Proposed Registration Decision PRD2010-03

FeHEDTA

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Overview

Proposed Registration Decision for FeHEDTA

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of NEU1173H TGAI and the end-use products; NEU1173H RTU with Pull'N Spray Applicator, NEU1173H RTU with Quick Connect Sprayer, NEU1173H RTU, Fiesta Lawn Weed Killer Ready to Spray, Fiesta Lawn Weed Killer, NEU1173H Ready to Spray Large Size, NEU1173H Ready to Spray, NEU1173H Large Size, and NEU1173H, containing the technical grade active ingredient iron present as FeHEDTA (herein referred to as FeHEDTA), to control several broadleaved weed species that commonly occur in turf.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

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 NEU1173H TGAI and the end-use products; NEU1173H RTU with Pull'N Spray Applicator, NEU1173H RTU with Quick Connect Sprayer, NEU1173H RTU, Fiesta Lawn Weed Killer Ready to Spray, Fiesta Lawn Weed Killer, NEU1173H Ready to Spray Large Size, NEU1173H Ready to Spray, NEU1173H Large Size, and NEU1173H.

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.

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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."

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 (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). 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 PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on FeHEDTA, the PMRA will consider all comments received from the public in response to this consultation document[3]. The PMRA will then publish a Registration Decision[4] on FeHEDTA, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA'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 FeHEDTA?

Iron is a metallic chemical element (symbol "Fe") that acts as a selective herbicide when chelated with hydroxyethylenediaminetriacetic acid (HEDTA) to form FeHEDTA. Broadleaved plants are generally more susceptible to the herbicidal effects of FeHEDTA than are grass species. The mechanism of selectivity is not entirely understood but is believed to relate in part to differences in uptake. As Fe can function as a catalyst for oxygen reduction, thereby producing unstable and highly reactive oxygen species, including hydroxyl radicals that cause cellular damage, the excessive uptake of FeHEDTA by many broadleaved species leads to tissue necrosis and ultimately plant death.

Health Considerations

Can Approved Uses of FeHEDTA Affect Human Health?

FeHEDTA is unlikely to affect your health when used according to label directions.

Exposure to FeHEDTA may occur when handling and applying the product. 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). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

[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 technical grade active ingredient, FeHEDTA, is of low acute toxicity by the oral, dermal and inhalation routes and is minimally irritating to eyes, but non-irritating to skin. There is potential for skin sensitization to occur when skin is repeatedly exposed to FeHEDTA products. Therefore, cautionary statements alerting users to this sensitization concern are required on all product labels.

Dermal exposure is likely for commercial applicators, domestic users or anyone entering sprayed areas before the spray is dried. Children may also be exposed to FeHEDTA by direct dermal or hand-to-mouth contact if they were to play on freshly treated lawn surfaces. Therefore, a restricted entry statement is required on all product labels to mitigate this exposure concern.

Waivers were granted for short-term dermal toxicity, prenatal development toxicity and genotoxicity studies based on the low application rates, low dermal absorption, low toxicity of FeHEDTA, and on the strength of toxicological information on chemically similar EDTA compounds.

Residues in Water and Food

Dietary risks from food and water are not of concern.

End-use products containing FeHEDTA are not applied directly to food or feed crops, so residues on food are expected to be negligible.

Occupational Risks From Handling FeHEDTA

Occupational risks are not of concern when FeHEDTA is used according to label directions, which include protective measures.

Occupational and residential exposure is expected to be brief, and is not likely to result in unacceptable risk to commercial applicators, occupational workers, and domestic users if the end-use products are used according to label directions.

The proposed use of the end-use products may result in exposure to the commercial applicators, domestic-users, mixers, loaders, and those responsible for clean-up and maintenance activities, but significant risks from such exposures are not anticipated due to the low toxicity of FeHEDTA and adequate exposure mitigation measures recommended on the labels. For bystanders, exposure is expected to be negligible. Therefore, health risks to bystanders are not of concern.

Precautionary and hygiene statements on the labels are considered adequate to protect individuals from any unnecessary risk from occupational exposure.

Environmental Considerations

What Happens When FeHEDTA Is Introduced Into the Environment?

FeHEDTA is expected to be non-persistent in the environment (terrestrial and aquatic) under neutral to alkaline aerobic conditions. FeHEDTA has a potential for high mobility in sandy soil with negligible organic matter. FeHEDTA is expected to impact broadleaf terrestrial plants; therefore, a precautionary label statement is needed for the protection of desirable plants.

Iron is ubiquitous in the environment. FeHEDTA is widely used as a plant micronutrient fertilizer in agricultural industries. Based on its low volatility, FeHEDTA is not expected to enter the atmosphere. FeHEDTA is soluble in water where it is rapidly degraded by natural light. FeHEDTA is transformed by micro-organisms in soil and aquatic systems, although it is relatively stable in anaerobic soils. No major products are formed in soil and water. From the proposed use pattern, the amount of FeHEDTA entering the environment will be lower than for other agricultural uses.

FeHEDTA is expected to pose negligible risk to terrestrial and aquatic organisms under conditions of use for application to turf.

Value Considerations

What Is the Value of FeHEDTA

FeHEDTA controls several broadleaved weed species that commonly occur in turf. It is an alternative to conventional herbicides. FeHEDTA is compatible with integrated weed management practices in that it is applied only when weeds have emerged and is not used as a "preventative" treatment.

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 labels of the end-use products NEU1173H RTU with Pull'N Spray Applicator, NEU1173H RTU with Quick Connect Sprayer, NEU1173H RTU, Fiesta Lawn Weed Killer Ready to Spray, Fiesta Lawn Weed Killer, NEU1173H Ready to Spray Large Size, NEU1173H Ready to Spray, NEU1173H Large Size, and NEU1173H to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with domestic-users coming into direct contact with FeHEDTA on the hands and then transferring to mouth, the labels recommend “avoid hand-to-mouth contact” and require commercial applicators/domestic-users and workers to wash hands thoroughly with soap and water after handling the products and before eating, drinking, and chewing gum or chewing tobacco.

The labels specify that anyone handling or applying these products should “avoid breathing vapour or spray mist” and “avoid contact with skin or clothing.” Domestic product labels should include the statement “DO NOT get in eyes.”

To protect children and adults from dermal exposure to FeHEDTA from wet treated turf, the labels should include the restricted entry statement, “Do not re-enter or allow re-entry into treated areas until the spray is dried.”

The signal words “POTENTIAL SKIN SENSITIZER” and the statement “May cause skin sensitization” are required on the principal and the secondary display panels, respectively, of both the technical and end-use product labels.

To prevent inappropriate use, the secondary display panel of the technical label should include the statement “PREVENT ACCESS BY UNAUTHORIZED PERSONNEL.”

Personal protective equipment (PPE) recommended include protective eye-wear for commercial products and waterproof gloves for both commercial and domestic products which require loading, mixing, and for repair/clean-up activities.

The application of commercial products is recommended only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools, and recreational areas is minimal; taking into consideration wind speed, wind direction, temperature, application equipment, and sprayer settings.

Next Steps

Before making a final registration decision on FeHEDTA, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency’s response to these comments.

Other Information

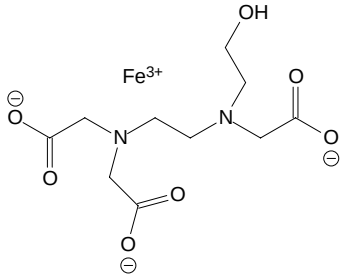
When the PMRA makes its registration decision, it will publish a Registration Decision on FeHEDTA (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's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

Science Evaluation

FeHEDTA

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	FeHEDTA
Function	Herbicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	Hydroxyethylethylenediaminetriacetic acid, ferric complex
2. Chemical Abstracts Service (CAS)	Iron, [N-(2-[bis[(carboxy-.kappa.O)methyl]amino-.kappa.N]ethyl]-N-[2-(hydroxy-.kappa.O)ethyl]glycinato(3-)--.kappa.N,.kappa.O]-
CAS number	17084-02-5
Molecular formula	$C_{10}H_{15}N_2O_7Fe$
Molecular weight	331.15
Structural formula	
Purity of the active ingredient	4.51 % as iron (present as FeHEDTA)

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

Technical Product—NEU1173H TGAI

Property	Result
Colour and physical state	Deep red liquid
Odour	Odourless
Melting range	Not applicable
Boiling point or range	106 °C
Density	1.396 g/mL
Vapour pressure at 20°C	Not applicable
Ultraviolet (UV)-visible spectrum	medium — λ_{max} (nm) — molar abs. (L/(mol*cm)) acidic — 210 — 6.60×10^3 neutral — 210 — 7.06×10^3 basic — 219 — 4.27×10^3
Solubility in water at 20°C	Miscible in all proportions
Solubility in organic solvents at 20°C	Solvent — Solubility Hexanes — completely immiscible Diethyl ether — completely immiscible Acetone — FeHEDTA immiscible aqueous portion miscible Methanol — completely soluble
n-Octanol-water partition coefficient (K_{ow})	log $K_{ow} < 0$,
Dissociation constant (pK_a)	pKa_1 =2.4, pKa_2 = 5.4, pKa_3 = 9.9
Stability (temperature, metal)	Stable at 54 °C, non-corrosive to glass, plastic, stainless steel, brass and aluminum. Corrosive to galvanized steel, zinc and copper.

