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Proposed Registration Decision

PRD2022-05

Prohexadione-calcium and Anuew Plant Growth Regulator

(publié aussi en français)

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Overview

Proposed Registration Decision for Prohexadione-calcium

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 Nufarm Prohexadione Calcium Technical Plant Growth Regulator and Anuew Plant Growth Regulator, containing the technical grade active ingredient prohexadione-calcium, for growth management of the following turfgrass species: Bentgrass, annual and perennial *Poa annua*, Kentucky bluegrass, perennial ryegrass, tall fescue and fine fescue, growing on golf courses, sod farms, sports fields, municipal sites and cemeteries.

Prohexadione-calcium is currently registered for use on apple, cherry and strawberry. For details, see Regulatory Note REG2006-07, *Prohexadione Calcium* and Proposed Registration Decision PRD2009-05, *Prohexadione Calcium*.

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 prohexadione-calcium and Anuew Plant Growth Regulator.

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 acceptable¹ 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 value² 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.

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."

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 section](#) of Canada.ca.

Before making a final registration decision on prohexadione-calcium and Anuew Plant Growth Regulator, 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 Decision⁴ on prohexadione-calcium and Anuew Plant Growth Regulator, 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 Prohexadione-calcium?

Prohexadione-calcium is a plant growth regulator used for growth management of select turfgrass species.

Health considerations

Can approved uses of Prohexadione-calcium affect human health?

Anuew Plant Growth Regulator, containing Prohexadione-calcium, is unlikely to affect your health when used according to label directions.

Potential exposure to prohexadione-calcium may occur through the diet (food and drinking water), when handling and applying the end-use product, or when coming into contact with treated surfaces. When assessing health risks, two key factors are considered: the levels at which 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.

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*.

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 dose levels 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 prohexadione-calcium was of low acute toxicity by the oral, dermal, and inhalation routes of exposure. It was minimally irritating to the eyes and non-irritating to the skin, and did not cause an allergic skin reaction.

The acute toxicity of the end-use product Anuew Plant Growth Regulator containing prohexadione-calcium 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.

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 prohexadione-calcium 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 kidneys, decreased body weight, and abortions. 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.

Risks in residential and other non-occupational environments

Residential risks are not of concern when Anuew Plant Growth Regulator is used according to the proposed label directions and re-entry intervals are observed.

Adults, youth and children golfing or playing on treated turf can come into direct contact with Anuew Plant Growth Regulator residues. Therefore, the label requires that all individuals not enter treated golf courses, sports fields, municipal fields and cemeteries until sprays have dried. Taking into consideration the label statements, number of applications and duration of exposure, risks to individuals golfing and playing on treated turf are not a concern.

Occupational risks from handling Anuew Plant Growth Regulator

Occupational risks are not of concern when Anuew Plant Growth Regulator is used according to the proposed label directions, which include protective measures.

Workers who mix, load and apply Anuew Plant Growth Regulator as well as postapplication workers entering freshly treated sites can come in direct contact with Anuew Plant Growth Regulator residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying Anuew Plant Growth Regulator must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks.

The label also requires that workers not enter treated fields until sprays have dried, except for sod farms where re-entry is permitted following the restricted-entry interval (REI) of 12 hours. Taking into consideration these label statements, the number of applications and the exposure period for workers, risks to these individuals are not a concern.

To address potential exposure to bystanders, best practice label statements are required to prohibit the presence of individuals in the treated area during application and to minimize human exposure from spray drift.

Environmental considerations

What happens when Anuew Plant Growth Regulator is introduced into the environment?

When Anuew Plant Growth Regulator, containing prohexadione-calcium, is used according to the label, the risks to the environment are acceptable.

Prohexadione-calcium is not expected to build-up in the environment, and toxicity to non-target organisms is expected to be low. When used as per the label directions, the product Anuew Plant Growth Regulator is expected to pose acceptable risks to the environment.

Value considerations

What is the value of Anuew Plant Growth Regulator?

Anuew Plant Growth Regulator is a plant growth regulator used for slowing vertical growth, reducing mowing frequency and enhancing colour and quality of select turfgrass species growing on golf courses, sod farms, sports fields, municipal sites and cemeteries.

Anuew Plant Growth Regulator will serve as an additional option for turfgrass growth management and align with an option that is presently available to users in the United States.

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 Anuew Plant Growth Regulator to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Human health

Because there is a concern with users coming into direct contact with Anuew Plant Growth Regulator on the skin or through inhalation of spray mists, anyone mixing, loading and applying Anuew Plant Growth Regulator must wear a long-sleeved shirt, long pants, chemical-resistant gloves, shoes and socks. In addition, a restriction from applying in and around homes and a standard label statement to protect against drift during application were added to the label.

Environment

A precautionary label statement stating, “toxic to aquatic plants,” and 1 m aquatic spray buffer zones are required.

Next steps

Before making a final registration decision on prohexadione-calcium and Anuew Plant Growth Regulator, 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 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 prohexadione-calcium and Anuew Plant Growth Regulator (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. For more information, please contact the PMRA’s Pest Management Information Service.

Science evaluation

Prohexadione-calcium and Anuew Plant Growth Regulator

1.0 The active ingredient, its properties and uses

1.1 Identity of the active ingredient

Active substance Prohexadione-calcium

Function Plant growth regulator

Chemical name

1. International Union of Pure and Applied Chemistry (IUPAC) calcium bis(3,5-dioxo-4-propionylcyclohexanecarboxylate)

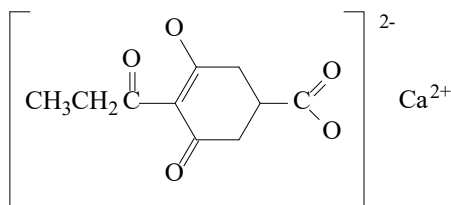
2. Chemical Abstracts Service (CAS) cyclohexanecarboxylic acid, 3,5-dioxo-4-(1-oxopropyl)-, ion(1-), calcium, calcium salt (2:1:1)

CAS number 127277-53-6

Molecular formula C₂₀H₂₂CaO₁₀

Molecular weight 250.26

Structural formula



Purity of the active ingredient 94%

1.2 Physical and chemical properties of the active ingredient and end-use product

Technical product—Nufarm prohexadione calcium technical plant growth regulator

Property	Result
Colour and physical state	Pale yellow solid
Odour	Sweet odour
Melting range	> 360°C
Boiling point or range	Not applicable
Density	1.46 g/mL at 22°C

