Registration Decision RD2023-08

Florpyrauxifen-benzyl, Milestone NXT Herbicide, Restore NXT Herbicide, GF-3206 Herbicide, GF-3301 Aquatic Herbicide, and ProcellaCOR FX Herbicide

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Table of Contents

Under the authority of the *Pest Control Products Act,* pesticides must be assessed before they are sold or used in Canada in order to determine that they do not pose unacceptable risks to humans or the environment and have value when used according to the label instructions. The pre-market assessment considers available data and information[1] from pesticide registrants, published scientific reports, other governments, and international regulatory agencies, as well as comments if received during public consultations. Health Canada applies internationally accepted current risk assessment methods as well as risk management approaches and policies. More details, on the legislative requirements, risk assessment and risk management approach, are provided under the Section of Evaluation Approach of this document.

Registration decision statement[2] for florpyrauxifen-benzyl

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is granting registration for the sale and use of Rinskor Active, Milestone NXT Herbicide, Restore NXT Herbicide, GF-3206 Herbicide, GF-3301 Aquatic Herbicide and ProcellaCOR FX Herbicide, containing the technical grade active ingredient florpyrauxifen-benzyl, for weed management in hazelnut and non-agricultural/industrial vegetation management including many invasive species, as well as for aquatic vegetation management to control invasive plants both in and around water.

The Proposed Registration Decision PRD2022-17, *Florpyrauxifen-benzyl, Milestone NXT Herbicide, Restore NXT Herbicide, GF-3206 Herbicide, GF-3301 Aquatic Herbicide, and ProcellaCOR FX Herbicide*, containing the detailed evaluation of the information submitted in support of this registration, underwent a 45-day consultation period ending on 30 January 2023. The evaluation found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable. Health Canada received comments relating to the chemistry, health and environmental assessments during the public consultation period conducted in accordance with section 28 of the *Pest Control Products Act*.

Comments and responses

Comments on the chemistry assessment

Comment on the level of toluene

EcoJustice indicated that the PMRA did not appear to address potential impurities from toluene as identified in a European Union review published in 2019. EcoJustice asked the PMRA to establish a maximum limit to the levels of toluene as a condition of registration and consider the EU limit of 3 g/kg.

[1] Information Note – *Determining Study Acceptability for use in Pesticide Risk Assessments*

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

Health Canada response

Under the *Pest Control Products Act*, the identity and concentration of impurities in a pest control product are considered to be confidential business information (CBI), with the exception of those identified on the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*. As toluene is not included on that list, the PMRA cannot disclose levels of this impurity in specific registered pest control products as it is currently considered confidential business information. Please note that impurities of concern are taken into consideration as part of PMRA's health and environmental assessments, and pest control products containing such impurities are acceptable for registration only if the levels of the impurities are within acceptable limits.

Comments on the health assessment

Comment on the cumulative health risk assessment

EcoJustice stated that two pyridine-carboxylate herbicides, clopyralid and picloram, should be considered as part of the cumulative assessment of florpyrauxifen-benzyl, which they also state is a pyridine-carboxylate herbicide. They also noted that florpyrauxifen-benzyl is a Group 4 herbicide and state that the Group 4 herbicides are associated with neurotoxic responses.

