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Paclobutrazol

Review Conducted by MDAR and MassDEP for Use in Sensitive Areas of Rights-of-Way in Massachusetts

January 2012

Massachusetts Department of Environmental Protection

Massachusetts Department of Agricultural Resources

Active Ingredient Paclobutrazol:

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1. INTRODUCTION

The review presented here was initiated by the request for the addition of Cambistat® (EPA Reg. No. 74779-3), containing the active ingredient paclobutrazol, to the Massachusetts Rights-of-Way Sensitive Area Materials List. Paclobutrazol is a tree growth regulator that provides a tool for utility arborists to limit the size and growth of trees and shrubs in power line and utility rights-of-way corridors. Tree growth regulator products such as Cambistat® are regularly applied in high visibility locations such as parks, historic downtowns, residential areas and other areas where trees have a cultural value (Paul Sellers, NSTAR, pers. comm.). The utility industry is seeking approval of Cambistat® for use in sensitive areas in order to have the ability to use this product in the same locations that happen to be located within areas of rights-of-way that are regulated by 333 CMR 11.00.

The regulations specified in 333 CMR 11.00 provide standards, requirements and procedures for the use of herbicides in vegetation management in areas of rights-of-way, while minimizing the potential impacts to human health and the environment. Specific restrictions exist for sensitive areas within rights-of-way, including the list of herbicides that have been specified as acceptable for use in these sensitive areas. The herbicides included on the Sensitive Area Materials List have been evaluated to further scrutinize potential risks to sensitive receptors in these areas. The review presented here is the evaluation of the active ingredient paclobutrazol and products for use in sensitive areas of rights-of-way.

Paclobutrazol (PBZ) was first registered by U.S. EPA in 1985. At the time of preparation of this review in 2011, PBZ was undergoing registration review by U.S. EPA to determine whether it continues to meet the FIFRA standard for registration (U.S. EPA, 2007A). As part of the registration review process, a summary document was issued (U.S. EPA, 2007B). This document includes a factsheet describing the use of this active ingredient, the status of human health and ecological risk assessments, and the problem formulation and scope of work necessary to support the registration review at U.S. EPA.

Additional information was obtained from documents issued by the European Food Safety Authority (EFSA) that evaluated PBZ for use as a plant growth regulator on winter oilseed rape. The evaluation data package of the EFSA assessment included various documents describing data summaries, scientific evaluations, risk assessments, and conclusions of the peer review. The documents consulted for the review presented here included the Draft Assessment Report (DAR) (EFSA, 2006), the Additional Report to the DAR (EFSA, 2010A) and the Conclusion of the Peer Review (EFSA, 2010B).

The secondary review documents generated by the regulatory agencies U.S. EPA and EFSA are primarily based on the consideration of registrant-submitted studies in support of product registration. These studies are generally classified as Confidential Business Information (CBI) and therefore not available for review outside of these agencies. Additional information from scientific publications and other government documents was also considered, when available and as needed, for the assessment described in this review.

This document describes a review of the chemical and physical properties, product use characteristics, environmental fate characteristics and toxicity data. Environmental concentrations of PBZ were estimated using screening-level simulation models and calculation

methods. The risks to classes of organisms that are most likely to be exposed, including aquatic organisms and soil invertebrates, were characterized. The exposure to groundwater resources was also assessed.

The review described herein was conducted according to the established procedures and criteria for review of herbicide products for use within sensitive areas of Rights-of-Way (ROW) (MDAR, 2011). These review procedures and criteria address both the herbicide active ingredients as well as the “inert” or “other” ingredients, more specifically the surfactants.

2. CHEMICAL AND PRODUCT IDENTITY AND PROPERTIES

2.1. Chemical Identity and Properties

- Common Chemical Name: Paclobutrazol (***PBZ*** *acronym will be used*)
- IUPAC name: 2*RS*,3*RS*-1-(4-chlorophenyl)-4,4-dimethyl-2-(1*H*-1,2,4-triazol-1-yl) pentan-3-ol
- CAS No.: 76738-62-0

Paclobutrazol (PBZ) is a plant growth regulator belonging to the triazole chemical class (U.S. EPA, 2007B). The nomenclature is summarized in Table A1.1 in Appendix 1. PBZ is a racemic mixture of the (2R, 3R) and (2S, 3S) enantiomers. Chemical and physical properties are listed in Table A1.2 in Appendix 1.

2.2. Formulated Product

The product considered in this review, Cambistat®, is a suspension concentrate containing 22.3% PBZ. The MSDS document (Rainbow Treecare, 2011) for this product indicates that the formulation also contains propylene glycol at an unspecified concentration. No other ingredients were specified in the MSDS document (Rainbow Treecare, 2011).

Propylene glycol (PG) is a colorless, odorless liquid which is generally recognized as safe (GRAS) by the U.S. Food and Drug Administration (FDA) in 21 CFR § 184.1666 for use as a direct food additive under the conditions prescribed. It is approved by the U.S. FDA for certain indirect food additive uses. PG has a wide range of practical applications such as antifreezes, coolants and aircraft deicing fluids; solvents; food; flavors and fragrances; cosmetics and personal care products; pharmaceuticals; chemical intermediates; plasticizers; and thermoset plastic formulations (DOW, 2006). PG is not acutely toxic (single dose, high exposure). It is essentially non-irritating to the skin and mildly irritating to the eyes. Available data indicate that propylene glycol is not a skin sensitizer or a carcinogen. PG is not volatile and is miscible with water. It is not expected to bioaccumulate and it is not acutely toxic to water organisms except at very high concentrations (OECD/SIDS, 2001). Given the characteristics and regulatory status of this ingredient, propylene glycol was not further evaluated for this review.

Proprietary information on the other formulation ingredients was obtained. Two of the proprietary ingredients can be classified as surfactants. One of the surfactants belongs to a class of surfactants that has been approved for use in sensitive areas of rights-of-way in Massachusetts (MDAR, 2010A and B). Consequently, this ingredient did not have to undergo additional review and passed the surfactant policy portion of the review process for the sensitive area materials list. Nevertheless, both surfactants were included in the evaluation of proprietary ingredients.

The proprietary ingredients were evaluated as part of the review process for addition to the Sensitive Area Materials List, but cannot be disclosed here for proprietary reasons. In most cases, a quantitative or semi-quantitative evaluation was conducted based on available toxicity

endpoints and estimates for maximum soil, surface water and ground water concentrations. In some cases, only a qualitative evaluation was possible. Based on these evaluations, it was concluded that these compounds are of a nature and/or present at levels in the product such that use of it as directed would not cause unreasonable adverse effects to human health and the environment.

2.3. Mode of Action

PBZ is a cell elongation and internode extension inhibitor that retards plant growth by inhibition of gibberellins biosynthesis. Gibberellins stimulate cell elongation. When gibberellin production is inhibited, cell division still occurs, but the new cells do not elongate. The result is shoots with the same numbers of leaves and internodes compressed into a shorter length. Reduced growth in the diameter of the trunk and branches has also been observed. Another response of trees to treatment with PBZ is increased production of the hormone abscisic acid and the chlorophyll component phytol, both beneficial to tree growth and health. PBZ may also induce morphological modifications of leaves, such as smaller stomatal pores, thicker leaves, and increased number and size of surface appendages, and increased root density that may provide improved environmental stress tolerance and disease resistance (Chaney, 2005). PBZ also has some fungicidal activity due to its capacity as a triazole to inhibit sterol biosynthesis (Chaney, 2005; U.S. EPA, 2007B; BCPC, 2000).