Property	Result														
Vapour pressure at 20°C	1.335×10^{-5} Pa														
Ultraviolet (UV)-visible spectrum	No UV absorption observed at $\lambda > 300$ nm														
Solubility in water at 20°C	174.2 g/L														
Solubility in organic solvents at 20°C	<table> <tr> <th>Solvent</th><th>Solubility (mg/L)</th></tr> <tr> <td>methanol</td><td>1.11 ± 0.24</td></tr> <tr> <td>acetone</td><td>0.038 ± 0.01</td></tr> <tr> <td>toluene</td><td>0.004 ± 0.003</td></tr> <tr> <td>hexane</td><td>< 0.003</td></tr> <tr> <td>dichloromethane</td><td>0.004 ± 0.001</td></tr> <tr> <td>propan-2-ol</td><td>0.105 ± 0.009</td></tr> </table>	Solvent	Solubility (mg/L)	methanol	1.11 ± 0.24	acetone	0.038 ± 0.01	toluene	0.004 ± 0.003	hexane	< 0.003	dichloromethane	0.004 ± 0.001	propan-2-ol	0.105 ± 0.009
Solvent	Solubility (mg/L)														
methanol	1.11 ± 0.24														
acetone	0.038 ± 0.01														
toluene	0.004 ± 0.003														
hexane	< 0.003														
dichloromethane	0.004 ± 0.001														
propan-2-ol	0.105 ± 0.009														
<i>n</i> -Octanol-water partition coefficient (K_{ow})	$\log K_{ow} = -2.9 \pm 0.08$														
Dissociation constant (pK_a)	5.15														
Stability (temperature, metal)	Stable when exposed to temperatures of 21°C and 54°C for 14 days each, to sunlight for 48 hours and to metals (tin, aluminium and iron).														

End-use product—Anuew plant growth regulator

Property	Result
Colour	Tan
Odour	Not provided
Physical state	Solid
Formulation type	Wettable granule
Label concentration	27.5%
Container material and description	0.5 kg to bulk plastic bags and pouches
Density	0.265 kg/L at 23.3°C
pH of 1% dispersion in water	6.83 at 23.4°C
Oxidizing or reducing action	This product does not contain any oxidizing or reducing agents
Storage stability	Stable when stored for 12 months at room temperature
Corrosion characteristics	Non-corrosive
Explodability	Not explosive

1.3 Directions for use

Anuew Plant Growth Regulator is applied at 38.5 to 308.5 g a.i./ha in mixture with a non-ionic surfactant at 0.125% v/v (125 mL/100 L water) using ground application equipment to turfgrass that is green and actively growing. The upper end of the rate range (154 g a.i./ha or greater) may be used for select turfgrass species growing on golf courses (fairways and roughs) and sod farms, sports fields, municipal cites and cemeteries, including Kentucky bluegrass, perennial ryegrass, tall fescue and fine fescue. For these use sites, reapplications may be made after 1–4 weeks (with a 280–350 growing degree day (GDD) interval). The lower end of the rate range (up to 154 g a.i./ha) may be used for bentgrass and annual and perennial *Poa annua* cultivars growing on golf courses (fairways, roughs, greens and tees). For golf course fairways and roughs, reapplications may be made after 1–4 weeks (with a 280–350 GDD interval), whereas greens and tees may have reapplications after a 280–300 GDD interval. Regardless of use site, an annual maximum of 6000 g a.i./ha may be made per year.

1.4 Mode of action

Prohexadione-calcium blocks certain stages of the biosynthesis of active gibberellins. Gibberellin is a phytohormone that promotes growth of various plant organs. The resulting lower content of growth-active gibberellins leads to a decrease in cell elongation and hence a slowing of vertical growth.

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.

3.0 Impact on human and animal health

3.1 Hazard assessment

3.1.1 Toxicology summary

A detailed review of the toxicology database for prohexadione-calcium was conducted previously and is summarized in the Regulatory Note, REG2006-07, *Prohexadione Calcium*. The acute toxicity of Apogee Plant Growth Regulator, is also summarized in REG2006-07, and is considered adequate to characterize the acute toxicity of Anuew Plant Growth Regulator. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes, as well as two additional rabbit developmental toxicity studies. The studies

were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is acceptable and the database is considered adequate to characterize the potential health hazards associated with prohexadione-calcium.

No new toxicology studies were provided to support the proposed expansion of use for prohexadione-calcium. In order to ensure that the risk assessment provides adequate protection against potential effects in the young, the results of the reproductive and developmental toxicity studies were revisited. No changes were made to the effect levels in the previous assessment of the developmental toxicity studies in the rat or rabbit. In the 2-generation reproductive toxicity study in rats, the offspring NOAEL was revised to reflect changes in F1 pup body weight at the mid-dose level, in the presence of parental toxicity. There was no evidence of increased sensitivity of the young in the database.

Results of the reproductive toxicity study are summarized in Appendix I, Table 1. The toxicology reference values for use in the human health risk assessment are summarized in Appendix I, Table 2.

3.1.2 *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 an oral gavage developmental toxicity study in rats and multiple studies in rabbits and a dietary 2-generation reproductive toxicity study in rats.

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 gavage prenatal developmental toxicity studies or dietary reproductive study. In the 2-generation rat reproductive toxicity study, a decrease in body weight of F1 pups was observed in the presence of parental toxicity. No developmental effects were observed in the rat developmental toxicity study; however, a serious effect, abortions, was observed in rabbits in the presence of other maternal toxicity (body weight loss prior to aborting and maternal death).

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 on the young are well-characterized and occurred in the presence of maternal toxicity. The abortions were considered a serious endpoint, although the concern was tempered by the presence of maternal toxicity.

Therefore, the *Pest Control Products Act* (PCPA) factor was reduced to threefold when using the rabbit developmental toxicity studies to establish the point of departure for human health risk assessment. Where the point of departure from the rabbit developmental toxicity studies not used for risk assessment, the PCPA factor was reduced to onefold.

3.2 Toxicology reference values

3.2.1 Occupational and residential toxicology references values

Occupational exposure to Anuew Plant Growth Regulator is characterized as intermediate- to long-term duration, with the exception of postapplication activities characterized as long-term duration. Exposures are predominantly by the dermal and inhalation routes for mixers/loaders/applicators, by the dermal route for postapplication workers and adults, youth and children, as well as, the incidental oral route for children (1<2 years).

Short- and intermediate-term dermal and inhalation (adults)

For the short- to intermediate-term dermal and inhalation risk assessments of subpopulations excluding children, a combined NOAEL of 150 mg/kg/day from the three available rabbit developmental toxicity studies was selected. At dose levels of 200 mg/kg bw/day and higher, increased abortions were observed in the presence of maternal toxicity. The existing 28-day dermal toxicity study did not address the endpoint of concern, and no repeat-exposure inhalation toxicity study was available, thus necessitating the use of an oral study for risk assessment.