Health Canada response

Health Canada Science Policy Note (SPN2018-02) entitled *Cumulative Health Risk Assessment Framework* describes the framework and methodology that Health Canada's Pest Management Regulatory Agency (PMRA) uses for assessing the cumulative health effects of pesticides that have a common mechanism of mammalian toxicity. Consistent with the approach outlined in SPN2018-02, Health Canada followed a weight-of-evidence approach to explore the potential for a common mechanism of mammalian toxicity for this active ingredient with other pesticides. Health Canada considered chemicals within the same class of herbicides, which takes into consideration similarities with respect to structure and pesticidal mode of action. Florpyrauxifen-benzyl is an arylpicolinate herbicide. The two pesticides noted in the comment are pyridine-carboxylate herbicides, which, while in the same greater class of synthetic auxins, do not share structural similarities with florpyrauxifen-benzl. Furthermore, Health Canada examined the toxicology databases of the general class of auxin herbicides and compared apical endpoints among the available toxicity studies. Although some adverse effects observed were common among some of the pesticides, such as decreased body weight and body weight gain, these findings were indicative of more generalized toxicity and are not linked to a specific common mechanism of mammalian toxicity. There are no indications of neurotoxicity in the database for florpyrauxifen-benzyl or in that of the pyridine-carboxylate herbicides. Florpyrauxifen-benzyl and the pyridine-carboxylate herbicides do not have similar mammalian toxicity profiles, and as a result, no common mechanism of toxicity was identified. Overall, for the current evaluation, Health Canada did not identify information indicating that florpyrauxifen-benzyl shares a common mechanism of mammalian toxicity with other pest control products.

This is consistent with the approach outlined in SPN2018-02, which indicates that effects which may have many possible unrelated causes, or that could be considered nonspecific in origin, are not appropriate as the primary basis for grouping chemicals for cumulative risk assessment. Health Canada thus determined that a cumulative risk assessment was not required at this time.

Comment on the acceptable daily intake (ADI)

EcoJustice questioned the setting of an ADI of 2 mg/kg bw/d when the European Food Safety Authority (EFSA) set an ADI of 0.5 mg/kg bw/d stating that Health Canada's chronic reference dose appears to underestimate chronic toxicity.

Health Canada response

In EFSA's (2018) "Peer review of the pesticide risk assessment of the active substance florpyrauxifen (variant assessed florpyrauxifen-benzyl)", it is stated that the no observed adverse effect level (NOAEL) in the 2-year toxicity study in rats was 50 mg/kg bw/day based on an increased incidence of mammary gland tumours observed in males at the lowest observed adverse effect level (LOAEL) of 200 mg/kg bw/day. This was the only finding cited at that dose level. It was further stated in the document that there was a lack of consensus within the Expert Peer Review and with the Rapporteur Member State as to whether the tumours were treatment-related. While the EFSA decision was to call the tumours treatment-related, it did not propose classification regarding carcinogenicity and the overall uncertainty factor was retained at 100. Other regulatory authorities including the United States Environmental Protection Agency (2019) and the Australian Pesticides and Veterinary Medicines Authority (2018), did not consider these tumours to be treatment-related or adverse.

At the time of Health Canada's review of florpyrauxifen-benzyl, the presence of very low incidences of mammary adenocarcinomas in males was noted in the 50 and 200 mg/kg bw/day dose groups in the 2-year combined chronic toxicity and carcinogenicity study in rats. These tumours occurred in the absence of any other findings in the study up to the highest dose tested (200 mg/kg bw/day). Health Canada reviewed the incidences of tumours, the historical control data for the tumour type in the performing laboratories, the histopathology of the tissue and any incidences of tumours or equivalent histopathology in females given the same doses. The weight-of-evidence considered the lack of expected treatment-related pre-neoplastic lesions in males or females, the lack of statistical significance of the finding, the lack of mammary adenocarcinomas in females in any of the treated groups, and that florpyrauxifen-benzyl was not mutagenic in a standard battery of genotoxicity assays. In contrast to the EFSA evaluation, Health Canada concluded that the tumours were not treatment-related. The chronic toxicological potential of florpyrauxifen-benzyl is well-characterized and an ADI of 2 mg/kg bw/day is considered appropriate, given the lack of treatment-related effects observed in this study up to the highest dose tested.

Comments on the environmental assessment

Comment on the Toxic Substances Management Policy considerations

EcoJustice commented that "The active meets track 1 criteria: Actives in this group are also persistent and there is the potential for groundwater and surface water contamination and soil contamination. This particular active has assessed as being persistent in the soil for up to 348 days. There is a history of compost contamination with actives in this group. As the metabolites of this active are bioaccumulative we submit that the PMRA should reconsider whether this meets Track 1 criteria."