3. USE PATTERN AND APPLICATION CHARACTERISTICS

3.1. Use as Tree Growth Regulator

The use pattern of PBZ considered in this review is as a tree growth regulator, more specifically as a tree growth retardant (TGR). PBZ was one of the three active ingredients that were used by utility arborists in the 1980s. The products were applied by trunk injection as a formulation containing alcohol solvents. Due to problems associated with trunk injection of these products (e.g., tree injury and wood discoloration) there was a decline of the use of TGRs. In 2005, PBZ was the only remaining TGR for use on trees. Modifications in formulations and application methods, satisfactory performance as a TGR and benefits to overall tree health resulted in a rebound in the use of PBZ. Current formulations of PBZ TGRs such as Cambistat® for TGR use, such as Cambistat®, are applied as a water suspension by soil injection or basal drench (Chaney, 2005).

PBZ is also registered for use on ornamental plants grown in containers in nurseries, greenhouses and interior landscapes. It is also used on turf to control annual grasses and broadleaf weeds, to reduce the mowing frequency and to increase turf density.

3.2. Application Methods and Rates

PBZ formulated as Cambistat® is applied by soil injection or application as a basal drench. The species-specific dose rate is determined by measuring the tree diameter at breast height (DBH). Based on the dose rate information on the product label, it can be calculated that the dose rate of active ingredient is in the range of 4.1 g (0.009 lbs) to 202.5 g (0.446 lbs) PBZ per individual tree. Dose rates may be reduced by 25 to 30% based on consideration of canopy size and structure, stressed or declining tree status, or the presence of a confined or compromised root system. Given the use pattern of treating individual trees, the application rate expressed in mass use per acre has not been established. The water suspension of PBZ can be injected approximately 2-6 inches deep at 50 to 200 psi as close to the tree trunk as possible. Alternatively, the water suspension can be poured into a shallow trench around the tree. Retreatment may be done every 3 years or until the effects from the previous application subside (Rainbow Treecare, 2011).

4. ENVIRONMENTAL FATE OF PACLOBUTRAZOL

4.1. Environmental Fate Parameter Summary

The environmental fate properties of PBZ are summarized in Table A2.1 in Appendix 2. The mobility and persistence characteristics are described in more detail in the following two sections.

4.2. Mobility

PBZ has been characterized as a compound with a moderate potential for mobility in soil and water environments (U.S. EPA, 2007B). The summary document for registration review prepared by U.S. EPA (2007B) documents that laboratory batch equilibrium studies indicated that PBZ has the capacity to be mobile under certain conditions. Studies with nine US soils ranging in texture from sand to silt loam indicated values for the soil adsorption coefficient K_D in the range from 1.3 to 23.0 ml/g. Adsorption appeared to increase with an increase in soil organic matter content and a decrease in soil pH. In the draft assessment report prepared by the United Kingdom (EFSA, 2006) adsorption data for 13 soils are summarized that show K_D values in the range of 0.8 – 21.3 ml/g with a geometric mean of 4.3 ml/g. The ketone metabolite showed on average a slightly higher affinity for adsorption to soil with K_D values in the range of 2.1 – 13.5 with a mean of 8.0 across 6 soils.

Results from laboratory soil column leaching experiments summarized in U.S. EPA (2007B) indicated low mobility in the experiments using methine-labeled PBZ in soils ranging in texture from sand to clay-loam. The experiments using triazole-labeled PBZ showed low mobility in columns of sand and sandy loam soils, and mobility in loamy sand and clay loam soils. In all cases, the majority (58.6 – 90.7%) of applied PBZ aged residue did not leach out of the upper 10 cm of the treated soil columns.

An issue noted in the draft assessment report (EFSA, 2006) was the identification in a column leaching study of the degradate hydroxyl triazole at a concentration of 12 μg/L in the leachate. Even though this degradate was not detected in the soil metabolism experiments, the observation in the column leaching experiment raised concerns for risks to groundwater and a data gap was identified. This data gap was addressed in the additional report to the DAR (EFSA, 2010A). Groundwater exposure modeling using additional soil degradation and adsorption data for the degradate hydroxyl triazole showed a maximum concentration of the degradate in groundwater (80^{th} percentile annual average concentration in leachate leaving the top 1 m soil layer) did not exceed 0.1 μg/L except in one of the six scenarios, where it was modeled at a concentration of 0.1192 μg/L. The modeling study concluded that the potential for the degradate hydroxyl triazole to reach groundwater at high concentrations is low.

PBZ is unlikely to volatilize to any significant extent owing to a low estimated vapor pressure. The octanol-water partitioning coefficient (log K_{OW}) of 3.2 indicates a potential for this chemical to bioaccumulate in fish. A fish bioaccumulation study, which was only conducted for 14 days, showed BCF factors of 20x for edible tissues (day 3), 248x for non edible tissues (day 3), and 44x for whole fish (day 10) (U.S. EPA, 2007B).

Although characterized as moderately mobile in laboratory studies, no significant movement of PBZ was detected in field studies in agricultural soils. In the orchard studies, PBZ residues (parent plus degradate) were detected at 10% or less of total applied in soils with depths of 48 inches in the California study, 24 inches in West Virginia study, and 48 inches in the Florida study. These depths are the maximum depths sampled at each study. No information was provided on the nature or type of soils in the summary document. The PBZ ketone metabolite was predominately detected in the subsurface soil layers, also at insignificant levels (U.S. EPA, 2007B).

A scientific publication by Baris et al. (2010) provided information regarding the potential of PBZ to impact groundwater from its use on turf areas. PBZ was included in a comprehensive evaluation of water quality monitoring data and assessment. This evaluation considered water quality data for a large number of turf-related pesticides from 44 studies involving 80 golf courses in the US over a 20-year period. PBZ was found in 3/440 groundwater samples, with the highest detection at 4.2 μg/L.

4.3. Persistence

PBZ has been characterized as an environmentally stable compound in soil and water environments (U.S. EPA, 2007B). Laboratory studies with US loam and silt-loam soils indicated that PBZ degraded with a half-life of more than 1 year under both aerobic and anaerobic conditions.

Summaries of laboratory half-lives, normalized to 20 °C with moisture content at field capacity, show values in the range of 43 to 618 d with a mean of 183 d (6 soils) (EFSA, 2006). Data from field studies in the UK and Italy indicated dissipation half-lives of 58 to 389 d with a mean of 114 d. Field accumulation studies conducted for a period of 4 to 8 years with annual applications of PBZ showed no apparent build up of PBZ residues except in one of the 7 sites.

The degradation pathway of PBZ, described in EFSA (2006), occurs via the ketone analog, (2RS)-1-(4-chlorophenyl)-4,4-dimethyl-2-(1,2,4-triazol-1-yl)-pentan-3-one, which was detected in the aerobic soil metabolism study at approximately 18% of total applied and at less than 10% in other soil studies. The ketone analog is degraded via separation of the 1-H-1,2,4-triazole moiety. The 1,2,3-triazole moiety was only observed at a maximum of 3%. Degradation of the 1,2,4-triazole proceeds via triazole acetic acid and hydroxyl triazole. Hydroxy triazole was identified in a soil column leaching study but was not observed in any of the soil metabolism studies (EFSA, 2006).

