.3,IIIA 2.6.1,IIIA 2.7.4,IIIA 2.8.2,IIIA 2.8.3.1,IIIA 2.8.3.2,IIIA 2.8.4,IIIA 2.8.5.2,IIIA 2.8.6.1,IIIA 2.8.8.2

2827883 2016, GLP Validation of Analytical Method AFR0108/01: Determination of BAS 450 I in BAS 450 00 I Formulations by GC-FID, DACO: 3.4.1,IIIA 5.2.1

2827884 2017, Method AFR0108/02: Determination of BAS 450 I in Suspension Concentrate (SC) Formulations by GC-FID, DACO: 3.4.1,IIIA 5.2.1

2827926 2017, DACO 3.1 - Product Identification, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,IIIA 1.1,IIIA 1.2.1,IIIA 1.3

2827928 2017, Formulation Type of Teraxxa F4, DACO: 3.5.4,IIIA 1.5

2827932 2017, Physical and chemical properties of BAS 453 UF I: Accelerated storage stability and corrosion characteristics in commercial type containers, DACO: 3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.5,3.5.6,3.5.7,IIIA 2.1,IIIA 2.13,IIIA 2.14,IIIA 2.4.2,IIIA 2.6.1,IIIA 2.7.1

2827933 2017, Miscibility of Teraxxa F4, DACO: 3.5.13,IIIA 2.11

2827934 2017, Dielectric Breakdown Voltage - Teraxxa F4, DACO: 3.5.15,IIIA 2.12

2827935 2017, Container Material and Description, DACO: 3.5.5,IIIA 2.14

2827936 2017, Explodability of Teraxxa F4, DACO: 3.5.12,IIIA 2.2.1

2827937 2016, BAS 453 00 I - Determination of physico-chemical properties according to UN transport regulation and Directive 94/37/EC (Regulation (EC) No. 440/2008), DACO: 3.5.11,3.5.12,IIIA 2.2.1,IIIA 2.3.1,IIIA 2.3.2,IIIA 2.3.3

2827938 2017, BAS 453 00 I: Determination of physical properties and oxidation reduction, DACO: 3.5.8,3.5.9,IIIA 2.2.2,IIIA 2.5.1,IIIA 2.5.2

2827939 2017, Teraxxa F4- Storage Stability Supplemental Information, DACO: 3.5.10,IIIA 2.7.2

2827942 2017, GLP validation of analytical method AFR0117/02: Determination of Fluxapyroxad, Pyraclostrobin, Triticonazole, Metalaxyl, and Broflanilide in FS formulations by HPLC, DACO: 3.4.1,IIIA 5.2.2

2827943 2017, Method AFR0117/02: Determination of Fluxapyroxad, Pyraclostrobin, Triticonazole, Metalaxyl, and Broflanilide in FS formulations by HPLC, DACO: 3.4.1,IIIA 5.2.2

2827880 2015, BAS 450 00 I, BAS 450 01 I: Determination of oxidation/reduction, DACO: 3.5.8,IIIA 2.2.2

2827987 2017, DACO 3.1 - Product Identification, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,IIIA 1.1,IIIA 1.2.1,IIIA 1.3

2827989 2017, Formulation Type of Teraxxa, DACO: 3.5.4,IIIA 1.5

2828000 2017, Determination of physical / chemical properties of BAS 450 07 I: Accelerated storage stability and corrosion characteristics, 2 weeks @ 54C in commercial containers, DACO: 3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.5,3.5.7,3.5.9, IIIA 2.1,IIIA 2.13,IIIA 2.14,IIIA 2.4.2,IIIA 2.5.1,IIIA 2.5.2,IIIA 2.7.1

2828001 2017, Miscibility of Teraxxa, DACO: 3.5.13,IIIA 2.11

2828002 2017, Dielectric Breakdown Voltage - Teraxxa, DACO: 3.5.15,IIIA 2.12
2828003 2017, Container Material and Description, DACO: 3.5.5,IIIA 2.14
2828004 2017, Explodability of Teraxxa, DACO: 3.5.12,IIIA 2.2.1
2828005 2014, BAS 450 01 I - Determination of physico-chemical properties according to Directive 94/37/EC (Regulation (EC) No. 440/2008), DACO: 3.5.11,3.5.12,IIIA 2.2.1,IIIA 2.3.1,IIIA 2.3.2,IIIA 2.3.3
2828007 2017, Physical and chemical properties of BAS 450 01 I: Storage stability and corrosion characteristics in commercial type containers, DACO: 3.5.10,3.5.6,3.7,8.2.2.1,8.2.3.6,IIIA 2.5.3,IIIA 2.6.1,IIIA 2.7.4,IIIA 2.8.2,IIIA 2.8.3.1,IIIA 2.8.3.2,IIIA 2.8.4,IIIA 2.8.5.2,IIIA 2.8.6.1,IIIA 2.8.8.2
2828010 2016, GLP Validation of analytical method AFR0119/01: Determination of BAS 450 I in BAS 450 01 I formulations by GC-FID, DACO: 3.4.1,IIIA 5.2.1
2828011 2017, Method AFR0119/02: Determination of BAS 450 I in flowable concentrate for seed treatment (FS) formulations by GC-FID, DACO: 3.4.1,IIIA 5.2.1