Health Canada response

To be considered a Track 1 substance under the Toxic Substances Management Policy, a substance must meet all Track 1 criteria (persistent, bioaccumulative, toxic, and predominantly anthropogenic).

Although florpyrauxifen-benzyl met the criterion for persistence in soil under laboratory conditions, it dissipated rapidly under field conditions. It also did not meet the criterion for bioaccumulation based on a laboratory study in fish, even though its log K_{ow} (octanol-water partition coefficient) was greater than 5. As indicated in PRD2022-17, footnote 6 below Table 56, the results of laboratory data are preferred over chemical properties when evaluating the potential for bioaccumulation.

None of the major transformation products met the bioaccumulation criterion based on their log K_{ow} values. Although laboratory bioconcentration factor (BCF) data were not available for these substances, their structural similarity to florpyrauxifen-benzyl and estimated BCFs calculated using EPISuite v4.11 (BCFBAF v3.01) indicate they are unlikely to bioaccumulate.

As neither florpyrauxifen-benzyl nor its transformation products meet **all** Track 1 criteria, they are not considered Track 1 substances.

Comment on the environmental risk assessment

EcoJustice commented that "The active exceeded levels of ecological concern: major metabolites of this active exceeded the level of concern for freshwater vascular plants. GF-3206 herbicide exceeded the level of concern for bees and leaf-dwelling invertebrates. Levels of concern were dramatically exceeded for terrestrial plants from GF-3206 and florpyrauxifen acid. There were also exceeded levels of concern for freshwater benthic invertebrates. Rangeland and pasture uses exceeded levels of concern for drift from aerial spraying for freshwater vascular plants. The PMRA can only register a product where it has reasonable certainty that no harm will occur to the environment. As the PMRA has identified harm to milfoil species and other species it does not have discretion to register this active (or its associated end use products) for any of the use patterns such as rangeland and filbert uses/aerial applications that would result in those effects."

Health Canada response

The PMRA uses a tiered approach when conducting environmental risk assessments of pesticides. Initially, a screening-level risk assessment was performed to identify the chemicals and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment used simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate), and sensitive effect metrics. If potential risks were identified at the screening-level, a refined assessment was conducted, which took into consideration more realistic exposure scenarios and effects metrics. When both a screening-level and refined assessment are performed for a given taxon or use pattern, the overall risk conclusions are based on the results of the refined risk assessment.

Effects to bees and leaf-dwelling invertebrates

In the assessment of terrestrial end-use products (including GF-3206), the conservative screening level risk quotients (RQs) for bees did not exceed the level of concern (LOC).

For leaf-dwelling invertebrates, screening-level RQs (2.5) slightly exceeded the LOC of 2. When considering higher tier data (with acute and chronic exposure to GF-3206 on leaf surfaces), the RQs did not exceed the level of concern. Based on these results, the terrestrial end-use products are not expected to pose a risk to bees or leaf-dwelling invertebrates.

In the screening-level assessment of risk from irrigation with surface waters treated during aquatic applications, some RQs for bees and leaf-dwelling beneficial invertebrates exceeded LOCs. This assessment incorporated the conservative assumptions of no pesticide degradation in the surface water source where pesticide was applied and daily irrigation over a 60-day period. More realistic exposure scenarios for irrigation were considered in the refined assessment, and included both a single irrigation event at peak concentrations of the pesticide, and daily irrigation over a 60-day period using average pesticide concentrations that accounted for degradation over the exposure duration. RQs calculated using the refined scenarios for irrigation did not result in any LOC exceedances for bees or leaf-dwelling invertebrates. Based on these results, risks are not expected for bees and leaf-dwelling invertebrates exposed to treated surface water used for irrigation following application of the aquatic end-use products.