End-Use Product— NEU1173H, Fiesta Lawn Weed Killer, Fiesta Lawn Weed Killer Ready to Spray, NEU1173H Large Size, NEU1173H Ready to Spray, NEU1173H Ready to Spray Large Size

Property	Result
Colour	Deep Red
Odour	Odourless
Physical state	Liquid
Formulation type	SN - solution
Guarantee	4.43 % nominal
Container material and description	HDPE bottles
Density	1.40 – 1.42 g/mL
pH	5.93 ± 0.12
Oxidizing or reducing action	No significant reaction with water, a 10 % monoammonium phosphate solution, iron powder or kerosene. Reducing activity seen with a 10 % potassium permanganate solution.
Storage stability	Accelerated storage shows a relative loss in assay of Fe of <1 % after 2 weeks storage at 54 °C and ~4.3 % loss after 2 months storage at 40 °C.
Corrosion characteristics	No evidence of corrosive effects on HDPE bottles used to store the product at ambient temperature for one year.
Explodability	Non-explosive

End-Use Product— NEU1173H RTU, NEU1173H RTU With Pull'N Spray Applicator, NEU1173H RTU with Quick Connect Sprayer

Property	Result
Colour	Deep Red
Odour	Odourless
Physical state	Liquid
Formulation type	SN - solution
Guarantee	0.25 % nominal

Property	Result
Container material and description	HDPE bottles
Density	1.01 – 1.03 g/mL
pH	5.81 ± 0.04
Oxidizing or reducing action	No significant oxidizing or reducing activity observed
Storage stability	Accelerated storage shows a relative loss in assay of Fe of <1 % after 2 weeks storage at 54 °C and ~3.4 % loss after 2 months storage at 40 °C.
Corrosion characteristics	No evidence of corrosive effects on HDPE bottles used to store the product at ambient temperature for one year.
Explodability	Non-explosive

1.3 Directions for Use

There are a total of nine herbicide end-use products that contain FeHEDTA in Concentrate, Ready-to-Spray and Ready-to-Use formats (Table 1.3).

Table 1.3 Herbicides containing FeHEDTA

Products by format (marketing class)	Guarantee
Concentrate products Fiesta Lawn Weed Killer (Commercial) NEU1173H Large Size (Domestic) NEU1173H (Domestic)	4.43% Fe
Ready-to-Spray Products Fiesta Lawn Weed Killer Ready To Spray (Commercial) NEU1173H Ready-To-Spray Large Size (Domestic) NEU 1173H Ready-To-Spray (Domestic)	4.43% Fe
Ready-to-Use products NEU1173H RTU with Pull'N Spray Applicator (Domestic) NEU1173H RTU with Quick Connect Sprayer (Domestic) NEU1173H RTU (Domestic)	0.25% Fe

Each of these products is a selective herbicide for the control of several emerged broadleaved weed species in established turf (residential and commercial lawns, non-crop areas, including rights-of-ways, golf courses, parks, cemeteries, and athletic fields). Each of these products may be applied at up to two times per season, with no less than 4 weeks between applications, to control dandelion (*Taraxacum officinale*), English daisy (*Bellis perennis*), false dandelion (*Hypochaeris radicata*), white clover (*Trifolium repens*), black medic (*Medicago lupulina*), bull thistle (*Cirsium vulgare*), Canada thistle (*Cirsium arvense*), common chickweed (*Stellaria media*), creeping buttercup (*Ranunculus repens*), narrow-leaved plantain (*Plantago lanceolata*), dovefoot geranium (*Geranium molle*), slender speedwell (*Veronica filiformis*), lawn burweed (*Soliva pterosperma*), moss (various species), and algae (various species), as well as to suppress broad-leaved plantain (*Plantago major*).

1.3.1 Concentrate products containing FeHEDTA

These products require dilution before application: 1 part of concentrate is to be mixed with 24 parts of water for a 4% solution. The mixed solution is to be applied at 200 - 400 ml/m^2 with a standard handheld or backpack sprayer. This equates to 0.5 - 1.0 g a.i./m^2. The lower rate is intended for control of smaller weeds and the higher rate is intended for control of larger weeds and on some perennial weeds. These products are intended for application over a large area or to larger patches of weeds.

1.3.2 Ready-to-Spray products containing FeHEDTA

These products are automatically diluted to the correct concentration when applied via a hose connected to a water source. The spray is to be applied at 200 - 400 ml/m^2. Similar to the concentrate products, these products are intended for application over a large weed-infested area or to larger patches of weeds.

1.3.3 Ready-to-Use products containing FeHEDTA

These products are ready to use and require no further dilution. They are intended for application to individual weeds or patches of weeds. Application is made until weed foliage is thoroughly wetted, just to the point of run-off.

1.4 Mode of Action

The exact mode of action of iron is unknown but it may in part be based on differential uptake and transport of iron, when present in chelated form. Synthetic chelates of iron are known to be more available than non-chelated iron for uptake by broadleaved plants which may result in excessive iron uptake. Uptake of synthetic chelates of iron by grasses may be inefficient relative to that in broadleaved species thereby conferring a greater level of tolerance, although not all grass species are equally tolerant of synthetic chelates of iron. Iron is known to function as a catalyst for oxygen reduction, thereby producing unstable and highly reactive oxygen species, including hydroxyl radicals that cause cellular damage, leading to cell death. Chelated iron has not been classified into a mode of action group e.g. WSSA or HRAC.

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 the impurities in FeHEDTA have been validated and assessed to be acceptable for the determinations.

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

Not required.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

The PMRA has conducted a detailed review of the submitted data and publicly available toxicological information for FeHEDTA. The database is considered adequate, consisting of an array of laboratory animal (in vivo) and cell culture (in vitro) toxicity studies and/or waiver requests for specific elements of information currently required for health hazard assessment purposes. The submitted toxicology studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is such that the database is considered adequate to qualitatively assess the toxicological hazards of this pest control product.

The applicant submitted acute toxicity, irritation, and sensitization studies performed with NEU1173H, one of the proposed end-use products which is similar to the technical product, to support registration of the technical grade active ingredient and the nine associated end-use products. The substance tested in the submitted studies was FeHEDTA (26.52% w/w). Although the PMRA requires toxicity and irritation studies to be conducted with each end-use product, given that none of the formulations contain formulants of toxicological concern, testing with NEU1173H representing all the formulations was considered acceptable.

FeHEDTA was of low acute toxicity by the oral, dermal, and inhalation routes in rats. It was minimally irritating to eyes and non-irritating to skin in rabbits. In a Local Lymph Node Assay (LLNA) in mice, FeHEDTA was a dermal sensitizer. There is apparent potential for skin sensitization associated with repeated dermal exposure to the technical and end-use products.

The applicant requested study waivers for short-term dermal (90-day, rodent), prenatal developmental toxicity (rodent), bacterial reverse mutation assay, and genotoxicity (in vitro mammalian cell assay) on the following basis:

1) The low toxicity of FeHEDTA as observed in the acute toxicology studies; 2) the low dermal absorption of FeHEDTA; 3) the information in the published literature on chemically similar EDTA compounds (PMRA PRD2007-13); 4) the low application rate of FeHEDTA (concentrate is diluted 1 in 25; concentration of iron in the end-use products ranges from 0.25–4%); 5) non-use on food or feed crops; 6) iron sodium EDTA (chemically similar substance) is used as a source of dietary iron for food fortification purposes in the United States and such a use is approved by the World Health Organization; 7) no report of toxicological concerns from the high volume use of this chemical worldwide as a fertilizer for counteracting iron deficiency in plants; 8) trisodium HEDTA which is the source of the HEDTA in the active ingredient is used in soaps and cosmetics.

Furthermore, the applicant provided a summary of the toxicity profile for ferric sodium EDTA, evaluated and registered by the PMRA as a molluscicide, from the PMRA document PRD2007-13 to support the waiver requests (Table 2, Appendix I).

Published information demonstrating the chronic toxicity potential of FeHEDTA was not available for evaluation; therefore, information available from the evaluation on ferric sodium EDTA was used. HEDTA of the proposed compound differs from EDTA of the registered ferric sodium EDTA in that one of the carboxyl groups (COOH) of the EDTA has been replaced with a hydroxyl (CH_2OH) group (Figure 1, Appendix I). Due to the close chemical similarity, biological effects of these iron chelates are not expected to be different, and the toxicity of HEDTA and its salts and EDTA and its salts is expected to be similar and low.

In the gastrointestinal tract (GI tract), ferric sodium EDTA, like other EDTA complexes, dissociates to form iron and an EDTA salt which are absorbed independently. Compounds of EDTA are poorly absorbed in the GI tract, do not undergo significant metabolic conversion, and have a low degree of acute oral toxicity. Metal ions on the EDTA-metal complex are freely exchanged in the GI tract; therefore, the toxicological effects of EDTA salts are likely to be similar irrespective of the salt form. In chronic toxicity studies, diets containing as much as 5% EDTA were without adverse effects. EDTA compounds were not carcinogenic in animal bioassays and are not directly genotoxic.