2.0 Human and Animal Health

2827889 2014, BAS 450 00 I - Acute oral toxicity study in rats, DACO: 4.6.1,IIIA 7.1.1
2827890 2014, BAS 450 00 I - Acute dermal toxicity study in rats, DACO: 4.6.2,IIIA 7.1.2
2827891 2014, BAS 450 00 I: 4-hour acute inhalation toxicity study in the rat, DACO: 4.6.3,IIIA 7.1.3
2827892 2014, BAS 450 00 I - Acute dermal irritation / corrosion in rabbits, DACO: 4.6.5,IIIA 7.1.4
2827893 2015, BAS 450 00 I - Acute eye irritation in rabbits (Including amendment no. 1), DACO: 4.6.4,IIIA 7.1.5
2827894 2014, BAS 450 00 I - Test for delayed contact hypersensitivity in the guinea pig using the BUEHLER test, DACO: 4.6.6,IIIA 7.1.6
2827945 2016, BAS 453 00 I - Acute oral toxicity study in rats, DACO: 4.6.1,IIIA 7.1.1
2827946 2016, BAS 453 00 I - Acute dermal toxicity study in rats, DACO: 4.6.2,IIIA 7.1.2
2827947 2016, BAS 453 00 I - Acute inhalation toxicity in rats, DACO: 4.6.3,IIIA 7.1.3
2827948 2017, BAS 453 UD I - Acute dermal irritation / corrosion in rabbits, DACO: 4.6.5,IIIA 7.1.4
2827949 2017, BAS 453 UD I - Acute eye irritation in rabbits, DACO: 4.6.4,IIIA 7.1.5
2827950 2017, BAS 453 UD I - BUEHLER Test in guinea pigs, DACO: 4.6.6,IIIA 7.1.6
2828019 2014, BAS 450 01 I - Acute oral toxicity study in rats, DACO: 4.6.1,IIIA 7.1.1
2828020 2014, BAS 450 01 I - Acute dermal toxicity study in rats, DACO: 4.6.2,IIIA 7.1.2
2828021 2014, BAS 450 01 I: 4-hour acute inhalation toxicity study in the rat, DACO: 4.6.3,IIIA 7.1.3
2828022 2014, BAS 450 01 I - Acute dermal irritation / corrosion in rabbits, DACO: 4.6.5,IIIA 7.1.4
2828023 2015, BAS 450 01 I - Acute eye irritation in rabbits (Including amendment no. 1), DACO: 4.6.4,IIIA 7.1.5
2828024 2014, BAS 450 01 I - Test for delayed contact hypersensitivity in the guinea pig using the BUEHLER test, DACO: 4.6.6,IIIA 7.1.6
2828152 2017, MCI-8007 (BAS 450 I, Broflanilide): Metabolism and pharmacokinetics in rats after single oral and intravenous doses, DACO: 4.5.9,IIA 5.1.1

2828153 2017, MCI-8007 (BAS 450 I, Broflanilide): Biliary excretion in rats, DACO: 4.5.9,IIA 5.1.1

2828154 2017, MCI-8007 (BAS 450 I, Broflanilide): Tissue depletion in rats after single oral doses, DACO: 4.5.9,IIA 5.1.1

2828155 2012, Single dose toxicokinetics of (14C)LS 5672774 after oral administration in male and female wistar rats, DACO: 4.5.9,IIA 5.1.1

2828156 2017, MCI-8007 (BAS 450 I, Broflanilide): Metabolism and pharmacokinetics in rats after repeat oral doses, DACO: 4.5.9,IIA 5.1.3

2828157 2015, MCI-8007 - Immunotoxicity study in male Wistar rats - Administration via the diet for 4 weeks, DACO: 4.2.9,4.3.8,4.4.5,4.5.8,4.8,IIA 5.10

2828158 Various, 2017, Scientific studies cited in support of Broflanilide: Toxicology, DACO: 4.2.9,4.3.8,4.4.5,4.5.8,4.8,IIA 5.10

2828159 2012, MLP-8607 - Acute oral toxicity study in the female rat (up and down method), DACO: 4.2.1,IIA 5.2.1

2828160 2012, MLP-8607 - Acute dermal toxicity study in the rat, DACO: 4.2.2,IIA 5.2.2

2828161 2014, An acute inhalation toxicity study of MCI-8007 in rats, DACO: 4.2.3,IIA 5.2.3

2828162 2012, MLP-8607 - Assessment of skin irritation, DACO: 4.2.5,IIA 5.2.4

2828163 2012, MLP-8607 - Assessment of ocular irritation, DACO: 4.2.4,IIA 5.2.5

2828164 2012, MLP-8607 - Murine local lymph node assay (LLNA), DACO: 4.2.6,IIA 5.2.6

2828165 2012, MLP-8607 - Local lymph node assay in the mouse, DACO: 4.2.6,IIA 5.2.6

2828166 2014, MCI-8007 - Skin Sensitization Preliminary Study in Guinea Pigs - Maximization Test-, DACO: 4.2.6,IIA 5.2.6

2828167 2015, MCI-8007: Skin sensitization study in guinea pigs - Maximization test -, DACO: 4.2.6,IIA 5.2.6

2828168 2010, MLP-8607: Oral (dietary) maximum tolerated dose (MTD) study in the rat, DACO: 4.3.3,IIA 5.3.1

2828169 2014, MCI-8007 - 4 Week Oral (Dietary) Administration Range-finding Study in the Mouse, DACO: 4.3.3,IIA 5.3.1

2828170 2014, MLP-8607 - Oral (Dietary) Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test in the Rat, DACO: 4.3.3,IIA 5.3.1

2828171 2013, Summary report: Range-finding study in beagle dogs - Oral administration (capsule), DACO: 4.3.3,IIA 5.3.1

2828172 2015, MCI-8007 - Repeated-dose 28-day oral toxicity study in Beagle dogs Oral administration (capsule), DACO: 4.3.3,IIA 5.3.1

2828173 2016, MCI-8007: 13 Week Toxicity Study in the Mouse for Dose Range Finding, DACO: 4.3.1,IIA 5.3.2

2828174 2017, MCI-8007 - Repeated-dose 90-day toxicity study in Wistar rats including a recovery period of 4 weeks - Administration via the diet, DACO: 4.3.1,IIA 5.3.2

2828175 2015, Summary report: Repeated dose 90-day oral toxicity study in Wistar rats - Administration via the diet, DACO: 4.3.1,IIA 5.3.2

2828176 2010, MLP-8607: Development/validation of an analytical method and the determination of homogeneity and stability in dietary formulations, DACO: 4.3.1,IIA 5.3.2

2828177 2016, Validation of an Analytical Procedure for the Determination of MCI-8007 and DM-8007 in Mouse Plasma using Protein Precipitation followed by Liquid Chromatography with Tandem Mass Spectrometric Detection (LC-MS/MS), DACO: 4.3.1,IIA 5.3.2

2828178 2015, Determination of MCI-8007 (Reg. No. 5672774) and its metabolite DM-8007 (Reg. No. 5856361) in rat plasma sampled during the course of Project No. 50C0219/10S117, DACO: 4.3.1,IIA 5.3.2

2828179 2017, BAS 450 I (Reg.No. 5672774, MCI-8007) - Validation of an analytical method for the analysis of BAS 450 I (Reg.No. 5672774, MCI-8007) in ground Kliba maintenance diet mouse/rat GLP meal using HPLC-MS (control procedure: 10/0219_05), DACO: 4.3.1,IIA 5.3.2