Effects of GF-3206 to freshwater benthic invertebrates

The assessments for aquatic and terrestrial end-use products identified risks to freshwater benthic invertebrates at the screening-level only. These assessments assumed no pesticide degradation, and RQs were calculated using environmental exposure concentrations (EECs) and effects metrics based on overlying water concentrations. As described on page 43 of PRD2022-17, this approach likely overestimates risk quotients when using effect metrics from spiked sediment studies.

Because florpyrauxifen-benzyl has very low water solubility and adsorbs to sediment, the low overlying water concentrations of florpyrauxifen-benzyl in the spiked sediment studies are likely not representative of the exposure concentrations associated with effects to benthic invertebrates. Effects metrics based on pore water concentrations are more representative of effects to benthic invertebrates and were used in the refined assessment.

In the refined assessment, RQs were calculated using modelled EECs in pore water (considering dissipation), and effects metrics based on pore-water concentrations. These RQs did not exceed the LOC. Based on these results, the aquatic and terrestrial end-use products are not expected to pose risk to benthic invertebrates.

Effects to aquatic and terrestrial vascular plants

Several preventative measures and use restrictions have been included on the product labels to mitigate risks to non-target aquatic and terrestrial plants from both aquatic and terrestrial uses. As outlined in PRD2022-17, while florpyrauxifen-benzyl and florpyrauxifen acid may pose some risks to sensitive non-target terrestrial plants and aquatic vascular plants, the PMRA recognizes that control of invasive species is necessary to help protect habitats for native species.

For the terrestrial end-use products applied to rangeland and pasture, and filberts, spray drift buffer zones are included on the label to mitigate risks to aquatic and terrestrial plants from spray drift.

For the aquatic end-use product, some potential risks to plants are considered acceptable in light of the risks to habitats posed by invasive species, such as non-native milfoil. The results of available higher tier mesocosm and field data indicate that most non-target plants are either unaffected, or recover following application of the product, and that effects are generally limited to the management area. Furthermore, increases in species richness were observed following applications to control invasive species. The use of the aquatic end-use products is restricted and these products can only be applied with appropriate permits from the federal, provincial and/or territorial agencies.

Comments on the aquatic vascular plant endpoints

The applicant, Corteva Agriscience Canada Company, submitted several comments related to the aquatic vascular plant endpoints used in the screening-level and refined environmental risk assessments. These comments indicated that:

1) For aquatic primary producers, growth rate endpoints are scientifically preferred over the more sensitive yield endpoints, as indicated in several OECD guidelines and open-literature sources (Nyholm, 1990; Eberius et al., 2002; Bergtold and Dohmen, 2010). Growth rate endpoints are therefore recommended for use in the environmental risk assessment.
2) In studies testing the effects of technical and end-use products containing florpyrauxifen-benzyl on aquatic vascular plants, measured concentrations of the major transformation product, florpyrauxifen acid, could have been considered and

used to determine ecotoxicity endpoints based on florpyrauxifen-benzyl equivalents rather than florpyrauxifen-benzyl concentrations alone.

3) In the study testing the effects of GF-3301 on *Myriophyllum spicatum* (PMRA# 3133022), a slight increase in shoot length yield (~3%) was observed at the lowest treatment level. Corteva indicated that the 4P log-logistic+hormesis model provided a lower AIC value (143.5) and therefore better fit compared to the 4P log-logistic model proposed by PMRA (AIC = 144.1).

Health Canada responses

1) **Relevance of endpoints based on growth rate versus yield:** The PMRA acknowledges that EC_{50}s based on yield will generally be lower than those based on growth rate for mathematical reasons, and that the OECD 201 and 221 guidelines for algae and *Lemna sp*. state that the use of average specific growth rate for estimating toxicity is scientifically preferred. However, no preference between growth rate and yield endpoints is specified in the OECD 239 guideline for water-sediment tests with *Myriophyllum spicatum*. The articles cited by Corteva (Nyholm, 1990; Eberius et al. 2002, Bergtold and Dohmen, 2010) studied the yield and growth rate endpoints in algae and *Lemna* species, but not in rooted macrophyte species, such as *Myriophyllum spicatum*.