For residential scenarios, the target margin of exposure (MOE) selected for this endpoint is 300. Tenfold factors were applied each for interspecies extrapolation and intraspecies variability. As outlined in the *Pest Control Products Act* hazard characterization section, the PCPA factor was reduced to threefold. The selection of this study and target MOE is considered to be protective of all populations, including females 13–49 years of age and the unborn children of exposed women.

For occupational scenarios, the target MOE for this endpoint is 300. Tenfold factors were applied each for interspecies extrapolation and intraspecies variability. As the worker population could include pregnant women, it is necessary to afford adequate protection of the fetus that may be exposed via its mother. In light of concerns regarding prenatal toxicity, as outlined in the *Pest Control Products Act* hazard characterization section, an additional threefold factor was applied to this endpoint to protect for a sensitive subpopulation, namely females 13–49 years of age.

Short- and intermediate-term dermal (children)

For short- and intermediate-term dermal risk assessments for children, an offspring NOAEL of 36 mg/kg bw/day from the dietary 2-generation reproductive toxicity study in rats was selected. At the dose level of 385 mg/kg bw/day, decreased offspring body weight was observed in the presence of parental toxicity. The existing short-term dermal toxicity study did not address the endpoint of concern in children, thus necessitating the use of an oral study for risk assessment.

For residential scenarios, the target MOE selected for this endpoint is 100. Tenfold factors were applied each for interspecies extrapolation and intraspecies variability. As outlined in the *Pest Control Products Act* hazard characterization section, the PCPA factor was reduced to onefold. The selection of this study and target MOE is considered to be protective of the target population, namely children.

Long-term dermal and inhalation (all populations)

For long-term dermal and inhalation risk assessments, a NOAEL of 20 mg/kg bw/day from the 1-year oral toxicity study in dogs was selected. At a dose level of 200 mg/kg bw/day, effects on the kidneys were observed. The use of the 28-day dermal toxicity study was not considered appropriate for a long-term dermal scenario as there was evidence of increased toxicity with increased duration of dosing in the database. With regards to the selection of a reference value for the long-term inhalation risk assessment, a repeat-dose inhalation toxicity study was not available, thus necessitating the use of an oral study for risk assessment.

The target MOE for these scenarios is 100, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The selection of this study and target MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

Short-and intermediate-term incidental oral (children)

For short- and intermediate-term incidental oral risk assessments for children, the offspring NOAEL of 36 mg/kg bw/day from the 2-generation dietary reproductive toxicity study in rats was selected. At a dose level of 385 mg/kg bw/day, there was a decrease in offspring body weight in the presence of parental toxicity.

For residential scenarios, the target MOE selected for this endpoint is 100. Ten-fold factors were applied each for interspecies extrapolation and intraspecies variability. As outlined in the *Pest Control Products Act* hazard characterization section, the PCPA factor was reduced to onefold. The selection of this study and target MOE is considered to be protective of the target population, namely children.

Long-term incidental oral (children)

For long-term incidental oral risk assessment for children, a NOAEL of 20 mg/kg bw/day from the 1-year oral toxicity study in dogs was selected. At a dose level of 200 mg/kg bw/day, effects on the kidneys were observed.

For residential scenarios, the target MOE selected for this endpoint is 100. Tenfold factors were applied each for interspecies extrapolation and intraspecies variability. As outlined in the *Pest Control Products Act* hazard characterization section, the PCPA factor was reduced to onefold. The selection of this study and target MOE is considered to be protective of the target population, namely children.

3.2.2 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. The abortions noted in rabbits occurred late in gestation and are not considered relevant to a single exposure.

3.2.3 Acceptable daily intake (ADI)

To estimate risk following repeated dietary exposure, the NOAEL of 20 mg/kg bw/day from the 1-year oral toxicity study in dogs was selected. At the LOAEL of 200 mg/kg bw/day, effects on the kidneys were observed. This study provides the lowest NOAEL in the database. 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 proposed is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{20 \text{ mg/kg bw/day}}{100} = 0.2 \text{ mg/kg/day of prohexadione-calcium.}$$

This ADI provides a margin of 750 to the combined NOAEL for abortions observed in the rabbits developmental toxicity studies.

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). Short-, intermediate-, and long-term aggregate exposure to prohexadione-calcium in children and adult populations may be comprised of food, drinking water and residential exposure via the incidental oral (children only) and dermal routes.

The toxicology endpoint selected for short- and intermediate-term aggregation for adults was abortions. For the oral and dermal exposure scenarios of all durations in adults, the NOAEL of 150 mg/kg bw/day from the oral developmental toxicity studies in rabbits was selected with a target MOE of 300. The PCPA factor for both routes was threefold as set out in the *Pest Control Products Act* hazard characterization section.

The toxicology endpoint selected for short- and intermediate-term oral and dermal exposure scenarios in children was decreased body weight. For the oral and dermal routes, the offspring NOAEL of 36 mg/kg bw/day from the dietary reproductive toxicity study in rats was selected with a target MOE of 100. The PCPA factor was onefold as set out in the *Pest Control Products Act* hazard characterization section.

The toxicology endpoint selected for long-term oral and dermal exposure scenarios in all populations was kidney effects. For long-term oral and dermal routes, the NOAEL of 20 mg/kg bw/day from the 1-year oral toxicity study in dogs was selected with a target MOE of 100. The PCPA factor was onefold as set out in the *Pest Control Products Act* hazard characterization section.

3.3 Dermal absorption

A chemical-specific dermal absorption study was not submitted and is not on file for prohexadione-calcium. Therefore, the default dermal absorption value of 100% was used in the occupational and residential exposure assessments.

3.4 Occupational and residential exposure assessment

3.4.1 Occupational exposure and risk assessment

3.4.1.1 Mixer, loader and applicator exposure and risk assessment

Workers have the potential for exposure to Anuew Plant Growth Regulator during mixing, loading and application. Dermal and inhalation exposure estimates for workers mixing and loading wettable granules and applying liquids were generated using the data from the Agricultural Handlers Exposure Task Force (AHETF) and Outdoor Residential Exposure Task Force (ORETF).

Exposure to workers mixing, loading and applying Anuew Plant Growth Regulator is expected to be of intermediate- to long-term duration and to occur primarily by the dermal and inhalation routes. Exposure estimates were derived for mixers/loaders and applicators applying Anuew Plant Growth Regulator to sod farms, golf courses, sports fields, municipal sites and cemeteries using groundboom and handheld equipment. The exposure estimates are based on mixers/loaders and applicators wearing a single layer plus chemical-resistant gloves.