In humans, iron absorption from ferric sodium EDTA is related to body iron reserves. Generally, ferric (Fe^{3+}) iron in food and supplements is poorly absorbed because it is precipitated from solution at a pH above 3.5, and insoluble precipitate is poorly absorbed in the upper small intestine by humans, where most non-heme iron is absorbed, unless suitable complexing agents are present. Publicly available information suggests that normal individuals are capable of controlling iron absorption and that chronic toxicity (namely, hemochromatosis) is generally limited to individuals with inherited metabolic disorders affecting maintenance of iron balance in the body. In swine, exposure to radiolabelled ferric sodium EDTA ($Na^{55}Fe$-[2-^{14}C] EDTA, 5 mg introduced into the esophagus) resulted in 95% recovery in the feces and 0.3% in the urine. Absorption of a single, nonlethal, oral dose of ferric sodium EDTA introduced into the

esophagus was anticipated to be poor, with nearly complete excretion in the feces. Metabolism of ferric sodium EDTA is anticipated to be negligible based on a review of published scientific information.

The requirement for short term dermal toxicity testing was waived because like other EDTA compounds iron HEDTA is not likely to be readily absorbed through the skin and has low acute dermal toxicity. A clinical study in human males reported almost no absorption of calcium disodium EDTA following dermal exposure.

The requirement for a prenatal developmental toxicity study was also waived based on the summary of reproduction and developmental toxicity studies for ferric sodium EDTA. Administration of a large quantity of disodium EDTA (954 mg/kg bw/day) in the diet of pregnant CD rats (day 7 through 14 of gestation) resulted in maternal effects marked by weight loss, decreased food consumption and diarrhea in all test animals and gross fetal malformations.

When disodium EDTA (3% by weight) was added to the diet of pregnant Sprague Dawley rats from days 6 to 14 of gestation or from day 6 to term, the majority of fetuses were grossly malformed. When the diet of exposed rats was supplemented with zinc (1000 ppm), no fetal malformations were noted, suggesting that the malformations were not directly caused by EDTA but were the result of secondary effects due to sequestering of zinc required for normal fetal development. It seems that by binding to divalent and trivalent cations EDTA in large amounts can cause mineral deficiencies; thereby, resulting in toxicological effects.

The requirement for a genotoxicity/mutagenicity study was waived based on the available information from the evaluation of ferric sodium EDTA. There was no evidence of genotoxicity/mutagenicity when trisodium EDTA was tested in *Salmonella typhimurium* strains (TA 98, TA100, TA1535, TA1537, and TA1538), *Escherichia coli* (WP2uvrA) and in mouse lymphoma cells with and without metabolic activation. This suggests that the EDTA moiety is not mutagenic/genotoxic. There was evidence of genotoxic potential of ferric sodium EDTA in mouse lymphoma cells in the presence and absence of metabolic activation. It should be noted, however, that it is anticipated that the Fe and EDTA will dissociate in solution and that Fe uptake by a transferrin independent transport system requires reduction of Fe^{3+} to Fe^{2+} at the cell surface. The ferrous ion is then subject to Fenton reaction: $Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + .OH + OH^-$. The hydroxyl free radical is expected to attack the DNA, resulting in the observed genotoxicity. The genotoxic reaction is therefore likely to be an indirect result of iron and not of the ferric sodium EDTA. The genotoxic nature of iron is not a concern because it is an essential element required by the human body and is readily available from food. The adverse effects of excess dietary iron in normal individuals have not been reported. For iron, the Recommended Dietary Allowance (RDA) is 8 mg/day for all age groups of men and postmenopausal women and 18 mg/day for premenopausal women. The tolerable upper intake level (UL) for adults is 45 mg/day iron, based on gastrointestinal distress as an adverse effect.

Results of the acute tests with FeHEDTA and chronic tests for ferric sodium EDTA conducted on laboratory animals, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Tables 1 and 2 of Appendix I.

3.2 Determination of Acceptable Daily Intake (ADI)

As the end-use products are not intended for direct application to food crops, determination of an acceptable daily intake is not required.

3.3 Determination of Acute Reference Dose (ARfD)

As the end-use products are not intended for direct application to food crops, determination of an acute reference dose is not required.

3.4 Occupational and Residential Risk Assessment

3.4.1 Use Description/exposure Scenario

Product use

The end-use products are to be applied onto individual weeds at a rate of 200–400 mL/m^2 (2000 to 4000 L/ha). For best results, the labels instruct to re-apply with no less than 4 weeks between applications up to a maximum of 2 applications per year per treatment site.

Ready-To-Use End-use products: NEU1173H RTU With Pull 'n Spray Applicator, NEU1173H RTU With Quick Connect Sprayer, NEU1173H RTU (Iron present as FeHEDTA 0.25%)

Application of these products does not involve mixing or loading as they are ready-to-use formulations applied with the integrated applicator on the product container. The nozzle is to be adjusted to achieve a desired spray pattern. For these products, on average, a residential user would be treating a lawn area of 0.0093 ha per treatment per day with18.6–37.2 L of the end-use products, and the estimated amount of active ingredient used would be 0.047 to 0.094 kg of iron present as FeHEDTA.

Ready-To-Spray: *NEU1173H Ready-to-Spray Large Size, NEU1173H Ready-to-Spray* (Iron present as FeHEDTA 4.43%)

Application of these products does not involve mixing or loading as they are ready-to-use formulations and will be applied using a hose-end sprayer attached to the product container. A garden hose is to be attached to the hose-end sprayer as per the label instructions and the sprayer is to be calibrated to achieve a dilution ratio of 1:24 in water. For these products, on average, a residential user would be treating a lawn area of 0.10 ha per treatment per day with 8–16 L of the end-use products, and the estimated amount of active ingredient used would be 0.51 to 1.02 kg iron present as FeHEDTA.

Hand-held or Backpack application: NEU1173H Large Size, NEU1173H (Iron present as FeHEDTA 4.43%)

The proposed application is by any standard hand-held or backpack sprayer. The product is to be loaded and mixed with water at 1:24 ratio and sprayed to achieve a uniform coverage of the area to be treated. To reduce spray drift, the labels instruct users to set sprayers to a coarse nozzle setting. For application, a residential user would be treating an average lawn area of 0.0093 ha per treatment per day with 0.74–1.48 L of the end-use products, and the estimated amount of active ingredient used would be 0.047 to 0.094 kg iron present as FeHEDTA.

Fiesta Lawn Weed Killer Ready to Spray (Iron present as FeHEDTA 4.43%)

There is no mixing or loading involved as the product is a ready-to-use formulation to be applied using a hose-end sprayer attached to the product container. A garden hose would be attached to the hose-end sprayer as per the label instructions, and the sprayer is to be calibrated to achieve a dilution ratio of 1:24 in water. At a maximum application rate, 20.2 ha can be treated in a day with 1616–3232 L of the end-use product, and the estimated amount of active ingredient handled by a commercial applicator in a day would be 101 kg to 202 kg iron present as FeHEDTA.

Fiesta Lawn Weed Killer (Iron present as FeHEDTA 4.43%)

The product is to be transferred to any standard hand-held or backpack sprayer and would be diluted with water at 1:24 ratio. To reduce spray drift, the label instructs users to set sprayers to a coarse nozzle setting. At a maximum application rate, 2.02 ha can be treated in a day with 161.6–323.2 L of the end-use product, and the estimated amount of active ingredient handled in a day by a commercial applicator would be 10.1 kg to 20.2 kg iron present as FeHEDTA.

3.4.2 Toxicological Endpoints

Occupational and residential exposures to end-use products are expected to be short-term in duration and predominantly by the dermal route during handling and application and from dermal contact of wet treated surfaces. Inhalation of spray mist is also possible, but is likely to be a minor route of exposure. The end-use products are anticipated to be of low acute toxicity by the oral, dermal, and inhalation routes. They are likely to be nonirritating to the skin, but minimally irritating to eyes, and are likely to be skin sensitizers. Repeated dermal exposure to end-use products can result in skin sensitization. The proper use and handling of the proposed end-use products, following label directions, is not likely to result in repeated or prolonged human exposure by any routes at a concentration that is likely to raise toxicological concerns. The publicly available information on the active ingredient suggests that the proposed use of end-use products is unlikely to have any short-term or prenatal developmental effects or genotoxic effects.

3.4.3 Dermal Absorption

As the available published literature suggests negligible dermal absorption for EDTA compounds, and since the product labels have adequate precautionary and hygiene statements to prevent repeated and prolonged dermal exposure, a dermal absorption study was not considered necessary to complete the health hazard assessment of FeHEDTA.

3.4.4 Mixer, Loader and Applicator Exposure and Risk Assessment

The proposed use of the commercial products may result in exposure to the mixer, loader, and applicator, as well as those responsible for clean-up and maintenance activities, but significant risks from such exposures are not anticipated due to the low toxicity of the end-use products and adequate exposure mitigation measures recommended on the labels. Loading and mixing is required only for one of the two commercial products. Applicators may be exposed through inhalation of spray drift and also dermally through contact with wet sprayed surfaces. The end-use products have low toxicity by the inhalation route, but may act as respiratory irritants. The end-use products are poorly absorbed through skin; they are not toxic or irritating to skin, but are potential skin sensitizers. Dermal exposure can be mitigated by restricting entry or re-entry to the freshly treated sites until the applied spray is dried. Ocular exposure to the end-use products is likely to cause minimal eye irritation.