2828180 2017, MCI-8007: Validation of an analytical method and determination of homogeneity in dietary formulations, DACO: 4.3.1,IIA 5.3.2

2828181 2017, BAS 450 I (Reg.No. 5672774, MCI-8007) - Validation of an analytical method for the analysis of BAS 450 I (Reg.No. 5672774, MCI-8007) in Ground Kliba maintenance diet mouse/rat GLP meal using HPLC-UV (control procedure 10/0219_03), DACO: 4.3.1,IIA 5.3.2

2828182 2016, MCI-8007 - Repeated-dose 90-day oral toxicity study in Beagle dogs Oral administration (capsule), DACO: 4.3.2,IIA 5.3.3

2828183 2017, MCI-8007 - Repeated-dose 12-months toxicity study in Beagle dogs Oral administration (capsule), DACO: 4.3.2,IIA 5.3.4

2828184 2015, Summary report: Range-finding study for a subchronic inhalation study, 5-day exposure wistar rats, dust exposure, DACO: 4.3.7,IIA 5.3.5

2828185 2017, MCI-8007 - Repeated dose 28-day inhalation toxicity study Wistar rats with recovery period; dust exposure, DACO: 4.3.7,IIA 5.3.5

2828186 2015, MCI-8007 - Repeated dose 28-day dermal toxicity study in Wistar rats, DACO: 4.3.5,IIA 5.3.7

2828187 2011, LS 5672774 - Salmonella typhimurium / Eschericia coli - Reverse mutation assay, DACO: 4.5.4,IIA 5.4.1

2828188 2010, Chromosome aberration test with MLP-8607 in cultured mammalian cells, DACO: 4.5.6,IIA 5.4.2

2828189 2014, MCI-8007 - In vitro gene mutation test in CHO cells (HPRT locus assay), DACO: 4.5.5,IIA 5.4.3

2828190 2013, MLP-8607 - Micronucleus test in bone marrow cells of the mouse, DACO: 4.5.7,IIA 5.4.4

2828191 2017, 14C-MCI-8007 - Study on kinetics in mice, DACO: 4.5.7,IIA 5.4.4

2828192 2017, Validation of an analytical method for the analysis of BAS 450 I (Reg.No. 5672774, MCI-8007) in a mixture of dimethyl sulfoxide and corn oil (2+3; V/V) using HPLC-UV (control procedure 10/0219_01) (Including amendment no. 1), DACO: 4.3.1,4.5.7,IIA 5.3.2,IIA 5.4.4

2828193 2017, MCI-8007 - Combined chronic toxicity/carcinogenicity study in Wistar rats - Administration via the diet up to 24 months, DACO: 4.4.1,4.4.2,4.4.4,IIA 5.5.1,IIA 5.5.2

2828194 2016, MCI-8007 - 78 week oral (dietary) administration carcinogenicity study in the mouse, DACO: 4.4.3,IIA 5.5.3

2828195 2017, MCI-8007: 90-day investigative toxicity study in wistar rats by dietary administration, DACO: 4.8,IIA 5.5.4

2828196 2017, Development and validation of an analytical method for the analysis of MCI-8007 in diet including diet analysis, DACO: 4.8,IIA 5.5.4

2828199 2017, An immunohistochemistry study to detect luteinizing hormone expression in the pituitary gland of rats from Charles River laboratories, DACO: 4.8,IIA 5.5.4

2828200 2017, Carcinogenic potential of Broflanilide based on genotoxicity, chronic term, life stages exposure, and dietary admixture investigative studies, DACO: 4.8,IIA 5.5.4

2828201 2017, MCI-8007 - Two-generation reproduction toxicity study in wistar rats - Administration via the diet, DACO: 4.5.1,IIA 5.6.1

2828202 2016, MCI-8007 - Prenatal developmental toxicity study in Wistar rats - Oral administration (gavage), DACO: 4.5.2,IIA 5.6.10

2828203 2017, BAS 450 I - Validation of an analytical method for the analysis of BAS 450 I (Reg.No. 5672774. MCI-8007) in 1.0% (w/v) Carboxymethylcellulose in drinking water using HPLC-UV (control procedure 10/0219_04), DACO: 4.5.2,IIA 5.6.10

2828204 2011, Summary report - LS 5672774, * - Test study in female, non-pregnant Wistar rats - Oral administration (gavage), DACO: 4.5.2,IIA 5.6.10

2828205 2011, Summary report - LS 5672774, * - Test study in female, non-pregnant Wistar rats - Oral administration (gavage), DACO: 4.5.2,IIA 5.6.10 CBI

2828206 2011, Summary report - LS 5672774, * - Maternal toxicity study in Wistar rats (range-finding) - Oral administration (gavage), DACO: 4.5.2,IIA 5.6.10

2828208 2011, Summary report - LS 5672774, * - Maternal toxicity study in Wistar rats (range-finding) - Oral administration (gavage), DACO: 4.5.2,IIA 5.6.10 CBI

2828210 2016, MCI-8007 - Prenatal Developmental Toxicity Study in New Zealand White Rabbits - Oral Administration (Gavage), DACO: 4.5.3,IIA 5.6.11

2828211 2016, MLP-8607 - Test study in female, non-pregnant New Zealand white rabbits - Oral administration (gavage), DACO: 4.5.3,IIA 5.6.11

2828212 2016, MLP-8607 - Maternal toxicity study in New Zealand white rabbits (range-finding) - Oral administration (gavage), DACO: 4.5.3,IIA 5.6.11

2828213 2017, Summary of results: MCI-8007: Peak-finding study in Wistar rats, single administration by gavage and 3-days observation period afterwards, DACO: 4.5.12,IIA 5.7.1

2828214 2017, MCI-8007 - Acute oral neurotoxicity study in Wistar rats - Administration gavage, DACO: 4.5.12,IIA 5.7.1

2828215 2015, MCI-8007 - Repeated Dose 90-day Oral Neurotoxicity Study in Wistar Rats Administration via the Diet, DACO: 4.5.13,IIA 5.7.4

2828216 2015, Acute oral dose toxicity study of DM-8007 in Wistar rats - (Up-and-down procedure), DACO: 4.8,IIA 5.8

2828219 2015, Bacterial reverse mutation test of DM-8007, DACO: 4.8,IIA 5.8

2828220 2016, DM-8007 - Test study in Wistar rats - Administration via the diet for at least 14 days, DACO: 4.8,IIA 5.8