The major ketone-metabolite is less persistent than the PBZ parent with half-lives of 23 – 90 d (mean of 54 d) in an aerobic degradation study with 3 soils. A minor metabolite 1,2,4-triazole is even less persistent as indicated by its half-life of 6.3 – 12.3 d (mean 9.5 d) in aerobic soil degradation studies.

Field dissipation studies from the US showed PBZ residues that were persistent and relatively mobile. Half-lives of PBZ residues ranged from 450-950 days for orchard soils in California,

West Virginia, Florida and 25 weeks to 36 weeks in agricultural soils in Mississippi, North Carolina, and Illinois.

Laboratory studies indicated that PBZ is relatively stable to degradation by hydrolysis. More than 94 percent of PBZ was still present after 30 d in pH 4, 7 and 9 solutions, respectively (U.S. EPA, 2007B). PBZ did not undergo appreciable photolysis in water when exposed to light in pH 7 buffer. More than 96 percent of PBZ was still present after 10 d of exposure (U.S. EPA, 2007B). In the presence of light, degradation of PBZ in soil was slightly accelerated with a calculated half-life of 188 d. It was concluded that soil photolysis is unlikely to be a significant route of dissipation (EFSA, 2006).

Degradation in a water-sediment system was reported in EFSA (2006). The data indicate a low degradation rate in both the water and the whole system. The half-life determined for the whole system was 164 d, with most of the PBZ remaining in the water phase.

5. MAMMALIAN TOXICITY

With regard to the existing toxicological data of PBZ, the work plan for registration review by U.S. EPA (2007B) makes reference to RfD/Peer Review reports from 1986 and 1994 among the primary resources for the status update. A more recent review and evaluation of toxicological information was organized by the European Food Safety Authority (EFSA) as part of the peer review of the pesticide risk assessment of PBZ in European Community. The more up-to-date information available in the EFSA-organized peer review documents was the primary source of information for review presented here. The EFSA-organized review was initiated in 2006 (EFSA, 2006), subsequently withdrawn, and then resubmitted along with additional toxicological information, and was completed in 2010 (EFSA, 2010A and B). Information on the mammalian toxicology from registrant-submitted studies considered in these review documents is summarized below.

Acute toxicity, irritation and sensitization

PBZ exhibits moderate acute toxicity by the oral route in the species tested. The LD_{50} is 1954 mg/kg in male rats and 1336 mg/kg in female rats; 490 mg/kg and 1219 mg/kg in male/female mice, respectively; 542 mg/kg and 400-640 mg/kg in male/female guinea pigs, respectively; and 835 mg/kg and 937 mg/kg in male/female rabbits, respectively. New data for rats indicated an oral LC_{50} > 2000 mg/kg.

Acute dermal LC_{50} values are greater than 2000 mg/kg in rats and greater than 1000 mg/kg in rabbits. Overall, PBZ is of low acute toxicity by the dermal route.

Acute inhalation studies showed a 4h-LC_{50} value of greater than 2 mg/L particulate to rat indicating moderate toxicity by inhalation.

Skin irritation studies with rats (5 repeated applications) and with rabbits (single application) indicated that PBZ is slightly irritating to skin. Eye irritancy studies with rabbits indicated mild irritancy to the eye. PBZ is not a skin sensitizer based on the results of studies with guinea pigs.

Overall, the acute toxicity data indicate that PBZ is of moderate acute toxicity by the oral and inhalation routes and of low acute toxicity by the dermal route. PBZ is slightly irritating to skin and eye and is not a skin sensitizer.

Toxicokinetics

In the rat, absorption was rapid and extensive (88-95%) and did not show saturation at a high dose. Absorbed material was readily oxidized to PBZ diol, which was subject either to excretion or to further oxidation to the carboxylic acid. Biotransformation was limited to the tertiary butyl moiety, with no metabolism detected in either the triazole or chlorinated phenyl rings. Male rats oxidized a greater proportion of PBZ to the carboxylic acid than did female rats.

A small proportion of radioactivity equilibrated into the tissues and was subsequently eliminated. The highest concentrations of radioactivity were seen in the liver after a high or low dose. There was no evidence of bioaccumulation.

Excretion at a low dose was relatively rapid with more than 70% of radioactivity excreted within 48 hours. The delay in excretion in the high dose animals (>70% excretion not achieved until 72 hours after dosing) and the significant amount of radioactivity in faeces (well beyond normal transit time) were due to significant enterohepatic recirculation. In cannulated rats, biliary excretion at a low dose represented >50% and 70% of the administered dose in females and males, respectively. In cannulated rats, 5% was excreted as unchanged parent.

In the dog, following a single oral low dose, radioactivity was rarely absorbed reaching peak concentrations in plasma and blood within 1 hour and declining below the limits of detection by 72 hours. Most of the radioactivity was associated with plasma. Elimination was faster than for rats with >75% of radioactivity eliminated in urine and faeces within 24 hours. At 168 hours after dosing, there was almost a complete absence of radioactivity in all tissues examined (with the exception of the liver in one animal). There was no evidence of bioretention of PBZ or its metabolites in dogs.

Short-term toxicity

The short-term toxicity of PBZ was investigated by the oral route in rats (90 days) and dogs (90 days and 1 year), and by the dermal route in rabbits (21 days).

The liver is the target organ of PBZ oral toxicity in the rat. Signs of liver toxicity (clinical chemistry changes, increased weight and marginal increases in hydropic and fatty changes) were observed in males and females at 1250 ppm (93 and 107 mg/kg/day in males and females, respectively). These effects were accompanied by decreases in food consumption and body weight gain. There were no effects at 250 ppm (20 mg/kg/day). An overall short-term NOAEL of 20 mg/kg/day was identified for the rat from this subchronic study.

Similar findings were observed in the dog. Liver toxicity (clinical chemistry changes, increased weight, enzyme induction and ballooned hepatocytes), accompanied by decreases in food consumption and body weight gain, was observed from a dose of 75 mg/kg/day (in the 1-year study). There were no effects at 15 mg/kg/day (1-year study). Therefore, an overall short-term NOAEL of 15 mg/kg/day was identified for the dog from the chronic study.

A repeat dose dermal toxicity study in rabbits showed no signs of systemic toxicity up to 100 mg/kg bw/day.

No short-term studies in the mouse were available; however, results from the mouse carcinogenicity study do not indicate that the mouse was more sensitive to PBZ than rats or dogs.

Genotoxicity

The mutagenic, clastogenic, and aneugenic potential of PBZ was studied in several *in vitro* test systems using bacteria and mammalian cells and *in vivo* test systems in rats and mice. PBZ was negative in an *in vitro* bacterial reverse mutation assay and an *in vitro* gene mutation test in mouse lymphoma cells. No clastogenic effects were seen in an *in vitro* human lymphocyte cytogenetics test, two *in vivo* rat cytogenetics tests and two *in vivo* mouse micronucleus tests. No evidence of DNA damage or repair was noted in an *in vivo* UDS assay. PBZ had no effect on

either fertility or dominant lethality in mice in a dominant lethality test. Based on these *in vitro* and *in vivo* mutagenicity tests, it was concluded that PBZ is not genotoxic.