   In the risk assessment of aquatic plants, rooted macrophytes were most sensitive to florpyrauxifen-benzyl and its transformation products, whereas few effects to algae and *Lemna gibba* were observed. As the available guideline for rooted macrophytes (OECD 239) does not specify a preference between endpoints, yield is considered an appropriate and conservative endpoint for these organisms.

2) **Concentrations used to calculate EC_{50} values for aquatic plants exposed to florpyrauxifen-benzyl:** Although in the studies with exposures to florpyrauxifen-benzyl, the PMRA calculated aquatic plant endpoints based on the measured concentrations of florpyrauxifen-benzyl alone and did not include the concentrations of florpyrauxifen acid measured during the test, the degradation of florpyrauxifen-benzyl was considered when calculating modelled EECs and when taking into account monitoring data in the refined assessment.

   Ecotoxicology studies for aquatic plants were available for both florpyrauxifen-benzyl and florpyrauxifen acid, and indicated that florpyrauxifen-benzyl has much higher toxicity than florpyrauxifen acid alone. The physical-chemical and environmental fate properties of the two substances also differ, with florpyrauxifen acid having much higher water solubility and lower K_d/K_{oc} values compared to the parent. For these reasons, the EECs and endpoints were calculated for each substance individually.

   As indicated by Corteva Agriscience Canada Company, for the studies where aquatic plants were exposed to florpyrauxifen-benzyl, the calculation of endpoints based solely on florpyrauxifen-benzyl concentrations is conservative. Although RQs for some aquatic plant species exceeded the LOC when using endpoints from laboratory toxicity studies and exposure estimates based on modelling and monitoring data, risks were determined

to be acceptable based on the refinements using available higher-tier field and mesocosm studies. These field and mesocosm studies demonstrated recovery of most plant species following application of the product. Additional protections are provided through the required risk mitigation measures and use restrictions on the product labels. Therefore, no further refinement of the aquatic plant endpoints is required to support the use of these products.

3) **Model selection for the study testing the effects of GF-3301 on *Myriophyllum spicatum,* PMRA# 3133022:** The PMRA generally assumes that the results of ecotoxicity tests will follow a monotone dose response relationship, but does account for non-monotone dose-response relationships (NMDR) under certain circumstances (for example, based on the considerations described in Varret et al. (2018) and EFSA (2021)). Varret et al. (2018) developed a set of six checkpoints to evaluate the evidence for NMDR for a given dataset, which were also considered in EFSA (2021). The shoot length data from the GF-3301 study on *Myriophyllum spicatum* (PMRA# 3133022) do not meet several of the checkpoints that would provide evidence of an NMDR. For instance, the apparent NMDR depends on a single treatment group and only a 2.8% increase in shoot length yield was observed at this treatment, which is below the effect size threshold of 5% specified in Varret et al. (2018). Furthermore, although a statistical method was not used to compare the fit of the 4P log-logistic+hormesis and 4P log-logistic models, the difference between the Akaike Information Criterion (AIC) values is small (143.5 vs. 144.1), and the CETIS output provided by Corteva indicates that the hormesis factor (ε) was a non-significant parameter in the analysis performed with the 4P log-logistic+hormesis model. As the CETIS User Guide recommends the selection of the model with the least number of parameters, where appropriate, PMRA considers the 4P log-logistic model to be more suitable.

Other information

The relevant confidential test data on which the decision is based (as referenced in PRD2022-17, *Florpyrauxifen-benzyl, Milestone NXT Herbicide, Restore NXT Herbicide, GF-3206 Herbicide, GF-3301 Aquatic Herbicide, and ProcellaCOR FX Herbicide*) are available for public inspection, upon application, in the PMRA's Reading Room. For more information, please contact the PMRA's Pest Management Information Service.