3.4.5 Residential Risk Assessment

The proposed use of the domestic products and also commercial products may result in exposure to users and bystanders, but significant risks from such exposures are not anticipated due to the low toxicity of the end-use products and adequate exposure mitigation measures recommended on the labels. Loading and mixing is required only for products using standard hand-held or backpack sprayer application; that is, two domestic end-use products. Applicators may be exposed through inhalation of spray drift and also dermally through contact with wet sprayed surfaces. The end-use products have low toxicity by the inhalation route, but may act as respiratory irritants. Prolonged dermal exposure is not likely and end-use products are poorly absorbed through skin. Exposure to children from direct dermal or hand-to-mouth contact is possible if they were to play on lawns freshly treated with FeHEDTA. Restricting entry or re-entry to the freshly treated sites until the spray has dried can mitigate this exposure.

Exposure reduction statements including the requirement for personal protective equipment and mitigative and hygiene statements on the labels are adequate to protect domestic users and bystanders against any unnecessary risk from residential exposure if label directions are followed.

3.5 Food Residues Exposure Assessment

FeHEDTA products are not applied directly to food. The risk from dietary exposure is considered negligible, so a food residue exposure assessment was not required.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

FeHEDTA is chemically similar to other iron salts of EDTA such as Ferric sodium EDTA and Ferric EDTA, based on their physical properties relevant to environmental chemistry and fate. In the terrestrial environment, FeHEDTA is not expected to volatilize under field conditions (i.e from dry, wet or moist surfaces). FeHEDTA is expected to be less stable in alkaline and

calcareous soils (pH 7-8) where iron ion is displaced by calcium ion and precipitates as $Fe(OH)_3$. FeHEDTA is expected to be rapidly transformed by natural light in water. Based on the proposed use pattern (mode of application, application rate and use areas), the risk for potential leaching and exposure of FeHEDTA to drinking water (surface or ground water) will be low.

Data on the fate and behaviour of FeHEDTA are summarized in Table 3 of Appendix I.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the 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. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take 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 (i.e. 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 those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (e.g. 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 = 1). If the screening level risk quotient is below the level of concern, 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 level of concern, 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 might 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.

4.2.1 Risks to Terrestrial Organisms

Risk to terrestrial organisms was based upon the evaluation of FeHEDTA toxicity data for the following (Appendix I, Table 4):

- one species of honey bee (oral and contact exposure) representing invertebrates; and
- two bird and one mammal species representing vertebrates (acute and dietary).

The uncertainty factors used in adjusting the toxicity values are summarized in Appendix I, Table 5.

For an assessment of bees, a screening level EEC for acute oral or contact exposure to residues is 62.4 kg FeHEDTA/ha. For bees, the LD_{50} values in µg/bee were converted to the equivalent rates in kg/ha by multiplying with 1.12. The converted LD_{50} value was 93.7 kg FeHEDTA/ha. The screening level RQ value was <0.66; therefore, negligible risk to honey bees is expected.

For the assessment of birds and small wild mammals, the EEC values for FeHEDTA in potential food items were determined for a direct application immediately after a spray of 59 kg FeHEDTA/ha. The screening level estimated daily exposure (EDE) values were dependent on the body weight of an organism (20, 100, 1000 g for birds and 15, 35, 1000 g for mammals), food preferences (100% small insects for insectivores, 100% fruits for frugivores, 100% grain and seeds for granivores, and 100% leaves and leafy crops for herbivores), and amount consumed on a daily basis. The FeHEDTA toxicity endpoints used were LD_{50} >530.4 mg/kg bw for acute exposure and >307.13 mg/kg bw/day for dietary assessment of birds, and LD_{50} > 1326 mg/kg bw for acute assessment of small mammals. Most of the screening level and refined RQ values were higher than 1 for birds and small wild mammals due to the high application rate for turf (Appendix I, Table 6 & Table 8). However, based on the limited exposure expected from use on turf, which involves localized foliar treatment using standard hand-held or backpack sprayers, and coarse droplets sprays, the risk to birds and mammals is expected to be minimal.

FeHEDTA, at appropriate rates, is used as a broadleaf herbicide. Thus, precautionary label statements are required to prevent damage to desirable plants.

4.2.2 Risks to Aquatic Organisms

Risks of FeHEDTA to aquatic organisms were based upon the evaluation of FeHEDTA data for the following (Appendix I, Table 4):

- one freshwater invertebrate daphnid species (acute exposure); and
- one freshwater fish species (acute exposure).

The uncertainty factors used in modifying the toxicity values are summarized in Appendix I, Table 5. Where no dose-related effects were observed, the uncertainty factors were not used.

Screening level EEC values for FeHEDTA in water were calculated assuming a reasonable conservative scenario of direct application to water bodies of two different depths (80 cm and 15 cm). The 80-cm water body is chosen to represent a permanent body of water and 15 cm is chosen to represent a seasonal body of water. The pesticide is assumed to be instantaneously and completely mixed within the water body.

For assessment of fish and aquatic invertebrates, a screening level EEC of FeHEDTA in permanent water body (80-cm water depth) is 7.8 mg/L based on an application rate of 59 kg FeHEDTA/ha, two times per year. All screening level RQ values were <1 (Appendix I, Table 8c). Therefore, there are negligible risks to fish and aquatic invertebrates, on an acute basis.

For assessment of amphibians, a screening level EEC of FeHEDTA in a seasonal water body (15-cm water depth) is 41.6 mg/L based on an application rate of 59 kg FeHEDTA/ha, two times per year. Based on fish toxicity data, RQ values were <1.5 for acute exposure (Appendix I, Table 7) indicating that the level of concern may be exceeded for amphibians.

Available information on the effects of iron in ferric sodium EDTA on non-target organisms indicates that the iron in these chelates interacts with the hemocyanin in the bloodstream of molluscs and crustaceans, and would be toxic to these organisms. However, exposure to freshwater molluscs and crustaceans as well as amphibians is unlikely to occur given the intended use of FeHEDTA as a broadleaf herbicide applied directly to targeted terrestrial plants.

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

Efficacy data were submitted from 35 trials conducted in 2005, 2006 and 2007. Nineteen of these trials were conducted in the field in Saanichton, British Columbia (17 trials), Ridgetown, Ontario, and Fresno, California. The remaining 16 trials were conducted in the greenhouse in Saanichton, B.C. The application rates tested varied by trial and included rates from 0.4 to 1.6 g a.i./m^2. A second application was made 2-4 weeks after the first in 17 of the 35 trials. All greenhouse trials were replicated 4 to 10 times with each treatment-replicate combination consisting of one plant in one pot. Treatments were replicated two or four times in field trials except for two trials that were unreplicated.

In greenhouse trials, applications were made to single plants in single pots by a hand trigger sprayer or a hand pump sprayer. In field trials, application was made by a hand pump sprayer, pressurized pump sprayer, hose sprayer, or hand trigger sprayer. Efficacy was visually assessed from 1 to 42 days after application, or 5-28 days after a second application, and was reported as percent phytotoxicity, percent injury, percent stand reduction, or percent control. The number and timing of evaluations was specific to trial.

The submitted efficacy data conditionally support the efficacy claims summarized in Table 5.1.1 for the NEU1173H products applied at 0.5 - 1.0 g a.i./m^2. The minimum rate is intended for application to smaller weeds while the maximum rate is intended for application to larger weeds or more difficult to control perennial weeds. Data were adequate to support a maximum of two applications per season with no less than 4 weeks between applications. Data were adequate to support a rainfast interval of 3 hours.

Table 5.1.1 Weed species for which efficacy claims are conditionally supported for the NEU1173H products applied at 0.5 - 1.0 g a.i./m^2.

Pest species or group	Scientific name	Other common names	Life cycle
Claim of control			
Dandelion	*Taraxacum officinale*	common dandelion	P
English daisy	*Bellis perennis*	European daisy	P
False dandelion	*Hypochaeris radicata*	spotted cat's ear, common cat's ear, hairy cat's ear, coast dandelion	P
White clover	*Trifolium repens*	Dutch clover, creeping white clover	P
Black medic	*Medicago lupulina*	hop clover	A or B
Bull thistle	*Cirsium vulgare*	common thistle,	WA, B, or MP
Canada thistle	*Cirsium arvense*	creeping thistle, field thistle	P
Common chickweed	*Stellaria media*	chickweed, common starwort	A, WA or SLP
Creeping buttercup	*Ranunculus repens*	buttercup, creeping crowfoot	P
Slender speedwell	*Veronica filiformis*	creeping speedwell	P
Narrow-leaved plantain	*Plantago lanceolata*	English plantain, buckhorn, buckhorn plantain, black plantain, lance-leaved plantain, ribgrass	P
Dovefoot geranium	*Geranium molle*	dove's-foot geranium, dove's-foot, crane's-bill, woodland geranium	A, B, or P
Lawn burweed	*Soliva pterosperma or S. sessilis*	spurweed	WA
Moss	various species		
Algae	various species		
Claim of suppression			
Broadleaf plantain	*Plantago major*	common plantain, plantain	P

A: annual; WA: winter annual; B: biennial; P: perennial; MP: monocarpic perennial; SLP: short-lived perennial.