Long-term toxicity and carcinogenicity

The chronic toxicity and carcinogenicity of PBZ was investigated in two standard dietary studies in rats and mice.

The liver is the target organ of PBZ oral chronic toxicity in the rat. Signs of liver toxicity (decreases in plasma triglycerides in females and increases in plasma BUN levels in females, increased liver weights in males and females and increased incidence of hepatocyte steatosis/hypertrophy in males and females) were seen at the top dose of 1250 ppm. These were accompanied by decreases in body weight gain and food consumption in females. At 250 ppm, body weight gains were still significantly reduced in females and liver steatosis was still significantly increased in males. There were no toxicologically significant effects at 50 ppm (2.2 and 2.8 mg/kg bw/day in males and females, respectively).

In mice, the target organ of PBZ oral chronic toxicity was also the liver (and related fat metabolism), as indicated by increased liver weights, increased severity of steatosis in males and reduced serum cholesterol in males and triglyceride levels in females at the top dose level of 750 ppm. There were no toxicologically significant effects at 125 ppm (14 and 16 mg/kg bw/day in males and females, respectively).

There was no evidence of carcinogenic effect of PBZ in rats or mice.

Reproductive and developmental toxicity

The reproductive toxicity of PBZ has been investigated in a 2-generation study in the rat and in pre-natal developmental toxicity studies in rats and rabbits.

In the 2-generation study, dietary administration of PBZ caused general toxicity in the parental animals at the top dose of 1250 ppm, observed as increased incidence of chromocryorrhea and thickened eyelids and increases in liver weights and associated histopatology (centrilobular fatty changes). PBZ also caused adverse effects in the young F_1 and F_2 offspring at the top dose of 1250 ppm, observed as a reduction in pup bodyweight gains, increased incidence of chromodacryorrhea, thickened eyelids, dental malocclusion and twisted snout and increases in liver weights and associated histopatology (centrilobular fatty changes). However, fertility mating performance, litter size and pup survival were not affected by treatment. Accordingly, on the basis of this study, it can be concluded that PBZ is not a specific hazard to fertility and reproductive performance, as no effects were seen up to the top dose of 1250 ppm (117 mg/kg/day in males and 124 mg/kg/d in females). Classification for effects on fertility was not required. However, a NOAEL of 250 ppm (23 mg/kg/day in males and 25 mg/kg/day in females) was identified for general parental toxicity and for effects on the offspring.

New information confirmed the increased incidence of dental malocclusion and twisted snout observed in the F1 and F2 offspring is unlikely to be a developmental effect of PBZ. As the same finding was detected in the treated adult animals of the F_O generation with a similar incidence, it

was considered that, at most, it represents a generalized, unspecific toxic effect of PBZ to pups and adult animals.

Two developmental toxicity studies in the rat are available. In the first study, a NOAEL for maternal toxicity of 100 mg/kg bw/day was identified on the basis of reduced food consumption and deaths at the next dose level of 250 mg/kg bw/day (top dose). Developmental toxicity was limited to delayed ossification of a number of bones. A no-effect level for developmental effects could not be established because a statistically significant, dose-related increase in partially ossified 7th transverse process was apparent at all dose levels (from 40 mg/kg bw/day = LOAEL). There was also an increased incidence of cleft palate (1.28% vs 0% in concurrent and historical controls) at the highest dose which may have been the consequence of maternal toxicity (including lethality); however a direct teratogenic effect could not be ruled out.

In a second study, conducted to determine a no-effect level for developmental toxicity, there were no effects on the dams up to the top dose tested (100 mg/kg bw/day = NOAEL for maternal toxicity). Developmental toxicity was limited to an increased incidence of partial ossification of the transverse processes of the 7th cervical vertebra and extra 14th rib at 40 and 100 mg/kg bw/day. There were no developmental effects at 10 mg/kg bw/day (NOAEL for developmental toxicity).

In two separate developmental toxicity studies in the rabbit, there was no evidence of developmental effects up to the top dose tested of 125 mg/kg bw/day at which maternal toxicity (reduced body weight gain and food consumption) was observed. Additional information confirmed that the reported skeletal variants are chance findings unrelated to treatment and that PBZ is not a developmental toxicant in the rabbit up to maternally toxic dose levels.

Overall, therefore, PBZ causes developmental toxicity in rats, manifested as a low incidence of cleft palate (1.28% affected foetuses vs 0% in concurrent and historical controls), seen in a preliminary study at 240 mg/kg bw/day and in one of the two definitive studies at the top dose of 250 mg/kg bw/day. The lack of the observation in the second definitive study is consistent with the findings of the other studies as the highest dose tested in the second study was only 100 mg/kg bw/day. Although the cleft palate occurred in the presence of severe maternal toxicity (including lethality), there is no evidence that the finding is a secondary non-specific consequence of maternal toxicity. PBZ also causes small changes in the incidences of common skeletal variants in the rat (partial ossification of the transverse processes of the 7th cervical vertebra and extra 14th rib). Although these occurred both in the absence of observable maternal toxicity and in the presence of maternal toxicity, they were observed in isolation, did not show a consistent pattern and were not accompanied by any effects on other foetal parameters, such as body weight. Nevertheless, as cleft palate toxicity is very rare in the rat and is not considered to be a secondary non-specific consequence of maternal toxicity, classification for developmental toxicity in a category representing substances with possible risk of harm to the unborn child was considered to be appropriate.

Tolerances and other guidelines

Since there are no food uses of PBZ, no maximum residue levels for PBZ have been established for agricultural commodities in the US (U.S. EPA, 2007A). A drinking water standard is also not

established in the US. The derivation of a maximum allowable concentration in drinking water of 66 μg/L is described in EFSA (2010A). This value is based on an allowable daily intake of 0.022 mg/kg/day.

In the context of the evaluation water quality data and assessment of pesticide impacts, Baris et al. (2010) calculated a lifetime health advisory level following procedures used by U.S. EPA and reported a value of 460 μg/L for PBZ.

6. ECOTOXICITY

Data on the ecotoxicity of PBZ were available in EPA's summary document for registration review (U.S. EPA, 2007B), in the draft assessment report (EFSA, 2006), and in the additional report to DAR (EFSA, 2010A). The toxicity data considered in these regulatory reviews were primarily obtained from registrant-submitted data. Summaries of these studies are available in review documents generated by EFSA (2006 and 2010A). The ecotoxicity information is described below. A data summary table is included in Appendix 3.

6.1. Acute and Chronic Toxicity of Paclobutrazol

Avian

PBZ is slightly toxic to practically non-toxic to avian species based on acute oral toxicity data (see Appendix 3) ranging from >2100 to >7913 mg/kg b.w. and the ecotoxicity categories as defined by U.S. EPA (2011A). The sub-acute dietary toxicity data indicate that PBZ is slightly toxic to mallard and bobwhite quail. The no-observed-effect-concentration (NOEC) corresponded to a daily dose of 3106 mg/kg/d for mallard and 101 mg/kg/d for bobwhite quail, respectively. A reproductive toxicity effect study with mallard ducks indicated a NOEC that corresponded to a daily dose of 38.8 mg/kg bw/d.