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

Total (dermal + inhalation) exposures were estimated by coupling the unit exposure values with the amount of active ingredient 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 (no observed adverse effects levels) to obtain the margins of exposure (MOE); the target MOEs are 300 for intermediate-term and 100 for long-term durations. Calculated MOEs were greater than the target MOEs; therefore, there are no health risks of concern (Appendix I, Table 3).

3.4.1.2 Exposure and risk assessment for workers entering treated areas

There is potential for exposure to postapplication workers entering areas treated with Anuew Plant Growth Regulator to complete such tasks as transplanting, mowing, watering, fertilizing and seeding. Given the nature of activities performed, contact with treated turf is expected to be primarily via the dermal route. Based on the number and frequency of applications, and in the absence of chemical-specific dissipation data for turf transferable residues, it was assumed that transferable residues of prohexadione-calcium would remain on turf several days/weeks following the final application; and therefore, the duration of exposure would be long-term.

Inhalation exposure is not considered to be a significant route of exposure for people entering or contacting treated turf due to the combination of the low vapour pressure of prohexadione-calcium (1.34×10^{-8} kPa at 20°C) and the expected dilution in outdoor air. In addition, any spray droplets in the air would be expected to have settled when entry is permitted and residues have dried.

Dermal exposure to workers entering treated areas is estimated by coupling the default turf transferable residue values with activity-specific transfer coefficients. Activity-specific transfer coefficients are based on data from the Agricultural Reentry Task Force (ARTF). Chemical-specific turf transferable residue data were not submitted. As such, a default turf transferable residue value, calculated assuming 1% of the application rate and 10% daily dissipation, was used in the exposure assessment.

Exposure estimates were compared to the toxicological reference value to obtain the MOE; the target MOE is 100. Calculated MOEs were greater than the target MOE of 100; therefore, there are no health risks of concern (Appendix I, Table 4).

3.4.2 Residential exposure and risk assessment

3.4.2.1 Postapplication exposure and risk assessment

There is potential exposure for adults, youth and children entering treated golf courses, sports fields, municipal sites and cemeteries treated with Anuew Plant Growth Regulator. Contact with treated turf via the dermal route is expected for individuals of all ages, as well as, the incidental oral route for children (1 to <2 years). Based on the potential for residues to remain several days/weeks after the final application, the duration of exposure is expected to be long-term.

Chemical-specific turf transferable residue data were not submitted. As such, a default turf transferable residue (TTR), estimated using 1% of the application rate coupled with a daily dissipation of 10% and 19 applications at the maximum supported rate of 0.308 kg a.i./ha, is used for the residential exposure assessments.

Dermal exposure to golfers (adults, youth 11<16 years, children 6<11 years) is estimated by coupling the default peak TTR value with the activity-specific transfer coefficient from the USEPA 2012 Residential SOP. Exposure estimates were compared to the toxicological reference value to obtain an MOE; the target MOE is 100. Calculated MOEs were greater than the target MOE on the day of application; therefore, there are no health risks of concern for golfers (Appendix I, Table 5).

For high-contact turf activities, risk assessments were conducted for two scenarios: 1) a short- to intermediate-term risk assessment using the peak TTR values, and 2) a long-term risk assessment using time-weighted average (TWA) TTR values. Peak residues would be expected to occur for a shorter duration of time, whereas for the long-term risk assessment the average exposure using the TWA TTR would be appropriate. The calculated dermal MOEs for adults and children were greater than the target MOEs on the day of application, when considering the default peak TTR value and comparing the exposures to the short- to intermediate-term reference values. Using the TWA TTR to calculate exposures and comparing these against the long-term reference values, the calculated MOEs were greater than the target MOEs on the day of application. As such, health risks are not of concern, and adults and children can enter the treated turf area once the sprays have dried (Appendix I, Tables 6 and 7).

Additionally, for high-contact turf activities, incidental oral exposure to children (1<2 years) is estimated via hand-to-mouth and object-to-mouth exposures using the peak TTR and TWA TTR as described above. The calculated MOEs for children exceed the target MOE on the day of application. As such, health risks are not of concern and children can enter the treated turf once the sprays have dried (Appendix I, Tables 8 and 9).

3.4.3 Bystander exposure and risk assessment

Any potential bystander dermal exposure would be expected to be less than from high-contact activities on treated turf which was assessed for adults and children and for which there were no risks of concern.

Furthermore, best practice label statements are required to prohibit the presence of individuals in the treated area during application and to minimize human exposure from spray drift.

3.5 Dietary exposure and risk assessment

3.5.1 Dietary risk assessment

Chronic (non-cancer) dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 4.02, 05-10-c), which incorporates consumption data from the National Health and Nutrition Examination Survey/What We Eat in America (NHANES/WWEIA) for the year 2005–2010.

3.5.1.1 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.

3.5.1.2 Chronic dietary exposure results and characterization

The following criteria were applied to the basic non-cancer chronic analysis for prohexadione-calcium: 100% crop treated, default processing factors, Canadian maximum residue limits (MRLs), and American tolerances for imported commodities. The basic chronic dietary exposure from all supported prohexadione-calcium food uses (alone) for the total population, including infants and children, and all representative population subgroups is less than 20% of the ADI. Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that chronic dietary exposure to prohexadione-calcium from food and drinking water (EEC value = 0.015 ppm, Level I, surface water) is 3% (0.0049 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 20% (0.0391 mg/kg bw/day) of the ADI.

3.6 Aggregate exposure and risk assessment

There is potential for individuals to be exposed concurrently to prohexadione-calcium via different routes and pathways of exposure. As such, the following exposure scenarios are aggregated:

- Long-Term Golfer Dermal Exposure + Dietary Exposure (Adults, Youth 11<16 years, Children 6<11 years)
- Short- to Intermediate Term High Contact Lawn Activities Dermal Exposure (Adults) + Dietary Exposure (Adults)
- Short- to Intermediate-Term High Contact Lawn Activities Dermal Exposure (Children 1<2 years) + High Contact Lawn Activities Hand-to-Mouth Exposure (Children 1<2 years) + Dietary Exposure (Children 1<2 years)
- Long-Term High Contact Lawn Activities Dermal Exposure (Adults) + Dietary Exposure (Adults)
- Long-Term High Contact Lawn Activities Dermal Exposure (Children 1<2 years) + High Contact Lawn Activities Hand-to-Mouth Exposure (Children 1<2 years) + Dietary Exposure (Children 1<2 years)

Exposure estimates are compared to the toxicological reference values to obtain an MOE. Calculated MOEs are greater than the target MOEs, therefore, there are no health risks of concern from aggregate exposure to adults, youth and children (Appendix I, Tables 10 and 11).