2828221 2017, DM-8007 - Repeated-dose 28 day toxicity study in Wistar rats - Administration via the diet, DACO: 4.8,IIA 5.8

2828222 2017, DM-8007 - Repeated-dose 90-day toxicity study in Wistar rats - Administration via the diet, DACO: 4.8,IIA 5.8

2828223 2015, Acute oral dose toxicity study of DC-DM-8007 in wistar rats (up-and-down procedure), DACO: 4.8,IIA 5.8

2828224 2015, Bacterial reverse mutation test of - DC-DM-8007, DACO: 4.8,IIA 5.8

2828225 2016, DC-DM-8007 - Test study in Wistar rats - Administration via the diet for at least 14 days, DACO: 4.8,IIA 5.8

2828226 2017, Summary of results: DC-DM-8007: Test study in wistar rats administration via the diet for at least 14 days, DACO: 4.8,IIA 5.8

2828229 2017, DC-DM-8007 - Repeated-dose 28-day toxicity study in Wistar rats - Administration via the diet, DACO: 4.8,IIA 5.8

2828230 2017, DC-DM-8007 - Repeated-dose 90-day toxicity study in Wistar rats - Administration via the diet, DACO: 4.8,IIA 5.8

2828231 2015, Acute oral dose toxicity study of S(PFP-OH)-8007 in Wistar rats - (Up-and-down procedure), DACO: 4.8,IIA 5.8

2828232 2015, Bacterial reverse mutation test of S(PFP-OH)-8007, DACO: 4.8,IIA 5.8

2828233 2016, S(PFP-OH)-8007 - Test study in Wistar rats - Administration via the diet for at least 14 days, DACO: 4.8,IIA 5.8

2828234 2017, S(PFP-OH)-8007 - Repeated-dose 28-day toxicity study in wistar rats - Administration via the diet, DACO: 4.8,IIA 5.8

2828236 2017, S(PFP-OH)-8007 - Repeated-dose 90-day toxicity study in wistar rats - Administration via the diet, DACO: 4.8,IIA 5.8

2828238 2017, Acute oral dose toxicity study of DC-8007 in Wistar rats (up-and-down procedure), DACO: 4.8,IIA 5.8

2828239 2017, Bacterial reverse mutation test of DC-8007, DACO: 4.8,IIA 5.8

2828240 2016, Acute oral dose toxicity study of MFBA in Wistar rats (up-and-down procedure), DACO: 4.8,IIA 5.8

2828241 2016, Bacterial reverse mutation test of MFBA, DACO: 4.8,IIA 5.8

2828242 2017, Chromosomal aberration study of MFBA in cultured mammalian cells, DACO: 4.8,IIA 5.8

2828243 2017, Bone marrow micronucleus assay of MFBA in rats, DACO: 4.8,IIA 5.8

2828244 2017, Reg.No. 5959600 (metabolite of BAS 450 I) = AB-oxa - Acute oral toxicity study in rats, DACO: 4.8,IIA 5.8

2828247 2017, Reg.No. 5959600 (metabolite of BAS 450 I) = AB-oxa - Salmonella typhimurium / Eschericia coli - Reverse mutation assay, DACO: 4.8,IIA 5.8

2828248 2017, Reg.No. 5959595 (metabolite of BAS 450 I) = S(Br-OH)-8007 - Acute oral toxicity study in rats (Including amendment no. 1), DACO: 4.8,IIA 5.8

2828249 2017, Reg.No. 5959595 (metabolite of BAS 450 I) = S(Br-OH)-8007 - Salmonella typhimurium / Escherichia coli - Reverse mutation assay, DACO: 4.8,IIA 5.8

2828250 2017, A 28-day repeated dose oral toxicity study of MFBA in rats, DACO: 4.8,IIA 5.8

2828251 2017, DM-8007- Validation of an analytical method for the analysis of DM-8007 in Ground Kliba maintenance diet mouse/rat GLP meal using HPLC-UV (control procedure 13/0292_01), DACO: 4.8,IIA 5.8

2828252 2017, DC-DM-8007 - Validation of an analytical method for the analysis fo DC-DM-8007 in Ground Kliba maintenance diet mouse/rat GLP meal using HPLC-UV (control procedure 15/0426_01), DACO: 4.8,IIA 5.8

2828253 2017, S(PFP-OH)-8007 - Validation of an analytical method for the analysis of S(PFP-OH)-8007 in Ground Kliba maintenance diet mouse/rat GLP meal using HPLC (control procedure 15/0427_01), DACO: 4.8,IIA 5.8

2923483 2016, Analytical report - DC-DM-8007 - Stability analysis in ground kliba maintenance diet mouse/rat GLP meal, DACO: 4.8,IIA 5.8

2923484 2018, DC-DM-8007 - Repeated-dose 28-day toxicity study in Wistar rats - Administration via the diet, DACO: 4.8,IIA 5.8

2828136 2017, Validation BASF Method Number D1417/01 for determination of residues of BAS 450 I and its metabolites S(PFP-OH)-8007 and DM-8007 in wheat grain, dry beans seed, tomato fruit, citrus fruit, soybean seed and coffee grain using LC-MS/MS (Including Amendment No. 1), DACO: 7.2.1,7.2.4,IIA 4.3

2828137 2017, Validation of method D1703/01: Analytical method for the determination of Broflanilide (BAS 450 I) metabolites Reg. No. 6066332 and 6065386 at LOQ of 0.01 mg/kg in plant matrices by LC-MS/MS, DACO: 7.2.1,7.2.4,IIA 4.3

2828138 2017, Validation of BASF method D1713/01: Multi-residue method using modified AOAC official method 2007.01 for the determination of residues of BAS 450 I (Reg. No. 5672774) and its metabolites S(PFP-OH)-8007 (Reg.No. 5959598) and DM-8007 (Reg.No. 5856361) in plant matrices using LC-MS/MS, DACO: 7.2.1,7.2.4,IIA 4.3

2828139 2017, Independent laboratory validation of BASF analytical method D1417/01 titled: Analytical method for the determination of BAS 450 I (Reg. No. 5672774) and metabolites (Reg. No. 5959598 and 5856361) in plant matrices by LC-MS/MS, DACO: 7.2.1,7.2.4,IIA 4.3