5.2 Phytotoxicity to Host Plants

5.2.1 Acceptable Host Tolerance Claims for the NEU1173H Products

Data were submitted from 11 trials in which the tolerance of turfgrasses to one or two applications of the NEU1173H products was evaluated. The tolerance of perennial ryegrass was evaluated in seven greenhouse trials conducted in 2006 and 2007 in Saanichton, British Columbia. The tolerance of established turf to the NEU1173H products was evaluated in three field trials conducted in 2005 and 2006 at Saanichton, B.C., two of which were situated on "Park" turf consisting of about 65% perennial ryegrass and 25% of a mixture of chewings fescue and creeping fescue; the turf species composition in the third trial was unknown. The tolerance of established turf consisting of mainly Kentucky bluegrass with some chewings fescue and perennial ryegrass was evaluated in one field trial conducted in 2005 at Ridgetown, Ontario. There were no studies in which the tolerance of fescue grasses to the NEU1173H products was specifically assessed.

The application rates tested varied by trial and ranged from 0.5 - 1.0 g a.i./m^2 in the greenhouse trials and from 0.56 - 1.66 g a.i./m^2 in the field trials. A second application was made 2-4 weeks after the first in three greenhouse trials and two weeks after the first in the one field trial that was conducted on turf of unknown species composition.

In greenhouse trials, there were ten pots (replicates) per treatment of perennial ryegrass seedlings from 3.5 - 9 weeks old. Applications were made by a hand trigger sprayer.

In field trials, application was made by a hand pump sprayer (2 trials), hand trigger sprayer (1 trial), or a hose sprayer (1 trial). Treatments were replicated twice in the three field trials conducted at Saanichton and four times in the trial at Ridgetown.

Phytotoxicity was visually assessed from 1 - 43 days after application, or 5 - 21 days after a second application (made 14 - 29 days after the first), and was reported as percent phytotoxicity or percent injury. The number and timing of evaluations was specific to trial.

Overall injury to turf was low and consisted mainly of leaf darkening and some necrosis. These effects had usually diminished by 4 weeks after application in field trials. In greenhouse trials, the low injury initially observed to perennial ryegrass seedlings did not decrease by the last evaluation conducted 2-4 weeks after a first application of 0.4 - 1.0 g a.i./m^2. In two of the three greenhouse trials, injury to perennial ryegrass one week following a second application of 0.8 or 1.0 g a.i./m^2 was greater than that observed one week following the first application. In the one field trial in which two applications of 0.8 g a.i./m^2 was made, injury was greater following the second application.

The submitted tolerance data conditionally support a claim of tolerance for established turf comprised of one or more of Kentucky bluegrass, perennial ryegrass, and fescue treated with 0.5 - 1.0 g a.i./m^2. The submitted tolerance data are adequate to support a maximum of two applications per season with no less than 4 weeks between applications.

5.3 Impact on Succeeding Crops

Not applicable as the NEU1173H products are for application to established turf.

5.4 Economics

No market analysis was conducted or reviewed for the NEU1173H products.

5.5 Sustainability

5.5.1 Survey of Alternatives

Where manual removal of weedy plants in turf is not considered to be practical, herbicides may be used. The most common conventional herbicides used for broadleaved weed control on turf are those that belong to the synthetic auxin group and include 2,4-D, mecoprop, mecoprop-p and dicamba. In many herbicide-only products as well as in fertilizer-herbicide combination products, 2,4-D is included alone, in combination with mecoprop, or in combination with both mecoprop and dicamba. The spectrum of weeds controlled varies by the herbicide or combination of herbicides included in the product. Products that contain three-way mixtures of 2,4-D, mecoprop, and dicamba, generally include control claims for the greatest number of weed species. Other herbicides, including clopyralid, picloram, triclopyr, and dichlorprop are registered for use on non-crop areas, including roadsides, but are not for use on fine turf.

Interest in alternative turf herbicides is increasing. Corn gluten is a registered 'natural' alternative to synthetic herbicides for domestic and commercial use. Corn gluten may inhibit the seed germination of crabgrass and dandelion when used in conjunction with a sound lawn maintenance program. Acetic acid (e.g. EcoClear) is registered for domestic and commercial use for control of broadleaved weeds in and around the garden, including as a spot application in turf. Potassium salts of fatty acids (e.g. Safer's De-Moss Moss Killer Herbicide) are registered for domestic and commercial use for the control of moss in turf. Ferrous sulfate (e.g. Greenleaf Moss Control) is registered for moss control in turf. No product is registered for the control of algae in turf.

5.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

Cultural measures can be taken to discourage weed infestations, including proper fertilization and watering regimes that encourage development of dense turf thereby inhibiting establishment of weeds, mowing at the correct height (no less than 5 cm) and frequency (removing no more than one-third of biomass), and aerating and dethatching when necessary. Use of the NEU1173H products is compatible with such practices, particularly in that it is applied only when weeds have emerged and is not used as a "preventative" treatment. Patches of broadleaved weeds may be treated with spot applications of the NEU1173H products. Small patches or individual weeds may be treated with the NEU1173H products in the Ready-to-Use format.

5.5.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

The excessive level of iron that occurs in susceptible plants treated with the NEU1173H products is believed to be the result of uncontrolled uptake of iron that is chelated with HEDTA. Development of resistance to uptake of this synthetic iron chelate is not expected.

5.5.4 Contribution to Risk Reduction and Sustainability

The availability of the NEU1173H products provides an alternative herbicide option and mode of action to commonly used herbicides for broadleaved weed control in turf.

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 [those that meet all four criteria outlined in the policy, i.e., 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*].

During the review process, FeHEDTA 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 following conclusions:

- FeHEDTA does not meet Track 1 criteria, and is therefore not considered a Track 1 substance. See Appendix 1, Table 10 for comparison with Track 1 criteria.

- Transformation of FeHEDTA does not result in any transformation products that meet Track 1 criteria.

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

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[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: DIR99-03; and DIR2006-02[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 following conclusions:

- Technical grade FeHEDTA and the NEU1173H end-use products do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette.*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02[9].

7.0 Summary

7.1 Human Health and Safety

The available information for FeHEDTA is adequate to qualitatively define the majority of toxic effects that may result from human exposure to FeHEDTA. Overall, FeHEDTA is of low acute toxicity irrespective of the exposure routes. It is not irritating to skin, but minimally irritating to eyes, and is a potential skin sensitizer. Repeated dermal exposure to technical product and associated formulations can result in skin sensitization.

Commercial applicators, loaders, mixers, and those involved in clean-up and maintenance activities, domestic-users, and/or bystanders are not likely to be exposed to levels of FeHEDTA that will result in unacceptable risk when the product formulations are used according to label directions. Children could be exposed to FeHEDTA by direct dermal or hand-to-mouth contact if they were to play on freshly treated lawn surfaces. To minimize this potential for exposure, a restricted entry statement will be added to the product labels prohibiting entry or re-entry to treated areas until the spray has dried. Exposure mitigation measures are adequate to protect

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6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 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, PMRA Formulants Policy.

9 DIR2006-02, PMRA Formulants Policy.

human health from residential and occupational exposure. A maximum residue limit was not promulgated because the proposed use is non-food; therefore, exposure from food is unlikely.

7.2 Environmental Risk

Limited environmental risks were identified as a result of the assessment of the proposed use of FeHEDTA. Use of FeHEDTA and the NEU1173H end-use products on turf at the maximum annual application rate is expected to pose negligible acute risk to aquatic and terrestrial organisms. This is due to the limited exposure to the environment resulting from hand-held or backpack sprayers on turf, which use a coarse nozzle size to minimize spray drift. As FeHEDTA does, however, act as a herbicide against broadleaf plants, a precautionary label statement is needed to prevent damage to desirable plants.

7.3 Value

The data submitted are adequate to conditionally support the registration of the NEU1173H products for use on established turf consisting of one or more of perennial ryegrass, Kentucky bluegrass, and fescue for control or suppression of several broadleaved weeds, moss, and algae.

The availability of the NEU1173H products provides an alternative herbicide option and mode of action to commonly used herbicides for broadleaved weed control in turf.

7.4 Unsupported Uses

No data were provided to support efficacy claims for the following weed species: heal-all (*Prunella vulgaris*), silver cinquefoil (*Potentilla anserina*), shepherd's purse (*Capsella bursa-pastoris*), Persian speedwell (*Veronica persica*), wild chamomile (*Matricaria chamomilla*), and liverworts (various species), and lichens (various species). No efficacy or tolerance data were provided to support more than two applications per season. Data were insufficient to support use on newly sown turf (turf grass seedlings).