3.7 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 prohexadione-calcium. Prohexadione-calcium is part of a group of plant growth regulators that acts as a gibberellin biosynthesis inhibitor. Other pesticides of the same class that are known to target the inhibition of gibberellic acid are registered in Canada; however the toxicological effects following exposure to this class of plant growth regulators are considered indicative of more generalized toxicity, and a common mechanism of mammalian toxicity has not been identified. Therefore, a cumulative risk assessment is not required at this time.

3.8 Health incident reports

As of 15 September 2021, no health incident reports have been submitted to the PMRA.

4.0 Impact on the environment

4.1 Fate and behaviour in the environment

Prohexadione-calcium is not expected to persist in the environment based on laboratory and field studies. Aerobic soil biotransformation is the major route of dissipation. Prohexadione-calcium has low to moderate mobility in soil. The potential to leach is considered to be low, mainly due to rapid degradation. Prohexadione-calcium is not expected to bioaccumulate.

For more details on environmental fate, please refer to the Regulatory Note for prohexadione-calcium (REG2006-07).

4.2 Environmental risk characterization

For details on ecotoxicity, please refer to the Regulatory Note and Proposed Registration Decision for prohexadione-calcium (REG2006-07 and PRD2009-05).

An environmental risk assessment was conducted by updating Estimated Environmental Concentrations (EECs) according to current protocols, and using the new maximum application rate in combination with previously published fate endpoints from REG2006-07. The revised EECs were compared to established ecotoxicity endpoints (also from REG2006-07) to generate the environmental risk profile for use on turf. Risk quotient (RQ) values were calculated by dividing the exposure estimate (in other words, EEC) by an appropriate toxicity value ($RQ = \text{exposure/toxicity}$), and the risk quotient was then compared to the level of concern (LOC).

It was determined that the LOC was not exceeded for all terrestrial organisms at the screening level, and the risk was considered acceptable for terrestrial habitats.

The LOC was also not exceeded at the screening level for the majority of aquatic organisms. However, it was exceeded for aquatic vascular plants ($RQ = 1.25$) and for freshwater and marine algae ($RQ = 1.25\text{--}1.36$). Thus, a refined risk assessment for drift and run-off into aquatic habitats was conducted. Once the risk assessment was refined, the risks were acceptable for run-off, and the risks for drift were acceptable with the addition of a one metre spray buffer zone (Appendix I, Tables 12, 13 and 14).

4.3 Environmental incident reports

As of 15 September 2021, there was one environmental incident reported to the PMRA involving the active ingredient prohexadione-calcium. This incident occurred when the water used to douse a fire in a chemical storage facility overflowed into a nearby stream and resulted in fish mortality. There were other chemicals involved and it was considered unlikely that the active ingredient prohexadione-calcium was associated with the reported fish mortality.

5.0 Value

Anuew Plant Growth Regulator may be applied to select turfgrass species growing on golf courses, sod farms, sports fields, municipal sites and cemeteries for growth management throughout the growing season.

The registration of Anuew Plant Growth Regulator will provide turfgrass managers another option to manage turfgrass growth and align with an option that is presently available to users in the United States.

Value information submitted for review consisted of research papers and use history information. The provided value information demonstrated that Anuew Plant Growth Regulator applied per label instructions would be expected to effectively manage turfgrass growth without turfgrass tolerance concerns.

Supported uses are summarized in Appendix I, Table 15.

6.0 Pest control product policy considerations

6.1 Assessment of the active ingredient under the Toxic Substances Management Policy

The Toxic Substances Management Policy (TSMP)⁵ 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.

The PMRA has reached the conclusion that technical grade prohexadione-calcium does not meet the TSMP Track 1 criteria, and is not expected to form any transformation products which would meet the TSMP Track 1 criteria. Please refer to REG2006-07 for further details on the TSMP assessment. These are also referenced in PRD2009-05.

6.1.1 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 Science Policy Note SPN2020-01⁷ and is based on existing policies and regulations, including the Toxic Substances 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 technical grade prohexadione-calcium does not contain any formulants or contaminants identified in the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern. Please refer to REG2006-07 and PRD2009-05 for further details on the assessment of formulants and contaminants for the technical product.

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

⁶ SI/2005-114, last amended on 24 June 2020. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

⁷ PMRA's Science Policy Note SPN2020-01, *Policy on the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* under paragraph 43(5)(b) of the Pest Control Products.

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

The new end-use product, Anuew Plant Growth Regulator, has also been assessed under the same TSMP Track 1 criteria. Based on the new formulation, it was determined that there are no new concerns under the Pest Control Product Policy.

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

7.0 Proposed regulatory decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of Nufarm Prohexadione Calcium Technical Plant Growth Regulator and Anuew Plant Growth Regulator, containing the technical grade active ingredient prohexadione-calcium, for growth management of the following turfgrass species: Bentgrass, annual and perennial *Poa annua*, Kentucky bluegrass, perennial ryegrass, tall fescue and fine fescue, growing on golf courses, sod farms, sports fields, municipal sites and cemeteries.

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.

List of abbreviations

↑	increased
↓	decreased
♂	male
♀	female
>	greater than
<	less than
% v/v	% volume by volume
µg	micrograms
a.i.	active ingredient
ADI	acceptable daily intake
AHETF	Agricultural Handler Exposure Task Force
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
ATPD	area treated per day
bw	body weight
CAF	composite assessment factor
CAS	Chemical Abstracts Service
cm	centimetres
DEEM-FCID	Dietary Exposure Evaluation Model-Food Commodity Intake Database
EC ₅₀	effective concentration on 50% of the population
Ecotox	Ecotoxicity
EEC	Estimated Environmental Concentration
F0	parental generation
F1	first filial generation
g	gram
GDD	Growing degree day
ha	hectare(s)
IC ₅₀	Inhibition Concentration – 50%
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
<i>K</i> _{ow}	<i>n</i> -octanol-water partition coefficient
L	litre
LOAEL	lowest observed adverse effect level
LOC	Level of Concern
m	metre
mg	milligram
mL	millilitre
M/L/A	Mixer/Loader/Applicator
MOE	margin of exposure
MRL	maximum residue limit
nm	nanometre
NOAEL	no observed adverse effect level
ORETF	Outdoor Residential Exposure Task Force
Pa	pascals