Aquatic Species

The acute toxicity data for bluegill sunfish, rainbow trout, mirror carp and sheepshead minnow listed in Appendix 3 show a range of LC_{50} values from 23.6 to 27.8 mg/L. These data indicate that PBZ is slightly acutely toxic to fish. Aquatic-phase amphibian toxicity data were available from a study with toad tadpoles that indicated a slight toxicity of PBZ with a LC_{50} value of 11 mg/L.

Chronic toxicity data for rainbow trout indicated a NOEC of 3.3 mg/L. The endocrine activity was studied in zebra fish (*Danio rerio*). No activity was found at levels up to and including the mean measured concentration of 3.2 mg/L. No NOEC could be established. However, statistically significant reductions in vitellogenin levels were observed at all test concentrations in male fish, while non-significant decreases were observed in top dose levels in female fish. Fish gonadal screening assays for endocrine activity in zebra fish showed no histopathological treatment-related effect on the gonads, liver, and kidneys.

Bioaccumulation

Bioaccumulation factors in bluegill sunfish were approximately 44 in whole fish, 20 in muscle, and 248 in viscera. During the depuration period the accumulated residues were rapidly eliminated, with ^{14}C-residue concentrations returning to background levels within 7 days.

Aquatic invertebrates

The toxicity data for aquatic invertebrates, including water fleas (*Daphnia magna*), mysid shrimp (*M. bahia*), and Pacific oyster larvae (*C. gigas*), indicate that PBZ is slightly toxic to this class of organisms with LC_{50} data in the range of >9 to 35 mg/L. Chronic toxicity data for water fleas (*D. magna*) indicated a 22-d NOEC value of 0.32 mg/L based on effect on *D. magna* length.

Aquatic plants

For non-vascular aquatic plants, the toxicity of PBZ to green algae (*Selenastrum capricornutum*) the 96-hr E_bC_{50} and E_rC_{50} [1] for PBZ were 7.2 mg/L and >15.2 mg/L, respectively. For blue-green algae (*Anabaena flos-aquae*) these values were estimated to be greater than 23.2 mg/L. PBZ is more toxic to vascular aquatic plants. The data for duckweed (*Lemma gibba*) 7-d E_bC_{50} and E_rC_{50} for PBZ were 8.2 μg/L (0.0082 mg/L) and 28.3 μg/L (0.0283 mg/L), respectively.

Terrestrial Vertebrates

Mammalian toxicity was presented in Section 5. The reader is referred to that section for information relative to the ecotoxicity for terrestrial invertebrates.

Bees

Honey bees (*Apis hellifera*) exposed to PBZ by contact with doses in the range of 2 to 40 μg per bee and orally by dosing at 2 μg per bee indicated contact and oral LD_{50} values that were determined to be >40 μg/bee and >2 μg/bee, respectively.

Earthworms

Clitelate adult earthworms (*Eisenia foetida*) were exposed at a single test concentration of 1000 mg/kg soil for 14 days. The 14 d LC_{50} value was >1000 mg/soil. No deaths, abnormalities in behavior or external condition were observed at the test concentration. There was a statistically significant 20% reduction in body weight. The 14 d LC_{50} value for the ketone degradate was also determined to be >1000 mg/soil.

6.2 Acute and Chronic Toxicity of Metabolites

Metabolites that are considered relevant for ecotoxicological risk assessment are the ketone analog of PBZ, 1,2,4,-triazole and hydroxyl triazole (EFSA, 2006 and 2010). The available toxicity data for these metabolites are listed in Table 6.1. The data for PBZ are included for comparison.

[1] The EbC50 value is the concentration at which 50% reduction of biomass is observed; the ErC50 is the concentration at which a 50% inhibition of growth rate is observed (Bergtold and Dohmen, 2011).

Table 6.1. Comparison of acute (LC_{50}/EC_{50}) and chronic (NOEC) ecotoxicity data of paclobutrazol and its metabolites ketone, 1,2,4-triazole, and hydroxy-triazole (EFSA, 2006 and 2010).

Species	Paclobutrazol (mg/L)	Ketone (mg/L)	1,2,4-triazole (mg/L)	Hydroxy-triazole (mg/L)
ACUTE				
Fish (*O. mykiss*, 96-h LC_{50})	23.6	-	498	-
Invertebrates (*D. magna*, 48-h EC_{50})	27.8	-	>100	-
Algae (*P. subcaptitata*, 72-h EC_{50})	7.2	-	12	-
Aquatic plants (*L. gibba*, 7-d EC_{50})	0.0283	0.57		>100
CHRONIC				
Fish (*O. mykiss*, NOEC)	3.3		100	

The data in Table 6.1 show that the metabolites are less toxic than the parent compound PBZ. In the case of the ketone metabolite, only aquatic plants have been tested. Such an approach was considered acceptable in the review by EFSA (2006) as this group of organisms is considered more sensitive to the parent compound than the other aquatic organism groups tested and the ketone is closer in structure to the parent and is formed higher up in the metabolic pathway.

7. EXPOSURE ASSESSMENT

In order to perform an ecological risk assessment, the exposure assessment is needed to estimate the environmental concentrations associated with the application of PBZ. Given the application method of PBZ as tree growth regulator by soil injection around the base of a tree, the exposure assessment was done for the environmental compartments surface water, ground water, and the soil in and immediately adjacent to the injection area. Potential off-site migration routes that are likely to be relevant for the applied product include runoff and leaching through the soil toward surface water and groundwater. Off-target migration through spray drift is not considered given that the application method is by soil injection.

7.1 Surface Water Exposure

The exposure to surface water was estimated using a Tier I screening-level exposure model that is used by the Environmental Fate and Effects Division of U.S. EPA's Office of Pesticide Programs (EFED-OPP) to assess the risk of a pesticide product to the environment. This Tier I model is designed as a coarse screen and estimates expected concentrations from several basic chemical and environmental fate parameters, and application information. This GENeric Expected Environmental Concentration Program (GENEEC) uses a candidate chemical's soil/water partition coefficient and degradation half-life values to estimate runoff from a ten hectare field into a one hectare by two meter deep pond. GENEEC is a program to calculate both acute and chronic generic expected environmental concentration values. It considers reduction in dissolved pesticide concentration due to adsorption of pesticide to soil or sediment, incorporation into the soil, degradation in soil before wash-off to a water body, direct deposition of spray drift into the water body, and degradation of the pesticide within the water body. It is designed to mimic the more sophisticated PRZM-EXAMS model simulation (Tier II model in EFED-OPP) (U.S. EPA, 2011B).

The model requires input values for parameters associated with application and the characteristics of the active ingredient. An application rate for Cambistat expressed in amount of product or active ingredient per acre has not been established because of its use pattern of treating individual trees. The application rate for the model input was set at 3 lbs per acre for a single application. This application rate was based on the annual maximum rate as for applications on turf (4 application per year of 0.75 lbs PBZ per acre = 3 lbs PBZ per acre) as was used with the exposure modeling described in U.S. EPA (2007B). This rate can be considered a reasonable high-end estimate of a per-acre rate considering the use pattern of treating individual trees. Since the product is injected into the soil, the option of granular application was selected in order to not simulate aerial spray drift. The incorporation depth of 6.0 inches was selected to be representative of the recommended injection depth used with the application of this product.