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of NEU1173H TGAI and the end-use products; NEU1173H RTU with Pull'N Spray Applicator, NEU1173H RTU with Quick Connect Sprayer, NEU1173H RTU, Fiesta Lawn Weed Killer Ready to Spray, Fiesta Lawn Weed Killer, NEU1173H Ready to Spray Large Size, NEU1173H Ready to Spray, NEU1173H Large Size, and NEU1173H, containing the technical grade active ingredient iron present as FeHEDTA (herein referred to as FeHEDTA), to control several broadleaved weed species that commonly occur in turf.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

µg	micrograms
a.i.	active ingredient
ADI	acceptable daily intake
ARfD	acute reference dose
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
BW	Body weight
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetres
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
dw	dry weight
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure
EDTA	ethylenediaminetetraacetic acid
EEC	estimated environmental exposure concentration
EC_{25}	effective concentration on 25% of the population
EP	end-use product
ER_{50}	effective rate for 50% of the population
Fe	iron
FeHEDTA	hydroxyethylenediaminetriacetic acid, ferric complex
g	gram
ha	hectare(s)
HDPE	high-density polyethylene
HEDTA	hydroxyethylenediaminetriacetic acid
HPLC	high performance liquid chromatography
HR_5	5^{th} percentile hazard rate
HRAC	Herbicide Resistance Action Committee
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOEC	low observed effect concentration
m^2	square metre(s)
mg	milligram
mL	millilitre
MAS	maximum average score
MRL	maximum residue limit
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration

NOEL	no observed effect level
OC	organic carbon content
PCPA	*Pest Control Product Act*
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PRD	proposed registration decision
RDA	recommended dietary allowance
RTU	ready-to-use
SSD	Species sensitivity distribution
$t_{1/2}$	half-life
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet
WSSA	Weed Science Society of America
2,4-D	2,4-dichlorophenoxyacetic acid

Appendix I Tables and Figures

Table 1 Toxicology Profile for FeHEDTA (26.52% w/w).*

Study	Species/Strain Doses	Result	Target Organ, Significant Effects, Comments
Oral Exposure by gavage Limit test 14-day observation	Rat – Wistar 3 ♀ rats/dose Dosed at 5000 mg/kg bw	LD_{50} ♀ > 5000 mg/kg bw	**Low toxicity**
Dermal Limit test, 24-hour exposure by topical application. 14-day observation	Rat – Wistar 5 rats/sex/dose Dosed at 5000 mg/kg bw	LD_{50} ♂ & ♀ > 5000 mg/kg bw	**Low toxicity**
Inhalation Limit test, 4-hour exposure (nose-only inhalation chamber). 14-day observation	Rat – Wistar 5 rats/sex/dose Dosed at 5.43 mg/L	LC_{50} ♂ & ♀ > 5.43 mg/L	**Low toxicity** Slight breathing abnormalities observed during exposure, and discolouration of fur observed on animals after exposure.
Eye irritation Draize method. 72-hour observation.	Rabbit - New Zealand White (3 ♀) Dose: 0.1mL; treated eye left unwashed and observed at 1 hour, 24, 48 and 72 hours post-instillation.	MAS [a] =2.2/110 MIS [b] = 4/110	**Minimally irritating to eye** Grade 1 redness of conjunctiva observed in all animals at 1-, 24-, and 48-hour observations. Grade 1 chemosis was observed in all animals at 24-hour observation. Irritation was completely resolved by 72-hour observation.
Dermal irritation 4-hour exposure	Rabbit - New Zealand White (3 ♀) Dose: 0.5 mL	MAS = 0/8 MIS = 0/8	**Non-irritating to skin**
Dermal Sensitization LLNA[c]	Mice: CBA/Ca01aHsd (5♀/group) Groups: 25% and 50% test substance with vehicle (3:1 acetone /olive oil), 100% test substance, and vehicle control.	Positive results Increase in lymph node weight in 25% and 50% dosage groups with SI[d] more than 3. SI: 3.2 (25%) 3.2 (50%) 1.3 (100%) EC3 value was calculated to be at a test item concentration of 33%.	**Dermal sensitizer**

*Test substance: Neu1173H (26.52% w/w FeHEDTA containing 4.43% w/w iron)

[a] MAS = Maximum Average Score for 24, 48, and 72 hrs
[b] MIS = Maximum Irritation Score
[c]LLNA = Local lymph node assay
[d]SI = Stimulation index

Table 2 Summary of toxicology from PRD2007-13.

Study	Species, Strain And Doses	Noael And Loael Mg/Kg Bw/Day	Target Organ, Significant Effects, Comments
REPRODUCTION AND DEVELOPMENTAL TOXICITY			
Single generation	F_0: 0, 0.5, 1 and 5% Na_2EDTA in diet for 12 weeks. Rats (number per dose not disclosed)	NOAEL 1% Na_2EDTA LOAEL 5% Na_2EDTA	Animals mated once they were 100 days old and 10 days after weaning. Diarrhea and ↓ food consumption at 5%. Test animals produced normal first and second litters, except at 5%, where dams failed to produce litters
Developmental toxicity	0 and 954 mg of EDTA/kg bw/day in diet for days 7 to 14 of gestation. Administered Na_2EDTA. CD rats	NOAEL < 954 mg of EDTA/kg w/day LOAEL 954 mg of EDTA/kg bw/day	<u>Maternal Toxicity</u> ↑ weight loss ($p < 0.001$) ↓ food consumption ($p < 0.001$) Severe diarrhea in all animals <u>Fetal Toxicity</u> ↓ fetal weight ($p < 0.001$) ↑ mean percentage of resorptions/litter ($p < 0.001$) ↑ mean percentage of malformed fetuses/litter ($p < 0.001$) Gross fetal malformations marked by cleft palate, micrognathia, microphthalmia, menigocoele, phocomelia, clubfoot and electrodactyly, umbilical hernia, and short curly tail. Internal malformations included great vessel anomalies, interventricular septal defects, small or missing lung lobes, missing thymus, small kidneys with associated hydronephrosis and hydroureter, and small undifferentiated gonads lateral to the kidneys. Skeletal malformations included extreme dysplasia, including shortened, missing or wavy ribs, misaligned and fused centra, as well as anomalies associated with external defects. Gross external brain malformations were also noted.
Developmental toxicity	3% (w/w) of Na_2EDTA in diet from day 6 to 14 of gestation or from day 6 to term.	Could not identify a NOAEL or LOAEL from the available information.	<u>Addition of 100 ppm zinc to the diet</u> Gross fetal malformations marked by cleft lip and palate, hydrocephalus, anencephalus, hydranencephalus, exencephalus, micro or anophthalimia, micro or agnathia, clubbed

Study	Species, Strain And Doses	Noael And Loael Mg/Kg Bw/Day	Target Organ, Significant Effects, Comments
	Sprague Dawley rats		legs, fused or missing digits, curly, short or missing tail were noted in a significant portion of the fetuses. <u>Addition of 1000 ppm zinc to the diet</u> No fetal malformations observed.
GENOTOXICITY			
STUDY	**SPECIES and STRAIN or CELL TYPE AND CONCENTRATIONS or DOSES**	**RESULTS**	
Gene mutations in bacteria	*Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538; *E. Coli* WP2uvrA Up to 1000 µg/plate without activation Up to 1000 µg/plate with activation **GENOTOXICITY**	Negative for Na_3EDTA.	
STUDY	**SPECIES and STRAIN or CELL TYPE AND CONCENTRATIONS or DOSES**	**RESULTS**	
Gene mutations in mammalian cells in vitro	L5178Y TK +/- mouse lymphoma cells 0–5000 µg/ml without activation 0–5000 µg/ml with activation	Negative for Na_3EDTA.	
Gene mutations in mammalian cells in vitro	L5178Y TK +/- mouse lymphoma cells 0–325 µg Fe/mL without activation 0–6.5 µg Fe/mL with activation	Positive for NaFeEDTA. Likely due to hydroxyl free radical produced from Fenton reaction of the available iron, not the direct result of NaFeEDTA.	

Table 3 Fate and Behaviour in the Environment

Property	Test substance	Value		Comments	Reference PMRA#
Biotransformation					
Biotransformation in aerobic soil Study carried out in aerated soil suspensions from 5 types of soils of different pHs.	FeEDTA Reaction between Fe and Na ^{14}C-labeled EDTA	pH 5.7 & 6.1 pH 6.75 pH 7.3 & 7.85	75-90 % remaining after 30 d 15-20% remaining after 30 d <5% remaining after 30 d	persistent* slightly persistent* non-persistent*	1122092
Biotransformation in anaerobic soil	FeEDTA	pH 6.0		stable (no CO_2 was	1566548

Property	Test substance	Value		Comments	Reference PMRA#
Study carried out in anaerobic soils from 3 types of agricultural soils of different pHs.	Reaction between $FeCl_3$ salt and [^{14}C]EDTA	pH 6.4 pH 7.4	not transformed	produced)	
Mobility					
Adsorption / desorption in soil Study carried out on Rehovot sand (sand, 88%; silt, 5%; clay, 7%) [pH 7.1 -7.2] in Batches equilibrium studies and column studies. Only results from column studies were valid.	FeEDTA	$K_{d\text{-}ads}$ values of K_d were estimated from break-through curves of column experiments No K_{oc} was calculated	$K_{d\text{-}ads:}$ 0.57	highly mobile in sand	1566532

Table 4 Toxicity to Non-Target Species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Reference PMRA #
Terrestrial					
Invertebrates: Bee	Oral	NEU 1173 H[b]	NOEL:12.5 µg FeHEDTA/bee LD_{50}: 83.68 µg FeHEDTA/bee	Relatively non-toxic	1566585
	Contact	NEU 1173 H	NOEC:100 µg FeHEDTA/bee LC_{50} >100 µg FeHEDTA/bee	Relatively non-toxic	1566585
Birds: Bobwhite quail	Acute	NEU 1173 H	LD_{50} >530.4 mg FeHEDTA/kg bw NOEL: 132.6 mg FeHEDTA/kg bw	Slightly toxicity	1566588
	Dietary	NEU 1173 H	LD_{50} > 307.13 mg FeHEDTA/kg bw/day NOEL: 307.13 mg FeHEDTA/kg bw/day	No toxicity at the highest dose	1566589
Rat	Acute oral	NEU 1173 H	LD_{50} > 1326 mg FeHEDTA/kg bw	No toxicity at the highest dose	1566576
Aquatic					
Invertebrates: *Daphnia magna*	Acute	NEU 1173 H	EC_{50}> 27.7 mg FeHEDTA/L NOEC: 27.7 mg FeHEDTA/L	No toxicity at the highest concentration	1566586

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Reference PMRA #
Fish: Rainbow trout	Acute	NEU 1173 H	LC_{50}> 27.7 mg FeHEDTA/L NOEC: 27.7 mg FeHEDTA/L	No toxicity at the highest concentration	1566587

[a] Atkins et al. (1981) for bees and US EPA classification for others, where applicable
[b] containing 26.52% FeHEDTA.