PCPA	<i>Pest Control Product Act</i>
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency
PND	post-natal day
PPE	personal protective equipment
ppm	parts per million
PRD	Proposed Registration Decision
REG	Regulatory Note
REI	Restricted-Entry Interval/Re-Entry Interval
RQ	Risk Quotient
RTI	retreatment interval
TC	Transfer Coefficient
TSMP	Toxic Substances Management Policy
TTR	turf transferable residue
TWA	time-weighted average
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and figures

Table 1 Results of the Reproductive Toxicity Study (revised from REG2006-07)

Study type/animal/PMRA#	Study results
2-generation reproductive toxicity study (dietary) Rat (CrI:CD VAF/Plus®) PMRA# 620685	<p>Parental Toxicity NOAEL = 36 mg/kg bw/day (♂/♀) LOAEL = 385 mg/kg bw/day (♂/♀)</p> <p>Effects at LOAEL: ↑ macroscopic and microscopic observations of the glandular and non-glandular stomach in F0 animals (♂/♀); ↓ bw in F1 animals (♀)</p> <p>Offspring Toxicity NOAEL = 36 mg/kg bw/day (♀) LOAEL = 385 mg/kg bw/day (♀)</p> <p>Effects at LOAEL: ↓ bw in F1 pups on PND 4 to 21, ↓ bw in F1 pups on PND 14 and 21, ↓ bw in F2 pups on PND 7 and PND 21 (♂/♀)</p> <p>Reproductive Toxicity NOAEL = 3850 mg/kg bw/day (♂/♀) LOAEL not determined</p> <p>No evidence of sensitivity of the young.</p>

Table 2 Toxicology reference values for use in health risk assessment for prohexadione-calcium

Exposure scenario	Study	Point of departure and endpoint	CAF ¹ or Target MOE
Acute dietary general population	Not required as an endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies		
Repeated dietary	1-year oral toxicity study in dogs (capsule)	NOAEL = 20 mg/kg bw/day Kidney effects	100
ADI = 0.2 mg/kg bw/day			
Short- and intermediate-term dermal ² and inhalation ³ (excluding children)	Developmental toxicity study in rabbits (gavage)	NOAEL = 150 mg/kg bw/day Abortions	300

Exposure scenario	Study	Point of departure and endpoint	CAF¹ or Target MOE
Short- and intermediate-term dermal (children)	2-generation reproductive toxicity study in rats (dietary)	Offspring NOAEL = 36 mg/kg bw/day Decreased bw	100
Long-term dermal and inhalation (all populations)	1-year oral toxicity study in dogs (capsule)	NOAEL = 20 mg/kg bw/day Kidney effects	100
Short- and intermediate-term incidental oral (children)	2-generation reproductive toxicity study in rats (dietary)	Offspring NOAEL = 36 mg/kg bw/day Decreased bw	100
Long-term incidental oral (children)	1-year oral toxicity study in dogs (capsule)	NOAEL = 20 mg/kg bw/day Kidney effects	100
Short- and intermediate-term aggregate (adults) Oral and dermal	Developmental toxicity study in rabbits (gavage)	Common endpoint: abortions NOAEL 150 mg/kg bw/day	300
Short- and intermediate-term aggregate (children) Oral and dermal	2-generation reproductive toxicity study in rats (dietary)	Common endpoint: body weight effects Offspring NOAEL = 36 mg/kg bw/day	100
Long-term aggregate (all populations) Oral and dermal	1-year oral toxicity study in dogs (capsule)	Common endpoint: kidney effects NOAEL = 20 mg/kg bw/day	100

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

² Since an oral NOAEL was selected, a dermal absorption factor of 100% was used in a route-to-route extrapolation.

³ Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Table 3 Mixer/loader/applicator exposure estimates and MOE

Site	Exposure scenario	Total (dermal and inhalation) unit exposure (µg/kg a.i. handled)*	ATPD (ha/day)	Rate (kg a.i./ha)	Daily exposure (mg/kg bw/day)‡	MOE¶
PPE: Single layer (and gloves when mixing/loading/applying)						
Long-term						
Sod Farm ¹	Open M/L + Groundboom	133.02	30 ¹	0.308	0.015	1302
	Handgun Lawn Sprayer (M/L/A)	1337.8	2	0.308	0.010	1942
Golf Courses	Open M/L + Groundboom	133.02	16	0.154	0.004	4882
	Handgun Lawn Sprayer (M/L/A)	1337.8	2	0.154	0.005	3883
Intermediate-term						
Golf Courses	Open M/L + Groundboom	133.02	16	0.308	0.008	18306
	Handgun Lawn Sprayer (M/L/A)	1337.8	2	0.308	0.010	14562

* Unit exposure values based on AHETF/ORETF

‡ Daily exposure = (total unit exposure × area treated per day (ATPD) × Rate) / (80 kg bw × 1000 µg/mg)

¶ Based on an intermediate-term NOAEL = 150 mg/kg bw/day, target MOE = 300 and a long-term NOAEL = 20 mg/kg bw/day, target MOE = 100

¹ The ATPD for sports fields, municipal sites and cemeteries are expected to be less than those for sod farms; therefore, sod farms were considered the appropriate surrogate for these sites.

Table 4 Postapplication long-term worker exposure estimates and MOE

Site/crop	Postapplication activity	Peak TTR (µg/cm ²) *	TC (cm ² /hr)	Dermal exposure ‡ (mg/kg bw/day)	MOE¶	REI ◇
Sod Farms ¹	Slab harvesting and transplanting/planting	0.0399	6700	0.0268	747	12 hours
	Mowing, watering and irrigation repair	0.0399	3500	0.0140	1431	
	Aerating, fertilizing, hand pruning, mechanical weeding, scouting and seeding	0.0399	1000	0.0040	5008	

Site/crop	Postapplication activity	Peak TTR ($\mu\text{g}/\text{cm}^2$) *	TC (cm^2/hr)	Dermal exposure ‡ ($\text{mg}/\text{kg bw}/\text{day}$)	MOE¶	REI ◇
Golf Courses	Transplanting/planting, mowing, watering, cup changing, irrigation repair and miscellaneous grooming	0.059	3500	0.0207	968	Until sprays have dried
	Aerating, fertilizing, hand pruning, mechanical weeding, scouting and seeding	0.059	1000	0.0059	3388	

TTR = Turf Transferrable Residue; TC = Transfer Coefficient; MOE = Margin of Exposure; REI = Restricted-Entry Interval (sod farms) / Re-entry Interval (golf courses)

* Calculated using the default values of 1% deposition on the day of application and 10% dissipation per day. The TTR value was calculated based on 19 applications of the maximum rate at a RTI of 14 days for sod farms and 7 days for golf courses.