The values of the chemical and environmental fate properties were a K_D of 2.7 (lowest non-sand value in EFSA (2006), soil half-life of 437 days (according to GENEEC manual instructions for selecting conservative parameter value), aquatic half-life of 164 d, and photolysis half-life of 365 d (stable). The GENEEC input and output for this scenario are included in Appendix 4.

The model output shows that the simulated peak generic environmental concentration was 19.98 µg/L (0.01998 mg/L), the maximum concentration was 19.34 µg/L at 21 d and 17.35µg/L at 90

days. It is important to note that the GENEEC model simulates conservative pesticide concentrations for aquatic ecological exposure assessments.

7.2. Groundwater Exposure Assessment

The exposure of herbicides to groundwater was evaluated by using the SCI-GROW model simulations. SCI-GROW (***S***creening ***C***oncentration ***I***n ***GRO***und ***W***ater) is a screening model which the Office of Pesticide Programs (OPP) in EPA frequently uses to estimate pesticide concentrations in vulnerable ground water (U.S. EPA, 2011C). The model provides an exposure value which is used to determine the potential risk to the environment and to human health from drinking water contaminated with the pesticide. The SCI-GROW estimate is based on environmental fate properties of the pesticide (aerobic soil degradation half-life and linear adsorption coefficient normalized for soil organic carbon content), the maximum application rate, and existing data from small-scale prospective ground-water monitoring studies at sites with sandy soils, low organic matter content (on average <1%) and shallow ground water (on average 14 ft).

Pesticide concentrations estimated by SCI-GROW represent conservative or high-end exposure values because the model is based on ground-water monitoring studies which were conducted by applying pesticides at maximum allowed rates and frequency to vulnerable sites (i.e., shallow aquifers, sandy, permeable soils, and substantial rainfall and/or irrigation to maximize leaching). In most cases, a large majority of the use areas will have ground water that is less vulnerable to contamination than the areas used to derive the SCI-GROW estimate.

The input parameters for SCI-GROW include the application rate, soil degradation (soil half-life value) and a soil mobility parameter (soil organic matter-water partitioning coefficient (K_{OC}). Following the instructions for input value selection, the annual application rate used was 3 lbs PBZ per acre (as described with surface water assessment), the soil half-life was 285 days (see surface water assessment), and the K_{OC} was 106 mL/g (determined from the lowest non-sand K_D value used above with surface water and the corresponding organic carbon content of 2.5%: K_{OC} = K_D/ fraction OC).

The SCI-GROW simulated screening-level groundwater concentration using the selected input values as described above was 14.3 µg/L(see also Appendix 5).

7.3. Soil Exposure at the Application Site

The exposure of PBZ in the soil following the injection of the product in a band around the trunk base of a tree was estimated by considering the amount of product applied according to label instruction to a tree with an assumed trunk diameter and assumed dimensions of a soil band around the trunk base of the tree that would received the initial application of the product. Details on the calculation of the PBZ concentration in the soil of the treated area around a tree are shown in Appendix 6. The initial peak concentration of PBZ in the treated soil band was calculated to be 150 mg/kg dry soil.

8. RISK CHARACTERIZATION

8.1 Ecological Risk Assessment

Ecological risk characterization integrates the results of the exposure and ecotoxicity data to evaluate the likelihood of adverse ecological effects. For most ecological risk assessments, U.S. EPA uses a deterministic approach or the quotient method to compare toxicity to environmental exposure. In the deterministic approach, a risk quotient (RQ) is calculated by dividing exposure estimates by ecotoxicity values, both acute and chronic. RQ values are then compared to established levels of concern (LOCs). The LOCs are criteria used by U.S. EPA to indicate potential risk to non-target organisms. The RQ ratio is a screening-level method that identifies high- or low-risk situations (U.S. EPA, 2011D).

As pointed out earlier, the environmental compartments that are most likely to be exposed to the products or residues thereof are the soil in and adjacent to the treatment area, and surface and ground water. The ecological risk assessment will therefore consider the risk to aquatic organisms and earthworms. Based on the localized application of product in the soil of tree rooting area it can be expected that the exposure to terrestrial vertebrates and birds is going to be minimal. The groundwater is not considered as a relevant environmental compartment for ecological risk, but will be addressed separately for a drinking water assessment.

The RQ values for the groups of organisms considered in this ecological risk assessment are listed in Table 8.1 along with the corresponding toxicity endpoint and EEC data. The RQ are compared with the established LOCs (U.S. EPA, 2011D).

Table 8.1. Ecological risk assessment data for paclobutrazol.

Species	Toxicity Endpoint	Endpoint Value	EEC	RQ	LOC[1]
AQUATIC INVERTEBRATES		(mg/L)	mg/L	EEC/ Endpoint	
Daphnia magna	Acute 96-h LC_{50}	35	0.01998	0.0006	0.5
Mysid Shrimp	Acute 96-h LC_{50}	>9	0.01998	>0.0022	0.5
Pacific oyster larvae	Acute 48-h EC_{50}	>10	0.01998	>0.0020	0.5
Daphnia magna	Chronic NOEC	0.32	0.0173	0.0541	1
FISH					
Bluegill sunfish	Acute 96-h LC_{50}	23.6	0.01998	0.0008	0.5
Rainbow trout	Acute 96-h LC_{50}	27.8	0.01998	0.0007	0.5
Mirror Carp	Acute 96-h LC_{50}	26.0	0.01998	0.0008	0.5
Sheepshead minnow	Acute 96-h LC_{50}	24.3	0.01998	0.0008	0.5
Rainbow trout	Chronic 22-d NOEC	3.3	0.01735	0.0053	1

Species	Toxicity Endpoint	Endpoint Value	EEC	RQ	LOC[1]
AMPHIBIAN (aquatic phase)					
Bufo bufo (toad)	Acute 72-h LC_{50}	11	0.01998	0.0018	0.5
AQUATIC PLANTS					
Green algae	Growth E_bC50	7.2	0.01988	0.0028	1
	Growth E_rC50	15.2	0.01988	0.0013	1
Blue-green algae	Growth E_bC50	>23.2	0.01988	>0.0009	1
	Growth E_rC50	>23.2	0.01988	>0.0009	1
Duck weed	Growth E_bC50	0.0082	0.01988	**2.4244**	1
	Growth E_rC50	0.0283	0.01988	0.7025	1
EARTHWORMS		mg/kg soil	mg/kg soil		
Eisenia foetida	Acute 14-d LC_{50}	>1000	150	0.15	0.5

[1] LOC values established by U.S. EPA, 2011D.

Comparison of the RQ values with the established LOCs indicates that all are well below the established LOCs, except for duckweed. The low RQ values indicate low potential for adverse effects on most aquatic organisms. The RQ value for growth effects on duckweed biomass indicates that there is some potential for adverse effects for vascular aquatic plants. This can be expected from exposure of plants to a growth retardant compound. Given the slight exceedance of the LOC and that the effect is on growth, it is not expected that the impact would be detrimental for this group of organisms. In addition, the estimated surface water concentration is a screening-level assessment that is based on conservative assumptions. The screening-level concentration can be considered to be representative of a high-end exposure and will not occur in most situations.