Table 5 Endpoints used for risk assessment and the uncertainty factors applied

Taxonomic group	Exposure	Endpoint	Uncertainty Factor
Earthworm	Acute	LC_{50}	0.5
	Chronic	NOEC	1.0
Bees	Acute	LD_{50}	1.0
Other non-target arthropods	Acute	LR_{50}	1.0
Birds	Acute oral	LD_{50}	0.1
	Dietary	LD_{50}	0.1
	Reproduction	NOEL	1.0
Mammals	Acute oral	LD_{50}	0.1
	Reproduction	NOEL	1.0
Non-target terrestrial plants	Acute	HR_5 of SSD of ER_{50}[10]	1.0
Aquatic invertebrates	Acute	EC_{50}	0.5
	Chronic	NOEC	1.0
Fish	Acute	LC_{50}	0.1
	Chronic	NOEC	1.0
Amphibians	Acute	Fish LC_{50}	0.1
	Chronic	Fish NOEC	1.0
Algae	Chronic	EC_{50}	0.5
Aquatic vascular plants	Chronic	EC_{50}	0.5

Table 6 Screening Level Risk Assessment on Non-target Species

Risks to birds and mammals								
Exposure type	**Toxicity endpoint (mg FeHEDTA /kg bw/d)**	**Food guild**	**In-field**		**Off-field**		**LOC exceeded**	
			EDE (mg FeHEDTA /kg bw)	**RQ**	**EDE (mg FeHEDTA /kg bw)**	**RQ**	**In-field**	**Off-field**
Small birds (0.02 kg)								
Acute	53.04	Insectivore (small insects)	7082.6	133.5	212.4	4.0	**Yes**	
	53.04	Granivore (grain and seeds)	1770.6	33.3	53.1	1.0		

[10] 5th percentile hazard rate of the species sensitivity distribution of ER50 values

Risks to birds and mammals								
Exposure type	**Toxicity endpoint (mg FeHEDTA /kg bw/d)**	**Food guild**	**In-field**		**Off-field**		**LOC exceeded**	
			EDE (mg FeHEDTA /kg bw)	**RQ**	**EDE (mg FeHEDTA /kg bw)**	**RQ**	**In-field**	**Off-field**
	53.04	Frugivore (fruit)	3541.3	66.7	106.2	2.0		
Dietary	307.13	Insectivore (small insects)	7082.6	23.0	212.4	0.7	**Yes**	No
	307.13	Granivore (grain and seeds)	1770.6	5.7	53.1	0.1		
	307.13	Frugivore (fruit)	3541.3	11.5	106.2	0.3		
Medium Sized Bird (0.1kg)								
Acute	530.4	Insectivore (small insects)	5527.2	104.2	165.8	3.1		**Yes**
	530.4	Insectivore (large insects)	1381.8	26.0	41.4	0.7	**Yes**	No
	530.4	Granivore (grain and seeds)	1381.8	26.0	41.4	0.7		
	530.4	Frugivore (fruit)	2763.6	52.1	82.9	1.5		**Yes**
Dietary	307.13	Insectivore (small insects)	5527.2	17.9	165.8	0.5		No
	307.13	Insectivore (large insects)	1381.8	4.4	41.4	0.1		
	307.13	Granivore (grain and seeds)	1381.8	4.4	41.4	0.1		
	307.13	Frugivore (fruit)	2763.6	8.9	82.9	0.2		
Large Sized Birds (1kg)								
Acute	530.4	Insectivore (small insects)	1613.7	30.4	48.4	0.9		No
	530.4	Insectivore (large insects)	403.4	7.6	12.1	0.2		
	530.4	Granivore (grain and seeds)	403.4	7.6	12.1	0.2		
	530.4	Frugivore (fruit)	806.8	15.2	24.2	0.4	**Yes**	
	530.4	Herbivore (short grass)	5767.4	108.7	173.0	3.2		
	530.4	Herbivore (long grass)	3521.4	66.4	105.6	1.9		**Yes**
	530.4	Herbivore (forage crops)	5336.1	100.6	160.0	3.0		
	530.4	Herbivore (leafy foliage)	10869.8	204.9	326.0	6.1		
Dietary	307.13	Insectivore (small insects)	1613.7	5.2	48.4	0.1		No
	307.13	Insectivore (large insects)	403.4	1.3	12.1	0.0		
	307.13	Granivore (grain and seeds)	403.4	1.3	12.1	0.0		

Risks to birds and mammals								
Exposure type	**Toxicity endpoint (mg FeHEDTA /kg bw/d)**	**Food guild**	**In-field**		**Off-field**		**LOC exceeded**	
			EDE (mg FeHEDTA /kg bw)	**RQ**	**EDE (mg FeHEDTA /kg bw)**	**RQ**	**In-field**	**Off-field**
	307.13	Frugivore (fruit)	806.8	2.6	24.2	0.0		
	307.13	Herbivore (short grass)	5767.4	18.7	173.0	0.5		
	307.13	Herbivore (long grass)	3521.4	11.4	105.6	0.3		
	307.13	Herbivore (forage crops)	5336.1	17.3	160.0	0.5		
	307.13	Herbivore (leafy foliage)	10869.8	35.4	326.0	1.0		**Yes**
Small Mammal (0.015 kg)								
Acute	1326	Insectivore (small insects)	4073.6	3.0	122.2	0.1	**Yes**	No
	1326	Granivore (grain and seeds)	1018.4	0.7	30.5	0.0	No	
	1326	Frugivore (fruit)	2036.8	1.5	61.1	0.0	**Yes**	
Medium Sized Mammal (0.035 kg)								
Acute	1326	Insectivore (small insects)	3571.0	2.7	107.1	0.0	**Yes**	No
	1326	Insectivore (large insects)	892.7	0.6	26.7	0.0	No	No
	1326	Granivore (grain and seeds)	892.7	0.6	26.7	0.0		
	1326	Frugivore (fruit)	1785.5	1.3	53.5	0.0	**Yes**	
	1326	Herbivore (short grass)	12762.9	9.6	382.8	0.2		
	1326	Herbivore (long grass)	7792.7	5.8	233.7	0.1		
	1326	Herbivore (forage crops)	11808.4	8.9	354.2	0.2		
	1326	Herbivore (leafy foliage)	24054.2	18.1	721.6	0.5		
Large Sized Mammal (1kg)								
Acute	1326	Insectivore (small insects)	1908.1	1.4	57.2	0.0	**Yes**	No
	1326	Insectivore (large insects)	477.0	0.3	14.3	0.0	No	
	1326	Granivore (grain and seeds)	477.0	0.3	14.3	0.0		
	1326	Frugivore (fruit)	954.0	0.7	28.6	0.0		
	1326	Herbivore (short grass)	6819.6	5.1	204.5	0.1	**Yes**	
	1326	Herbivore (long grass)	4163.9	3.1	124.9	0.1		
	1326	Herbivore (forage crops)	6309.6	4.7	189.2	0.1		
	1326	Herbivore (leafy foliage)	12852.9	9.7	385.5	0.2		

Table 7 Screening Level Risk Assessment on Non-Target Species

Risk to aquatic organisms					
Organism	**Exposure**	**Endpoint value** (mg FeHEDTA/L)	**EEC** (mg FeHEDTA/L)	**RQ**	**LOC exceeded**
Freshwater species					
Daphnia magna	Acute	$EC_{50} \div 2 > 13.85$	7.8	<0.56	No
Rainbow trout	Acute	$LC_{50} > 27.7$	7.8	<0.28	No
Amphibian	Acute	$LC_{50} > 27.7$	41.6	<1.5	Yes