‡ Exposure = (Peak TTR [$\mu\text{g}/\text{cm}^2$] \times TC [cm^2/hr] \times 8 hours/day) / (80 kg bw \times 1000 $\mu\text{g}/\text{mg}$)

¶ Based on a long-term NOAEL of 20 mg/kg bw/day; Target MOE = 100

◇ Minimum REI is 12 hours for sod farms and until sprays have dried for all other turf uses.

¹Postapplication worker exposure to maintenance workers of sports fields, municipal sites and cemeteries is not expected to exceed the postapplication exposure of workers performing similar duties on sod farms.

Table 5 Postapplication long-term golfer exposure estimates and MOE

Life stage	Peak TTR* ($\mu\text{g}/\text{cm}^2$)	TC (cm^2/hr)	Exposure time (hr/day)	Dermal exposure‡ ($\text{mg}/\text{kg bw}/\text{day}$)	MOE¶	REI
Adult (16+ yrs)	0.059	5300	4	0.0156	1300	Until sprays have dried
Youth (11<16 yrs)	0.059	4400	4	0.0182	1100	
Children (6<11 yrs)	0.059	2900	4	0.0214	930	

TTR = Turf Transferrable Residues; TC = Transfer Coefficient; MOE = Margin of Exposure; REI = Re-Entry Interval

* Calculated using the default values of 1% deposition on the day of application and 10% dissipation per day. The TTR value was calculated based on 19 applications of the maximum rate at a RTI of 7 days

‡ Dermal Exposure ($\text{mg}/\text{kg bw}/\text{day}$) = (Peak TTR [$\mu\text{g}/\text{cm}^2$] \times TC [cm^2/hr] \times Exposure Time [hours/day]) / (Body weight [80 kg for adults; 57 kg for youth; 32 kg for children] \times 1000 $\mu\text{g}/\text{mg}$)

¶ Based on a long-term NOAEL of 20 mg/kg bw/day; Target MOE of 100

Table 6 Postapplication short- to intermediate term residential high contact turf exposure estimates and MOE

Life stage	Activity	Peak TTR (µg/cm ²) *	TC (cm ² /hour)	Exposure time (hour/day)	Dermal exposure (mg/kg bw/day) ‡	MOE ¶	REI
Adult (16+ yrs)	High Contact	0.04	180 000	1.5	0.135	1100	Until sprays have dried
Children (1<2 yrs)			49 000	1.5	0.267	130	

TTR = Turf Transferrable Residues; TC = Transfer Coefficient; MOE = Margin of Exposure; REI = Re-Entry Interval

* Calculated using the default values of 1% deposition on the day of application and 10% dissipation per day. The TTR value was calculated based on 19 applications at the maximum rate of 0.308 kg a.i./ha and a RTI of 14 days

‡ Dermal Exposure (mg/kg bw/day) = (Peak TTR [µg/cm²] x TC [cm²/hr] x Exposure time [hours/day]) / (Body weight [80 kg for adults; 11 kg for children] x 1000 µg/mg)

¶ Based on a short- to intermediate-term NOAEL of 150 mg/kg bw/day; Target MOE of 300 for adults and a short- to intermediate-term NOAEL of 36 mg/kg bw/day; Target MOE of 100 for children

Table 7 Postapplication long-term residential high contact turf exposure estimates and MOE

Life stage	Activity	TWA TTR (µg/cm ²) *	TC (cm ² /hour)	Exposure time (hour/day)	Dermal exposure (mg/kg bw/day) ‡	MOE ¶	REI
Adult (16+ yrs)	High Contact	0.022	180 000	1.5	0.0729	270	Until sprays have dried
Children (1<2 yrs)			49 000	1.5	0.144	140	

TTR = Turf Transferrable Residues; TC = Transfer Coefficient; MOE = Margin of Exposure; REI = Re-Entry Interval; TWA = Time-Weighted Average

* Calculated using the default values of 1% deposition on the day of application and 10% dissipation per day. The TWA TTR value is the average residue calculated over 266 days, based on 19 applications at the maximum rate of 0.308 kg a.i./ha and a RTI of 14 days

‡ Dermal Exposure (mg/kg bw/day) = (TWA TTR [µg/cm²] x TC [cm²/hr] x Exposure time [hours/day]) / (Body weight [80 kg for adults; 11 kg for children] x 1000 µg/mg)

¶ Based on a NOAEL of 20 mg/kg bw/day; Target MOE of 100

Table 8 Postapplication child hand-to-mouth exposure estimates and MOE

Duration	Hand residue* (mg/hr)	Fraction of hand surface area mouthed/event	Exposure time (hrs/day)	Number of replenishments/hr	Saliva extraction factor	Frequency (events/hr)	Oral exposure‡ (mg/kg bw/day)	MOE¶
Short- to Intermediate-Term	0.05871	0.13	1.5	4	0.48	14	0.0009	38000
Long-Term	0.03177	0.12	1.5	4	0.48	8	0.0004	53000

*Hand Residue (mg/hr) = (Fraction ai on hands (6%) × lifestage specific dermal exposure (mg/hr))/2; Where Life stage specific dermal exposure (mg/hr) = dermal exposure (mg/day) / exposure time (hr)

‡Oral Exposure (mg/kg bw/day) = (residue (mg/hr) × fraction mouthed (%) × exposure time (hrs/day) × (1 – (1 - saliva extraction factor)^(frequency (events/hr) / # replenishments (#/hr)))) / 11 kg bw

¶Based on a short- to intermediate-term NOAEL of 36 mg/kg bw/day and a long-term NOAEL of 20 mg/kg bw/day; Target MOE = 100

Table 9 Postapplication child object-to-mouth exposure estimates and MOE

Duration	Object residue* (µg/cm²)	Object surface area mouthed / event (cm²/event)	Exposure time (hrs/day)	Number of replenishments/hr	Saliva extraction factor	Frequency (events/hr)	Oral exposure‡ (mg/kg bw/day)	MOE¶
Short- to Intermediate-Term	0.03994	10	1.5	4	0.48	9	0.00017	215000
Long-Term	0.02161	10	1.5	4	0.48	6	0.00007	271000

*Object Residue (µg/cm²) = Peak or TWA TTR

‡Oral Exposure (mg/kg bw/day) = (residue (µg/cm²) × 0.001 mg/µg × area mouthed (cm²/event) × exposure time (hrs/day) × (1 – (1 - saliva extraction factor)^(frequency (events/hr) / # replenishments (#/hr)))) / 11 kg bw