Earthworms are organisms that could be exposed to PBZ following a soil injection application around the perimeter of a tree trunk. However, the level of exposure associated with such an application would not exceed the LOC for this group of organisms. PBZ soil concentration and associated exposure by earthworms would also decrease over time as the PBZ is gradually taken up by the tree.

Acute and chronic risk to mammals from potential exposure to PBZ residues in food was assessed in the review by EFSA (2006). The exposure assessment was based on the application rate of 0.0557 lbs PBZ per acre as proposed for use on an oil seed crop. The food intake rate considered was for a medium-sized herbivorous mammal and residue characteristics were

representative for application to a leafy crop. The estimated theoretical exposure was 2.18 mg PBZ/kg bw/d (acute) and 0.51 mg PBZ/kg bw/d (chronic). The toxicological endpoints used in this risk assessment were the LD_{50} for male mouse (490 mg PBZ/kg bw) and developmental toxicity NOAEL of 10 mg/kg bw in rat. A developmental end-point was used as this was the lowest longer-term end-point and therefore considered to represent the worst-case scenario. Using this information, EFSA calculated a toxicity exposure ratio (TER) of 224.8 for acute risk and 19.6 for chronic risk. Based on comparison with the levels of concern (TER values of greater than 10 for acute risk and greater than 5 for chronic risk are not of concern), EFSA concluded that the acute and chronic risks to mammals were not a concern.

It should be pointed out that the developmental endpoint is toxicologically not considered a long-term or chronic endpoint. Developmental exposure is typically viewed as being of intermediate exposure. The evaluation of chronic toxicity using a toxicity value based on intermediate exposure is not protective.

Alternative long-term toxicological end-points for mammalian species identified by EFSA were the NOAEL of 23.2 mg/kg bw/d for parental toxicity and 108 mg/kg bw/d for reproductive toxicity. Evaluation of chronic risk based on these endpoints results in TER values of 45 (parental) and 212 (reproductive) which can be considered protective. Given that there was no estimated theoretical exposure of medium duration generated in the EFSA evaluation, it is not possible to properly evaluate the developmental endpoint, (i.e., the most sensitive endpoint) based on the available information. It is likely that if an exposure estimate of intermediate exposure were to be generated, that it would indicate that developmental effects would not be of concern—however, such a conclusion cannot be drawn based on the current information.

The risk to earthworm-eating mammals was assessed by considering the residue estimates in earthworms that were based on estimated bioconcentration factors and concentrations of PBZ in soil. The residue estimates were converted to a daily dose that had a value of 0.18 mg PBZ/kg bw/d. Compared to the long-term NOAEL of 10 mg/kg bw/d, the toxicity exposure ratio was 55.6. This value exceeds the trigger value (level of concern) of 5 (a TER value greater than 5 for chronic risk is not of concern) and therefore it was concluded that the risk to earthworm-eating mammals was not a concern.

The risk assessments described above were done assuming an application scenario representative for the use of PBZ on oilseed crops, which includes broadcast foliar applications resulting in residues that mostly occur on above ground plant material. The use scenario for tree treatments, in contrast, is by soil injection around the tree trunk perimeter, which results in a much more localized application of the material in the soil. It is likely that tree trunk application results in higher concentrations of PBZ occur in soil compared to soil concentrations associated with broadcast foliar applications. However, it is unlikely that small mammals would feed exclusively and permanently in a treated tree trunk area. It is therefore unlikely that the exposure of mammals to PBZ in a tree trunk treatment scenario would exceed the exposure levels as described above in the broadcast oil seed crop scenario. The risks to mammals from PBZ exposure associated with tree trunk applications is not expected to be significant.

8.2 Comparison of Estimated Groundwater Concentration with Drinking Water Standards

The screening-level groundwater concentration of 14.3 ppb is below the maximum allowable concentration in drinking water of 66 µg/L reported in EFSA (2010A). This screening-level concentration is also below the lifetime health advisory level of 460 µg/L calculated by Baris et al. (2010).

With the consideration of the risk to groundwater it is important to consider that the screening-level concentrations generated by the SCI-GROW model represent conservative or high-end exposure. In most cases, the use areas will have ground water that is less vulnerable to contamination than the areas used to derive the SCI-GROW estimate. In addition, the model does not consider buffer zones around a drinking water well as is required by ROW regulations.

9. RISK MITIGATION AND USE PRECAUTIONS

The product label (Rainbow Treecare, 2011) offers a number of precautionary practices that may be taken to mitigate potential risks to non-target organisms. Given that the product is a plant growth inhibitor, non-target plants have the highest potential to be affected by PBZ exposure through off-site movement of applied product. This potential risk to non-target plants is addressed by warning and precautionary language on the label:

Localized stunting or injury of turfgrass or other non-target plants immediately adjacent to the treatment site may occur if the product flows off of the application site.

Avoid basal drench applications on inclines and other areas where treated soil is likely to be washed away from the base of the tree by rainfall or irrigation.

Shrubs and/or herbaceous ornamentals next to treated trees may be affected if their roots extend into the treatment zone.

The risk to aquatic organisms is addressed by language that states that the product should not be applied directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark.

Other label language addresses the treatment of trees that produce products for human consumption such as maple trees, and fruit and nut trees.

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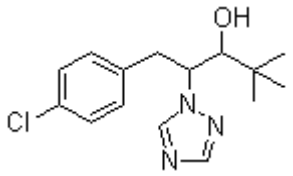
Appendix 1

Table A1.1. Paclobutrazol structure and nomenclature

Paclobutrazol	
Structure	
Molecular Formula	$C_{15}H_{20}ClN_3O$
IUPAC Name	(2*RS*,3*RS*)-1-(4-chlorophenyl)-4,4-dimethyl-2-(1*H*-1,2,4-triazol-1-yl)pentan-3-ol
CAS name	(a*R*,ß*R*)-*rel*-ß-[(4-chlorophenyl)methyl]-a-(1,1-dimethylethyl)-1*H*-1,2,4-triazole-1-ethanol
CAS Number	76738-62-0
PC Code	125601

Source: U.S. EPA, 2007B

Table A1.2. Physical and chemical properties of paclobutrazol

Parameter	Value	Source
Molecular Mass	293.8	EFSA, 2006[1)]
Melting/Boiling point	164 °C/ 384 °C	EFSA, 2006
Density	1.23 g/cm^3 (20 °C)	EFSA, 2006
Vapor Pressure	1.9 × 10^{-6} Pa (very slightly volatile)	EFSA, 2006
Volatility from water (Henry's constant	2.39 × 10^{-5} Pa m^3 mol^{-1}	EFSA, 2006
Solubility in water	26 mg/L (20 °C)	BCPC, 2000[2)]
Octanol-water partitioning constant (Log P)	3.2	BCPC, 2000

1) EFSA, 2006, Section B.2.1; [2)] British Crop Protection Council, 2000 (The Pesticide Manual).