2828140 2017, Validation of BASF Analytical Method D1604/01:Analytical Method for the Determination of BAS 450 I (Reg. No. 5672774), DM-8007 (Reg. No. 5856361) and DC-DM-8007 (Reg. No. 5936906) in Animal Matrices by LC-MS/MS, DACO: 7.2.1,7.2.4,IIA 4.3

2828141 2017, Independent laboratory validation of BASF analytical method D1604/01: Analytical method for the determination of BAS 450 I (Reg. No. 5672774), DM-8007 (Reg. No. 5856361) and DC-DM-8007 (Reg. No. 5936906) in animal matrices by LC-MS/MS, DACO: 7.2.1,7.2.4,IIA 4.3

2828142 2017, Validation of BASF analytical method D1710/01: Multi-residue method using modified AOAC official method 2007.01 for determination of residues of BAS 450 I (Reg. No. 5672774), DM-8007 (Reg. No. 5856361) and DC-DM-8007 (Reg. No. 5936906) in animal matrices by LC-MS/MS, DACO: 7.2.1,7.2.4,IIA 4.3

2828254 2017, Freezer Storage Stability of BAS 450 I (Reg. No. 5672774) and Metabolites S(PFPOH)- 8007 (Reg. No. 5959598) and DM-8007 (Reg. No. 5856361) in Plant Matrices, DACO: 7.3,IIA 6.1.1

2828255 2017, Freezer Storage Stability of BAS 450 I (Reg. No. 5672774) and Metabolites S(PFP-OH)-8007 (Reg. No. 5959598), DM-8007 (Reg. No. 5856361), B-oxam-acid (Reg. No. 6066332) and B-urea (Reg. No. 6065386) in Selected Plant and Bee Matrices, DACO: 7.3,IIA 6.1.1

2828257 2017, A metabolism study with [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I (2 radiolabels) in tomato (Lycopersicon esculentum), DACO: 6.3,IIA 6.2.1

2828258 2017, A metabolism study with [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I (2 radiolabels) in cabbage (Brassica oleracea), DACO: 6.3,IIA 6.2.1

2828259 2017, A metabolism study with [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I (2 radiolabels) in soybean (Glycine max), DACO: 6.3,IIA 6.2.1

2828260 2017, A metabolism study with [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I (2 radiolabels) in tea (Camelia sinensis), DACO: 6.3,IIA 6.2.1

2828261 2017, [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I: Metabolism in Japanese radish, DACO: 6.3,IIA 6.2.1

2828262 2017, Metabolism of 14C-BAS 450 I in wheat after seed treatment, DACO: 6.3,IIA 6.2.1

2828263 2017, [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I: Metabolism in rice, DACO: 6.3,IIA 6.2.1

2828264 2017, A metabolism study with [14C]Broflanilide also known as [14C]MCI-8007 and [14C]BAS 450 I (2 radiolabels) in laying hens, DACO: 6.2,IIA 6.2.2

2828265 2017, A metabolism study with [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I (2 radiolabels) in the lactating goat, DACO: 6.2,IIA 6.2.3

2828266 2017, Magnitude of the residue of Broflanilide, (BAS 450 I) in potatoes following foliar or in-furrow applications of BAS 450 00 I, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

2828267 2017, Magnitude of the residues of Broflanilide in or on field corn and sweet corn raw agricultural commodities following one in-furrow application of BAS 450 00 I, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.2

2828268 2017, Magnitude of the residues of Broflanilide in or on wheat raw agricultural commodities following seed treatment with BAS 450 01 I, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.3

2828269 2017, Magnitude of the residues of BAS 450I in barley following seed treatment with BAS 450 01 I, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.3

2828270 2017, Magnitude of the residues in eggs and tissues of laying hens following oral administration of BAS 450 I, DACO: 7.5,7.6,IIA 6.4.1

2828271 2017, A meat and milk magnitude of the residue study with BAS 450 I in lactating dairy cows, DACO: 7.5,7.6,IIA 6.4.2

2828274 2017, Magnitude and concentration of the residue of Broflanilide, (BAS 450 I) in potato processed commodities following in-furrow and foliar applications of BAS 450 00 I, DACO: 7.4.5,IIA 6.5.3

2828275 2017, Magnitude of the Residues of BAS 450 I in Wheat Processed Fractions Following Applications of BAS 450 00 I, DACO: 7.4.5,IIA 6.5.3

2828276 2017, Magnitude of the Residues of BAS 450 I in Corn Processed Fractions Following Applications of BAS 450 00 I, DACO: 7.4.5,IIA 6.5.3

2828277 2017, A Metabolism Study with [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I, (2 Radiolabels) in Rotational Crops, DACO: 7.4.4,IIA 6.6.2

2828278 2017, Magnitude of residues of BAS 450 I in field rotational crops following applications of BAS 450 00I (including analysis through the targeted 90-day plantback interval), DACO: 7.4.4,IIA 6.6.3

3004631 2019, Freezer Storage Stability of BAS 450 I (Reg. No. 5672774) and Metabolites S(PFPOH)- 8007 (Reg. No. 5959598) and DM-8007 (Reg. No. 5856361) in Plant Matrices, DACO: 7.3
3004632 2019, Freezer Storage Stability of BAS 450 I (Reg. No. 5672774) and Metabolites S(PFPOH)- 8007 (Reg. No. 5959598), DM-8007 (Reg. No. 5856361), B-oxam-acid (Reg. No. 6066332) and B-urea (Reg. No. 6065386) in Selected Plant and Bee Matrices, DACO: 7.3
3004633 2019, Magnitude of Residues of BAS 450 I in Field Rotational Crops Following Applications of BAS 450 00 I, DACO: 7.4.4
2827896 2016, 14C-MCI-8007 in BAS 450 00 I - Study of the dermal penetration in rats, DACO: 5.8,IIIA 7.6.1
2828009 2017, Use Site Description for Teraxxa and Teraxxa F4, DACO: 10.2.2,5.2,IIIA 3.3.1