¶Based on a short- to intermediate-term NOAEL of 36 mg/kg bw/day and on a long-term NOAEL of 20 mg/kg bw/day; Target MOE = 100

Table 10 Golfer aggregate exposure estimates and MOE

Life Stage	Dermal Golfer (mg/kg bw/day)	Dietary Exposure (mg/kg bw/day)	Aggregate Exposure‡ (mg/kg bw/day)	MOE¶
Adult (16+ yrs)	0.0156	0.00215	0.0178	1124
Youth (11<16 yrs)	0.0182	0.0042	0.0224	892
Child (6<11 yrs)	0.0214	0.00948	0.031	648

‡Aggregate Exposure (mg/kg bw/day) = sum of exposures / kg bw (80 kg adults; 57 kg youth; 32 kg child)

¶Based on a long-term NOAEL of 20 mg/kg bw/day; Target MOE = 100

Table 11 Residential aggregate exposure estimates and MOE

Duration	Life stage	Dermal high contact (mg/kg bw/day)	Hand-to-mouth (mg/kg bw/day)	Dietary exposure (mg/kg bw/day)	Aggregate exposure‡ (mg/kg bw/day)	MOE¶
Short- to intermediate-term	Adult (16+ yrs)	0.135	-	0.00215	0.137	1095
	Child (1<2 yrs)	0.267	0.0009	0.0434	0.311	116
Long-term	Adult (16+ yrs)	0.0729	-	0.00215	0.0751	266
	Child (1<2 yrs)	0.144	0.0004	0.0434	0.188	106

‡Aggregate Exposure (mg/kg bw/day) = sum of exposures / kg bw (80 kg adults; 11 kg child)

¶Based on a short- to intermediate-term NOAEL of 150 mg/kg bw/day; Target MOE = 300 for adults, a short- to intermediate-term NOAEL of 36 mg/kg bw/day; Target MOE = 100 for children and a long-term NOAEL of 20 mg/kg bw/day; Target MOE = 100 for all life stages

Table 12 Drift assessment for non-target fresh water macrophytes and algae exposed to Anuew Plant Growth Regulator

	ORGANISM	
	Aquatic Macrophyte (<i>Lemna gibba</i>)	Freshwater Algae (<i>S. capricornutum</i>)
Screening level - Seasonal maximum application rate (6000 g a.i./ha)		
Ecotox Endpoint Value - EC ₅₀ /IC ₅₀ (mg a.i./L)	1.2	1.1
Converted Ecotox Endpoint - 1/2 EC ₅₀ /IC ₅₀ (mg a.i./L)	0.6	0.55
Screening Level EEC (mg a.i./L)	0.75	0.75
Screening Level RQ	1.25	1.36
LOC Exceeded	Yes	Yes
Ground boom - Field sprayer - Coarse (3% drift)		
EEC Refined for Drift (mg a.i./L)	0.0225	0.0225
RQ Refined for Drift	0.038	0.041
LOC Exceeded	No	No
Ground boom - Field sprayer - Medium (6% drift)		
EEC Refined for Drift (mg a.i./L)	0.045	0.045
RQ Refined for Drift	0.075	0.082
LOC Exceeded	No	No

Table 13 Drift assessment for non-target marine algae exposed to Anuew Plant Growth Regulator

ORGANISM - Marine Algae (<i>Skeletonema costatum</i>)	
Screening level - Seasonal maximum application rate (6000 g a.i./ha)	
Ecotox Endpoint Value - EC ₅₀ (mg a.i./L)	1.1
Converted Ecotox Endpoint 1/2 EC ₅₀ (mg a.i./L)	0.55
Screening Level EEC (mg a.i./L)	0.75
Screening Level RQ	1.36
LOC Exceeded	YES
Due to tidal mixing, one application of 308.3 g a.i./ha (in other words, 100% drift)	
EEC Refined for Tidal Mixing (mg a.i./L)	0.039
RQ Refined for Drift	0.07
LOC Exceeded	No

Table 14 Run-off assessment for non-target aquatic macrophytes, freshwater and marine algae exposed to Anuew Plant Growth Regulator

	ORGANISM		
	Aquatic Macrophyte (<i>Lemna gibba</i>)	Freshwater Algae (<i>S. capricornutum</i>)	Marine Algae (<i>S. costatum</i>)
Screening level - Seasonal maximum application rate (6000 g a.i./ha)			
Ecotox Endpoint Value – EC ₅₀ /IC ₅₀ (mg a.i./L)	1.2	1.1	1.1
Converted Ecotox Endpoint 1/2 EC ₅₀ (mg a.i./L)	0.6	0.55	0.55
Screening Level EEC (mg a.i./L)	0.75	0.75	0.75
Screening Level RQ	1.25	1.36	1.36
LOC Exceeded	YES	YES	YES
Refined run-off assessment			
EEC Refined for Run-off (mg a.i./L)	0.015	0.016	0.016
RQ Refined for Run-off	0.025	0.029	0.029
LOC Exceeded	No	No	No

Table 15 List of supported uses

Items	Label claims that are supported
Crops	Bentgrass, annual and perennial <i>Poa annua</i> , Kentucky bluegrass, perennial ryegrass, tall fescue and fine fescue
Use Site	Golf courses, sod farms, sports fields, municipal sites and cemeteries
Anuew Plant Growth Regulator Rate (g a.i./ha)	38.5 to 308.3♦
Adjuvant	Use of a non-ionic surfactant in the spray mixture, such as Agral 90 or Ag-Surf, may improve coverage of the turf foliage and product performance consistency, especially under hot, quick drying conditions
Adjuvant Rate (% v/v)	0.125% v/v (125 mL/100L)
Other Spray Additives	Ammonium Sulphate†
AMS Rate	1:1 ratio with plant growth regulator
Application Timing	When the turf is green and actively growing. Delay application if the turf is entering

Items	Label claims that are supported
	stressful growing conditions.
Application Interval	280–350 Growing Degree Days 1–4 weeks after application. Re-application should occur no sooner than 7 days when applying to golf courses and 14 days when applying to other use sites.
Application Volume (L water/100 m ²)	2–20
Max Seasonal Rate (g a.i./ha)	6000
Application Method	Backpack sprayers, hand sprayers, boom sprayers and spray gun application devices
Efficacy Claims	- Slows vertical growth - Reduces mowing frequency - Often enhances colour and quality
Rainfastness	1-4 hours

† Use if the water source used for spray applications contains high levels of calcium (greater than 140 ppm or 140 mg/l).

♦ Rate chosen is dependent on the turf species and/or use site being treated.

References

PMRA References Document Number

A. List of studies/Information submitted by registrant

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