Appendix 2

Table A2.1. Environmental fate properties for mobility and persistence of paclobutrazol

Parameter	Value	Source
Hydrolysis	Stable: <6% degradation after 30 d at pH 4,7, and 9	U.S. EPA, 2007B
Photolysis in water	Stable: < 5% degradation after 10 d at pH 7	U.S. EPA, 2007B
Aerobic soil metabolism (half-life)	> 1 yr 43 – 618 d (mean 183 d)	U.S. EPA, 2007B EFSA, 2006 [1)]
Anaerobic soil metabolism (half-life)	> 1 yr	U.S. EPA, 2007B
Field dissipation (half-life)	450-950 d in orchard US soils 175 – 252 d in agricultural US soils	U.S. EPA, 2007B EFSA, 2006 [1)]
Aquatic metabolism (half-life)	164 d	EFSA, 2007B
Soil Adsorption Coefficient (K_D) mL/g	1.3 – 23.0 0.8 – 21.3 (mean of 4.3)	U.S. EPA, 2007B EFSA, 2006 [1)]

[1)] EFSA, 2006: Volume 3, Annex B, Section 8.

Appendix 3

Table A3.1. Summary of ecotoxicity data for paclobutrazol. Data were obtained from U.S. EPA (2007B), EFSA (2006) and EFSA (2010).

Species	Toxicity	Endpoint	Values
AVIAN			(mg/kg b.w.)
Mallard	Acute Oral[1]	LD50	>7913
Japanese Quail	Acute Oral	LD50	>2100
Mallard	Sub-acute dietary[2]	LD50	>3106
		NOEC	3106
Bobwhite Quail	Sub-acute dietary	LD50	>2791
		NOEC	101
Mallard	Long-term/ Reproductive[3]	NOEC	38.8
AQUATIC INVERTEBRATES			mg/L
Daphnia magna (flea)	Acute	48 hr EC50 static	35
Mysid Shrimp	Acute	96 hr EC50 semi- static	>9
Pacific oyster larvae	Acute	48 hr EC50 static	>10
Daphnia magna	Chronic	22-d NOEC semi-static	0.32
FISH			mg/L
Bluegill sunfish	Acute	96 hr EC50 semi- static	23.6
Rainbow trout	Acute	96 hr EC50 semi- static	27.8
Mirror Carp	Acute	96 hr EC50 semi- static	26.0
Sheepshead minnow	Acute	96 hr EC50 static	24.3
Rainbow trout	Chronic	28-d NOEC	3.3
AMPHIBIAN (aquatic phase)			mg/L
Bufo bufo (toad)	Acute	24-h LC50	11
VERTEBRATES (terrestrial)			mg/kg
Rat	Acute Oral[1]	LD50	1954 (male) 1336 (female)
Mouse	Acute Oral	LD50	490 (male) 1219 (female)
Guinea Pig	Acute Oral	LD50	542 (male) 400-640 (female)

Species	Toxicity	Endpoint	Values
Rabbit	Acute Oral	LD50	835 (male) 937 (female)
BEES			µg/bee
Honey bee *(Apis mellifera)*	Acute	48-hr LD50	>40 (contact) >2 (oral)
EARTHWORMS			mg/kg soil
Eisenia foetida	Acute	14-d LC50	>1000
AQUATIC PLANTS			mg/L
Green algae	Growth	96-h E_bC50 96-h E_rC50	7.2 15.2
Blue-green algae	Growth	96-h E_bC50 96-h E_rC50	>23.2 >23.2
Duck weed	Growth	7-d E_bC50 7-d E_rC50	0.0082 0.0283

[1] Exposed by a single oral dose

[2] Exposed by diets containing PBZ for 5 d

[3] Exposed by diets containing PBZ for 21 wks

Appendix 4

GENEEC Surface Water Model Input and Output:

```
RUN No.**** FOR Paclobutrazol  ON  Trees     * INPUT VALUES *
  ---------------------------------------------------------------------
  RATE (#/AC)  No.APPS &  SOIL SOLUBIL  APPL TYPE NO-SPRAY INCORP
  ONE(MULT)  INTERVAL   Kd  (PPM )  (%DRIFT)  ZONE(FT) (IN)
  ---------------------------------------------------------------------
 3.000( 3.000)  1  1    2.7  26.0  GRANUL(  .0)  .0  6.0


  FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)
  ---------------------------------------------------------------------
  METABOLIC DAYS UNTIL HYDROLYSIS  PHOTOLYSIS  METABOLIC COMBINED
  (FIELD)  RAIN/RUNOFF  (POND)   (POND-EFF)  (POND)   (POND)
  ---------------------------------------------------------------------
  437.00    2     N/A  365.00-45260.00  164.00  163.41


  GENERIC EECs (IN MICROGRAMS/LITER (PPB))   Version 2.0 Aug 1, 2001
  ---------------------------------------------------------------------
    PEAK   MAX 4 DAY   MAX 21 DAY  MAX 60 DAY  MAX 90 DAY
    GEEC   AVG GEEC    AVG GEEC   AVG GEEC   AVG GEEC
  ---------------------------------------------------------------------
    19.98    19.88     19.34     18.17     17.35
  ---------------------------------------------------------------------
```

Appendix 5

SCI_GROW model input and output for Paclobutrazol:

```
             SCIGROW
            VERSION 2.3
     ENVIRONMENTAL FATE AND EFFECTS DIVISION
        OFFICE OF PESTICIDE PROGRAMS
      U.S. ENVIRONMENTAL PROTECTION AGENCY
           SCREENING MODEL
       FOR AQUATIC PESTICIDE EXPOSURE

SciGrow version 2.3
chemical:Paclobutrazol
time is 6/13/2011 16:34:39
-------------------------------------------------------------------------
Application   Number of    Total Use  Koc   Soil Aerobic
rate (lb/acre) applications  (lb/acre/yr) (ml/g)  metabolism (days)
-------------------------------------------------------------------------
  3.000      1.0      3.000   1.06E+02   285.0
-------------------------------------------------------------------------
groundwater screening cond (ppb) =  1.43E+01
*************************************************************************
```

Appendix 6

Estimation of Paclobutrazol concentration in soil band around tree trunk:

Assumptions:

- Diameter of trunk at breast height of 50 inches
- Mass of applied PBZ is 202.5 g (calculated from information on Cambistat Label)
  (833 ml product x 1.09 g/ml x 22.3 % PBZ = 202.5 g PBZ)
- Diameter trunk at ground level is 60 inches
- Soil band treated begins 2 inches from trunk resulting in an inside diameter of soil band of 64 inches
- A 1-foot wide band will initially be exposed to product: Outside diameter of band is 76 inches
- Treatment reaches initially a depth of 1 ft
- Dry bulk density of soil to be 1.3 g/ml

Conversions:	Inside diameter:	64 inches =	162.56	cm
	Outside diameter:	76 inches =	193.04	cm
	Depth	12 inches =	30.48	cm

Calculations:

Area of treated soil band: Calculated by subtracting the areas of the circles with outside and inside diameters:

	Outside diameter:	Inside diameter:		
Circle areas (cm^2):				
(πR^2)	117069.7	83018.95		
Difference between circle areas is band area:			34050.74	cm^2
Volume of treated soil band: (area x depth):			1037867	cm^3
Mass of dry soil is volume x bulk density:			1349227	g
			1349.227	kg
Mass of applied PBZ in band area of soil:			202.5	g
Concentration of PBZ in soil (mg/kg or ppm)			150.086	ppm