3.0 Environment

2828123 2016, Hydrolysis of [14C]MCI-8007 at pH 4, 7 and 9, DACO: 8.2.3.2,IIA 2.9.1,IIA 7.5
2828126 2017, Direct aqueous photodegradation of [14C]MCI-8007 (also known as [14C]Broflanilide or [14C]BAS 450 I), DACO: 8.2.3.3.2,IIA 2.9.2,IIA 7.6
2828128 2017, Direct aqueous photodegradation of [14C]Broflanilide (also known as MCI-8007 and BAS 450 I) in pH 5 and pH 9 buffer, DACO: 8.2.3.3.2,IIA 2.9.2,IIA 7.6
2828280 2017, Aerobic soil metabolism of 14C-Broflanilide (MCI-8007 or BAS 450 I), DACO: 8.2.3.4.2,IIA 7.1.1,IIA 7.2.1
2828282 2017, Anaerobic soil metabolism of 14C-Broflanilide (MCI-8007 or BAS 450 I), DACO: 8.2.3.4.4,IIA 7.1.2,IIA 7.2.4
2828284 2017, Photodegradation of [14C] Broflanilide, also known as [14C] MCI-8007 and [14C] BAS 450 I in/on soil by artificial sunlight, DACO: 8.2.3.3.1,IIA 7.1.3
2828286 2017, Atmospheric degradation of Broflanilide (BAS 450 I or MCI-8007) by reaction with hydroxyl radicals and ozone: Structure-activity relationship calculations using AOPWIN v1.92, DACO: 8.2.3.3.3,IIA 7.10
2828290 2017, Aerobic soil metabolism of 14C-Broflanilide (MCI-8007 or BAS 450 I) in intact soil cores and processed soils, DACO: 8.2.3.4.2,IIA 7.2.1
2828292 2017, Terrestrial field dissipation of the insecticide Broflanilide (BAS 450 I or MCI-8007) following broadcast applications of BAS 450 00 I (SC), DACO: 8.3.2,IIA 7.3.1
2828295 2017, Outdoor aerobic soil metabolism of 14C-BAS 450 I on bare soil in California and Georgia, USA, DACO: 8.3.2,IIA 7.3.2
2828297 2017, Soil adsorption/desorption of [14C]MCI-8007 (also known as [14C]Broflanilide or [14C]BAS 450 I) by the batch equilibrium method, DACO: 8.2.4.2,IIA 7.4.1
2828299 2017, Soil adsorption coefficient of DM-8007, DACO: 8.2.4.2,IIA 7.4.2
2828300 2017, Soil adsorption coefficient of S(PFP-OH)-8007, DACO: 8.2.4.2,IIA 7.4.2
2828301 2017, Adsorption/desorption of [14C]DC-DM-8007 in US soils, DACO: 8.2.4.2,IIA 7.4.2
2828302 2017, Adsorption/desorption of [14C]DC-8007 in US soils, DACO: 8.2.4.2,IIA 7.4.2

2828303 2017, Aerobic aquatic metabolism of [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I, in two test systems, DACO: 8.2.3.5.2,8.2.3.5.4,IIA 7.8.1

2828305 2017, Anaerobic aquatic metabolism of [14C]Broflanilide, also known as [14C]MCI-8007 and [14C]BAS 450 I, DACO: 8.2.3.5.5,8.2.3.5.6,IIA 7.8.2

2828307 2016, Northern bobwhite (Colinus virginianus) acute oral toxicity test (LD50) with BAS 450 I, DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1

2828309 2015, BAS 450 I (Reg.No. 5672774, MCI-8007) - Acute toxicity in the mallard duck (Anas platyrhynchos) after single oral administration (LD50), DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1

2828311 2015, BAS 450 I (Reg.No. 5672774, MCI-8007) - Acute toxicity in the canary (Serinus canaria) after single oral administration (LD50), DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1

2828314 2017, BAS 450 I (MCI-8007): A dietary LC50 study with the mallard, DACO: 9.6.2.4,9.6.2.5,IIA 8.1.2

2828317 2017, BAS 450 I (MCI-8007): A dietary LC50 study with the northern bobwhite, DACO: 9.6.2.4,9.6.2.5,IIA 8.1.2

2828319 2017, BAS 450 I (MCI-8007): A reproduction study with the mallard, DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4

2828323 2017, BAS 450 I (MCI-8007): A reproduction study with the mallard, DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4

2828321 2016, BAS 450 I (MCI-8007): A reproduction study with the northern bobwhite, DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4

2828330 2016, BAS 450 I: A 96-hour toxicity test with the marine diatom (Skeletonema costatum), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

2828332 2016, BAS 450 I: A 96-hour flow-through acute toxicity test with the saltwater mysid (Americamysis bahia), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

2828334 2017, BAS 450 I - Acute toxicity test with eastern oyster (Crassostrea virginica) under flow-through conditions, DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

2828336 2017, BAS 450 I: A flow-through life-cycle toxicity test with the saltwater mysid (Americamysis bahia), DACO: 9.4.3,9.4.4,9.4.5,IIA 8.11.1

2828338 2016, BAS 450 I: A 96-hour flow-through acute toxicity test with the sheepshead minnow (Cyprinodon variegatus), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

2828340 2017, BAS 450 I Metabolite (S (Br-OH)-8007): A 96-Hour Flow-Through Acute Toxicity: Test With The Saltwater Mysid (Americamysis bahia), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

2828342 2017, BAS 450 I Metabolite (AB-oxa): A 96-Hour Flow-Through Acute Toxicity Test With The Saltwater Mysid (Americamysis bahia), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

2828344 2017, BAS 450 I metabolite (MFBA): A 96-hour flow-through acute toxicity test with the saltwater mysid (Americamysis bahia), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

2828347 2016, MCI-8007 technical (Broflanilide): A 96-hour static-renewal acute toxicity test with the rainbow trout (Oncorhynchus mykiss), DACO: 9.5.2.1,9.5.2.3,IIA 8.2.1.1

2828349 2016, MCI-8007 technical (Broflanilide): A 96-hour static-renewal acute toxicity test with the bluegill (Lepomis macrochirus), DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2

2828351 2016, BAS 450 I: A 96-hour flow-through acute toxicity test with the fathead minnow (Pimephales promelas), DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2

2828353 2017, MCI-8007 technical (Broflanilide): A 96-hour static-renewal acute toxicity test with the common carp (Cyprinus carpio), DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2

2828355 2017, BAS 450 I: An early life-stage toxicity test with the fathead minnow (Pimephales promelas), DACO: 9.5.3.1,IIA 8.2.4

2828357 2017, BAS 450 I: An early life-stage toxicity test with the sheepshead minnow (Cyprinodon variegatus), DACO: 9.4.3,9.4.4,9.5.3.1,IIA 8.11.1,IIA 8.2.4