Table 8 Refined Risk Assessment on Non-Target Species

Refined Risks to birds and mammals								
Exposure type	**Toxicity endpoint (mg FeHEDTA /kg bw/d)**	**Food guild**	**Mean nomogram residues**					
			In-field			**Off-field**		
			EDE (mg FeHEDTA /kg bw)	**RQ**	**LOC exceeded**	**EDE (mg FeHEDTA /kg bw)**	**RQ**	**LOC exceeded**
Small Birds (0.02 kg)								
Acute	53.04	Insectivore (small insects)	2156.1	40.6		64.6	1.2	**Yes**
	53.04	Granivore (grain and seeds)	460.9	8.6		13.8	0.2	
	53.04	Frugivore (fruit)	921.9	17.3	**Yes**	27.6	0.5	
Dietary	307.13	Insectivore (small insects)	2156.1	7.0		64.6	0.2	No
	307.13	Granivore (grain and seeds)	460.9	1.5		13.8	0.0	
	307.13	Frugivore (fruit)	921.9	3.0		27.6	0.1	
Medium Sized Birds (0.1 kg)								
Acute	53.04	Insectivore (small insects)	1682.6	31.7		50.4	0.9	
	53.04	Insectivore (large insects)	359.7	6.7		10.7	0.2	
	53.04	Granivore (grain and seeds)	359.7	6.7		10.7	0.2	
	53.04	Frugivore (fruit)	719.4	13.5		21.5	0.4	No
Dietary	307.13	Insectivore (small insects)	1682.6	5.4	**Yes**	50.4	0.1	
	307.13	Insectivore (large insects)	359.7	1.1		10.7	0.0	
	307.13	Granivore (grain and seeds)	359.7	1.1		10.7	0.0	
	307.13	Frugivore (fruit)	719.4	2.3		21.5	0.0	
Large Sized Birds (1kg)								
Acute	530.4	Insectivore (small insects)	491.2	9.2		14.7	0.2	No
	530.4	Insectivore (large insects)	105.0	1.9		3.15	0.0	
	530.4	Granivore (grain and seeds)	105.0	1.9		3.1	0.0	
	530.4	Frugivore (fruit)	210.0	3.9		6.3	0.1	
	530.4	Herbivore (short grass)	1118.0	21.0	**Yes**	33.5	0.6	
	530.4	Herbivore (long grass)	627.6	11.8		18.8	0.3	
	530.4	Herbivore (forage crops)	962.9	18.1		28.8	0.5	
	530.4	Herbivore (leafy foliage)	1961.4	36.9		58.8	1.1	**Yes**
Dietary	307.13	Insectivore (small insects)	491.2	1.5		14.7	0.0	
	307.13	Insectivore (large insects)	105.0	0.3		3.1	0.0	
	307.13	Granivore (grain and seeds)	105.0	0.3	No	3.1	0.0	
	307.13	Frugivore (fruit)	210.0	0.6		6.3	0.0	
	307.13	Herbivore (short grass)	1118.0	3.6		33.5	0.1	No
	307.13	Herbivore (long grass)	627.6	2.0	**Yes**	18.8	0.0	
	307.13	Herbivore (forage crops)	962.9	3.1		28.8	0.0	
	307.13	Herbivore (leafy foliage)	1961.4	6.3		58.8	0.1	
Small Mammal (0.015 kg)								
Acute	1326	Insectivore (small insects)	1240.1	0.9	No	37.2	0.0	
Medium Sized Mammals (0.035 kg)								
Acute	1326	Insectivore (small insects)	1087.1	0.8	No	32.6	0.0	
	1326	Frugivore (fruit)	464.8	0.3		13.9	0.0	

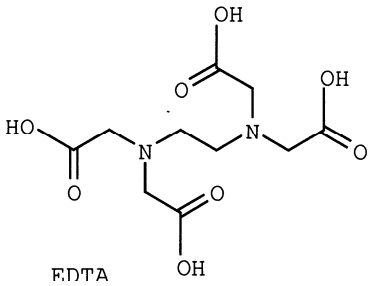
Refined Risks to birds and mammals								
Exposure type	Toxicity endpoint (mg FeHEDTA /kg bw/d)	Food guild	Mean nomogram residues					
			In-field			Off-field		
			EDE (mg FeHEDTA /kg bw)	RQ	LOC exceeded	EDE (mg FeHEDTA /kg bw)	RQ	LOC exceeded
	1326	Herbivore (short grass)	2474.2	1.8	Yes	74.2	0.0	No
	1326	Herbivore (long grass)	1388.9	1.0		41.6	0.0	
	1326	Herbivore (forage crops)	2130.8	1.6		63.9	0.0	
	1326	Herbivore (leafy foliage)	4340.6	3.2		130.2	0.0	
Large Sized Mammals (1 kg)								
Acute	1326	Insectivore (small insects)	580.8	0.4	No	17.4	0.0	No
	1326	Herbivore (short grass)	1322.0521	0.9		39.6	0.0	
	1326	Herbivore (long grass)	742.1880	0.5		22.2	0.0	
	1326	Herbivore (forage crops)	1138.5844	0.8		34.1	0.0	
	1326	Herbivore (leafy foliage)	2319.3386	1.7	**Yes**	69.5	0.0	

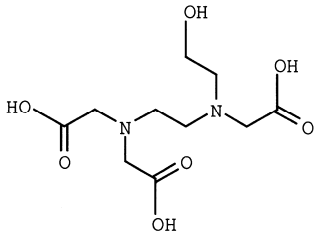
Table 9 Toxic Substances Management Policy (TSMP) Considerations-Comparison to Toxic Substances Management Policy

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	Not expected to be persistent
	Water	Half-life ≥ 182 days	14 - 56.8 min
	Sediment	Half-life ≥ 365 days	< 5 d (aerobic aquatic system)
	Air	Half-life ≥ 2 days or evidence of long range transport	Not expected to be volatile
Bioaccumulation[4]	Log $K_{OW} \geq 5$		<0
	BCF ≥ 5000		Not required
	BAF ≥ 5000		Not required
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 CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (id est, all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgment, 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 (exempli gratia, BAFs) are preferred over laboratory data (exempli gratia, BCFs) which, in turn, are preferred over chemical properties (exempli gratia, log K_{OW}).

Figure 1. Structural formulas of EDTA and HEDTA.





EDTA
(ethylenediaminetetraacetic acid)

HEDTA
(hydroxyethylethylenediaminetriacetic acid)

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
1753329	1753329 2009, Binder 2 Amended, DACO: 2.0, 2.1, 2.11, 2.11.1, 2.11.2, 2.11.3, 2.11.4, 2.12, 2.12.1, 2.12.2, 2.13, 2.13.1, 2.13.2, 2.13.3, 2.13.4, 2.14, 2.14.1, 2.14.10, 2.14.11, 2.14.12, 2.14.13, 2.14.14, 2.14.2, 2.14.3, 2.14.4, 2.14.5, 2.14.6, 2.14.7, 2.14.8, 2.14.9, 2.15, 2.16,2.2, 2.3, 2.3.1, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9 CBI
1791534	2009, NEU1173H TGAI Clarification Response, DACO: 0.1.6003, 2.11.2, 2.11.3, 2.12.2, 2.13.1 CBI
1753341	2009, 5-batch Analysis of NEU1173H TGAI - HEDTA, DACO: 2.13.3 CBI
1768339	2009, 5-Batch Analysis of Neu 1173H TGAI, DACO: 2.13, 2.13.1, 2.13.2, 2.13.3 CBI
1768340	2009, 5-Batch Analysis of Neu 1173H TGAI Appendices, DACO: 2.13, 2.13.1, 2.13.2, 2.13.3 CBI
1768341	2009, 5-Batch Analysis of Neu1173H TGAI for Nitrilotriacetate, Ethylenediaminetetraacetate and Hydroxyacetate, DACO: 2.13, 2.13.1, 2.13.2, 2.13.3 CBI
1753345	2009, Analysis of Iron in NEU1173H by ICP-MS in support of Eco-Care Study 1173-2W54-2M40-081216 "Accelerated (w weeks 54C, 2 months 40C) Storage Stability of NEU1173H", DACO: 2.14.14 CBI
1791535	2007, Method SOP IC/003, DACO: 2.13.1 CBI
1791536	2008, Method SOP 91-CM-006-00, DACO: 2.13.1 CBI
1791537	2009, NEU1173H TGAI Chromatograms, DACO: 2.11.3 CBI
1791534	2009, NEU1173H TGAI Clarification Response, DACO: 0.1.6003, 2.11.2, 2.11.3, 2.12.2, 2.13.1 CBI
1768838	Binder 2 Addendum June 23, 2009, DACO: 2.0, 2.11.4, 2.12, 2.12.1, 2.12.2, 2.13, 2.13.1, 2.13.2, 2.13.3, 2.13.4 CBI
1566571	2008, Binder 2, DACO: 2.0, 2.1, 2.11, 2.11.1, 2.11.2, 2.11.3, 2.11.4, 2.12, 2.12.1, 2.12.2, 2.13, 2.13.1, 2.13.2, 2.13.3, 2.13.4, 2.14, 2.14.1, 2.14.10, 2.14.11, 2.14.12, 2.14.13, 2.14.14, 2.14.2, 2.14.3, 2.14.4, 2.14.5, 2.14.6, 2.14.7, 2.14.8, 2.14.9, 2.2, 2.3, 2.3.1, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9 CBI
1566574	2008, Ambient (1 year) Storage Stability of NEU1173H, DACO: 2.14.14 CBI
1753343	2009, UV Visible Absorption, DACO: 2.14.12 CBI
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