2828359 2012, A flow-through bioconcentration screening test with the rainbow trout (Oncorhynchus mykiss) using 14C-MLP-9595 and 14C-MLP-8607, DACO: 9.5.6,IIA 8.2.6.1

2828362 2017, MCl-8007 (BAS 450 I, Broflanilide): Bioconcentration study in the rainbow trout (Oncorhynchus mykiss), DACO: 6.4,9.5.6,IIA 6.2.5,IIA 8.2.6.1

2828364 2016, MCI-8007 (BAS 450 I): A 48-hour static-renewal acute toxicity test with the Cladoceran (Daphnia magna), DACO: 9.3.2,IIA 8.3.1.1

2828366 2016, Acute immobilization test of MFBA with Daphnia magna, DACO: 9.3.2,IIA 8.3.1.1

2828368 2017, Chronic toxicity of BAS 450 I (MCI-8007) to Daphnia magna STRAUS in a 21 days semi-static test, DACO: 9.3.3,IIA 8.3.2.1

2828370 2016, Reproduction test of MFBA with Daphnia magna, DACO: 9.3.3,IIA 8.3.2.1

2828372 2017, MCI-8007 (Broflanilide): A 72-hour toxicity test with the freshwater alga (Pseudokirchneriella subcapitata), DACO: 9.8.2,9.8.3,IIA 8.4

2828374 2017, MCI-8007 (Broflanilide): A 96-hour toxicity test with the freshwater alga (Raphidocelis subcapitata), DACO: 9.8.2,9.8.3,IIA 8.4

2828376 2016, BAS 450 I: A 96-hour toxicity test with the Cyanobacteria (Anabaena flos-aquae), DACO: 9.8.2,9.8.3,IIA 8.4

2828378 2016, BAS 450 I: A 96-hour toxicity test with the freshwater diatom (Navicula pelliculosa), DACO: 9.8.2,9.8.3,IIA 8.4

2828380 2016, Growth inhibition test of MFBA with green algae (Pseudokirchneriella subcapitata), DACO: 9.8.2,9.8.3,IIA 8.4

2828382 2016, BAS 450 I - 10-day toxicity test exposing midge (Chironomus dilutus) to a test substance applied to sediment under static-renewal conditions, DACO: 9.9,IIA 8.5.1

2828384 2016, BAS 450 I - 10-day toxicity test exposing freshwater amphipods (Hyalella azteca) to a test substance applied to sediment under static-renewal conditions, DACO: 9.9,IIA 8.5.1

2828386 2016, BAS 450 I - 10-day toxicity test exposing estuarine amphipods (Leptocheirus plumulosus) to a test substance applied to sediment under static conditions, DACO: 9.9,IIA 8.5.1

2828388 2017, DC-8007 - 10-day toxicity test exposing midge (Chironomus dilutus) to a test substance applied to sediment under static-renewal conditions, DACO: 9.9,IIA 8.5.1

2828390 2017, Life-cycle toxicity test exposing midges (Chironomus dilutus) to BAS 450 I applied to sediment under static-renewal conditions following EPA test methods, DACO: 9.9,IIA 8.5.2

2828392 2017, BAS 450 I - 42-day toxicity test exposing freshwater amphipods (Hyalella azteca) to a test substance applied to sediment under static-renewal conditions following EPA test methods, DACO: 9.9,IIA 8.5.2

2828394 2017, BAS 450 I - 28-day toxicity test exposing estuarine amphipods (Leptocheirus plumulosus) to a test substance applied to sediment under static-renewal conditions following EPA test methods, DACO: 9.9,IIA 8.5.2

2828396 2016, BAS 450 I: A 7-day static-renewal toxicity test with Duckweed (lemna gibba G3), DACO: 9.8.5,IIA 8.6

2828398 2017, Determination of residues of BAS 450 00 I in pollen of corn after one in-furrow soil application in a field residue study in Germany 2016, DACO: 9.2.4.2,IIA 8.7.1

2828400 2017, Determination of residues in pollen and nectar of oilseed rape grown as a succeeding crop in a corn field previously treated once with BAS 450 00 I as a soil in-furrow application, DACO: 9.2.4.2,IIA 8.7.1

2828406 2017, Determination of residues of BAS 450 I in leaves and flowers of canola (Brassica napus) after seed treatment use under greenhouse conditions (NON-GLP), DACO: 9.2.4.2,IIA 8.7.1

2828408 2015, Acute toxicity of MCI-8007 (BAS 450 I) to the honeybee Apis mellifera L. under laboratory conditions, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2

2828411 2015, Acute toxicity of BAS 450 I (MCI-8007) to the bumblebee Bombus terrestris L. under laboratory conditions, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2

2828414 2016, Reg.No. 5856361 (metabolite of BAS 450 I): Effects (acute contact and oral) on honey bees (Apis mellifera L.) in the laboratory, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2

2828417 2016, Reg.No. 5959598 (metabolite of BAS 450 I): Effects (acute contact and oral) on honey bees (Apis mellifera L.) in the laborator?, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2

2828420 2017, Acute toxicity of Reg. No. 5936907 (metabolite of BAS 450 I) to the honeybee Apis mellifera L. under laboratory conditions (Including amendment no. 1), DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2

2828423 2017, Acute toxicity of Reg. No. 6065386 (metabolite of BAS 450 I) to the honeybee Apis mellifera L. under laboratory conditions, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2

2828426 2017, BAS 450 I (DC-DM-8007 Reg No. 5936906) - Apis mellifera acute laboratory, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2

2828429 2017, Reg.No. 6066332 (metabolite of BAS 450 I) - Acute oral and contact toxicity to the honey bee, Apis mellifera L. under laboratory conditions, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2

2828432 2015, Chronic toxicity of BAS 450 I (MCI-8007) to the honeybee (Apis mellifera L.) under laboratory condition, DACO: 9.2.4.1,IIA 8.7.3

2828434 2015, BAS 450 00 I (a.i. reg. no. 5672774): Toxicity of residues on foliage to the Honey bee, Apis mellifera, DACO: 9.2.4.1,IIA 8.7.3

2828436 2016, Acute toxicity of BAS 450 I (MCI 8007) to honeybee larvae Apis mellifera L. under laboratory conditions (in vitro), DACO: 9.2.4.3,IIA 8.7.4

2828438 2017, Repeated exposure of BAS 450 I (MCI-8007) to honey bee (Apis mellifera) larvae under laboratory conditions (in vitro), DACO: 9.2.4.3,IIA 8.7.4

2828440 2015, Acute toxicity of BAS 450 I (MCI-8007) to the earthworm Eisenia fetida in artificial soil with 10% peat, DACO: 9.2.3.1,IIA 8.9.1

2828442 2016, Reg.No. 5936907 (metabolite of BAS 450 I, DC-8007): Acute toxicity to the earthworm Eisenia fetida (Annelida, Lumbricidae) in artificial soil with 10% peat, DACO: 9.2.3.1,IIA 8.9.1

2828444 2017, Reg. No. 5936906 (Metabolite of BAS 450 I; DC-DM-8007): Acute toxicity to the earthworm Eisenia fetida (Annelida, Lumbricidae) in artificial soil with 10 % peat, DACO: 9.2.3.1,IIA 8.9.1

2828447 2017, Sublethal toxicity of BAS 450 I (MCI-8007) to the earthworm Eisenia fetida in artificial soil, DACO: 9.2.3.1,IIA 8.9.2

2827852 2016, Acute toxicity of BAS 450 00 I to the bumblebee Bombus terrestris L. under laboratory conditions, DACO: 9.2.8,IIIA 10.4.2.1,IIIA 10.4.2.2

2827855 2017, Acute toxicity of BAS 450 00 I to the honeybee - Apis mellifera L. under laboratory conditions, DACO: 9.2.8,IIIA 10.4.2.1,IIIA 10.4.2.2

2827856 2015, A rate-response laboratory test to determine the effects of BAS 450 00 I on the predatory mite Typhlodromus pyri (Acari: Phytoseiidae), DACO: 9.2.8,IIIA 10.5.1

2827858 2015, A rate-response laboratory test to determine the effects of BAS 450 00 I on the parasitic wasp Aphidius rhopalosiphi (Hymenoptera, Braconidae), DACO: 9.2.8,IIIA 10.5.1

2827860 2016, Effects of BAS 450 00 I on the predatory mite Typhlodromus pyri (Acari: Phytoseiidae) in an extended laboratory trial - dose response design, DACO: 9.2.8,IIIA 10.5.2

2827862 2016, Effects of BAS 450 00 I on the parasitic wasp Aphidius rhopalosiphi (DeStephani-Perez) (Hymenoptera: Braconidae) in an extended laboratory trial - Dose response design, DACO: 9.2.8,IIIA 10.5.2

2827864 2015, Acute toxicity of BAS 450 00 I to the earthworm Eisenia fetida in artificial soil with 10% peat, DACO: 9.2.8,IIIA 10.6.2

2827870 2016, BAS 450 00 I: A toxicity test to determine the effects on vegetative vigor of ten species of plants, DACO: 9.8.6,IIIA 10.8.1.2

2827872 2017, BAS 450 00 I: A toxicity test to determine the effects on seedling emergence and seedling growth of ten species of plants, DACO: 9.8.6,IIIA 10.8.1.3

2827991 2017, Assessment of dust and abrasion particles from BROFLANILIDE-treated seeds, DACO: 9.2.4.9

2827992 2016, Acute toxicity of BAS 450 01 I to the honeybee Apis mellifera L. under laboratory conditions, DACO: 9.2.8,IIIA 10.4.2.1,IIIA 10.4.2.2

2827994 2016, BAS 450 01 I, Acute Toxicity to the Earthworm Eisenia fetida (Annelida, Lumbricidae), in Artificial Soil with 10 % Peat, DACO: 9.2.8,IIIA 10.6.2

2827996 2016, Sublethal effects of BAS 450 01 I on the earthworm Eisenia andrei in artificial soil, DACO: 9.2.8,IIIA 10.6.3

2827998 2017, Potential effects of BAS 450 01 I on the reproduction of the soil mite Hypoaspis aculeifer in artificial soil with 5% peat, DACO: 9.2.8,IIIA 10.6.6

3027824 2019, Broflanilide Metabolite DC-8007: A 96-Hour Toxicity Test with the Freshwater Alga (Raphidocelis subcapitata), DACO: 9.8.2,9.8.3,IIA 8.4

3050587 2019, Amended final report: BAS 450 I metabolite (MFBA): A 96-hour flowthrough acute toxicity test with the saltwater mysid (Americamysis bahia), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

4.0 Value

2827851 2017, BAS 450 06 I - Minor change reasoning, DACO: 10.6,3.7, IIIA 1.7 CBI
2827882 2017, Use Site Description: Cimegra for In- furrow Applications on Corn and Potatoes, DACO: 10.2.2, 5.2, IIIA 3.3.1
2827885 2017, Petition for Application: CIMEGRA an insecticide for in-furrow use in potato and corn, DACO: 10.2.3.1, 10.2.3.2, 10.2.3.3, 10.2.3.4, 10.3.1, 10.3.2, 10.3.3, 10.4, 10.5.1, 10.5.2, 10.5.3, 10.6, IIIA 6.1.1, IIIA 6.1.2, IIIA 6.1.3, IIIA 6.1.4.1, IIIA 6.1.4.2, IIIA 6.1.4.3, IIIA 6.2.1, IIIA 6.2.2, IIIA 6.2.3, IIIA 6.2.4, IIIA 6.2.5, IIIA 6.2.6, IIIA 6.2.7, IIIA 6.2.8, IIIA 6.3, IIIA 6.4.1, IIIA 6.4.2, IIIA 6.5, IIIA 6.6, IIIA 6.7
2827887 2017, Field Data Trials, DACO: 10.2.3.4, 10.3.2,I IIA 6.1.3, IIIA 6.2.1
2827888 2017, Survey of Alternatives, DACO: 10.5.1, IIIA 6.4.1
2827929 2017, BAS 453 01 I Seed Treatment - Minor Change Reasoning, DACO: 10.6, 3.7, IIIA 1.7 CBI
2827930 2017, DACO 3.6- Teraxxa F4- Labelling of preservatives, DACO: 10.6, 3.7, IIIA 1.7 CBI
2827931 2017, Teraxxa F4 - Overview of SPSFs, DACO: 10.6,3.7,IIIA 1.7 CBI
2828008 2017, Dusting Off Study - Winter Wheat and Corn, DACO: 10.6, 5.14, IIIA 3.10
2828009 2017, Use Site Description for Teraxxa and Teraxxa F4, DACO: 10.2.2, 5.2, IIIA 3.3.1
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B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

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