Any person may file a notice of objection[3] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides section of the Canada.ca website (Request a Reconsideration of Decision) or contact the Pest Management Information Service.

[3] As per subsection 35(1) of the *Pest Control Products Act.*

Evaluation approach

Legislative framework

The Minister of Health's primary objective under the *Pest Control Products Act* subsection 4(1) is to prevent unacceptable risks to individuals and the environment from the use of pest control products.

As noted in the preamble of the Act, it is in the national interest that the attainment of the objectives of the federal regulatory system continue to be pursued through a scientifically-based national registration system that addresses risks to human health, the environment and value both before and after registration and applies to the regulation of pest control products throughout Canada; and that pest control products with acceptable risk and value be registered for use only if it is shown that their use would be efficacious and if conditions of registration can be established to prevent unacceptable risk impact to human health and the environment.

For the purposes of the Act, the health or environmental risks of a pest control product are acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from exposure to or use of the product, taking into account its conditions of registration as per subsection 2(2) of the Pest Control Products Act.

Risk for the human health and environment, and value are defined under the Act subsection 2(1) as follows:

> **Health risk**, in respect of a pest control product, means the possibility of harm to human health resulting from exposure to or use of the product, taking into account its conditions or proposed conditions of registration.
>
> **Environmental risk**, in respect of a pest control product, means the possibility of harm to the environment, including its biological diversity, resulting from exposure to or use of the product, taking into account its conditions or proposed conditions of registration.
>
> **Value**, in respect of a pest control product, means 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.

When evaluating the health and environmental risks of a pesticide and determining whether those risks are acceptable, subsection 19(2) of the *Pest Control Products Act* requires Health Canada to apply a scientifically-based approach. The science-based approach to assessing pesticides considers both the toxicity and the level of exposure of a pesticide in order to fully characterize risk.

Pre-market assessments are based on a required set of scientific data that must be provided by the applicants for pesticide registrations. Additional information from published scientific reports, other government departments and international regulatory agencies are also considered.[4]

Risk and value assessment framework

Health Canada uses a comprehensive body of modern scientific methods and evidence to determine the nature as well as the magnitude of potential risks posed by pesticides. This approach allows for the protection of human health and the environment through the application of appropriate and effective risk management strategies, consistent with the purpose described in the preambular text set out above.

Health Canada's approach to risk and value assessment is outlined in A Framework for Risk Assessment and Risk Management of Pest Control Products.[5] A high-level overview is provided below.

i) Assessing potential health risks

With respect to the evaluation and management of potential health risks, Health Canada's risk assessments follow a structured, predictable process that is consistent with international approaches and the Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks.[6]

The evaluation of potential health risks begins with a consideration of the toxicological profile of a pesticide to establish reference doses at which no adverse effect is expected and against which the expected exposure is assessed. This includes, where appropriate, the use of uncertainty (protection) factors to provide additional protection that accounts for the variation in sensitivity among members of human population and the uncertainty in extrapolating animal test data to humans. Under certain conditions, the *Pest Control Products Act* requires the use of another factor to provide additional protection to pregnant women, infants, and children. Other uncertainty factors, such as a database deficiency factor, are considered in specific cases. More details related to the application of the uncertainty factors are provided in SPN2008-01.[7]

Assessments estimate potential health risks to defined populations[8] under specific exposure conditions. They are conducted in the context of the proposed or registered conditions of use, such as the use of a pesticide on a particular field crop using specified application rates, methods and equipment. Potential exposure scenarios consider exposures during and after application of

4 Information Note – *Determining Study Acceptability for use in Pesticide Risk Assessments*

5 PMRA Guidance Document, *A Framework for Risk Assessment and Risk Management of Pest Control Products*

6 Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks – 1 August 2000

7 Science Policy Note: *The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides*

8 Consideration of Sex and Gender in Pesticide Risk Assessment

the pesticide in occupational or residential settings, food and drinking water exposure, or exposure when interacting with treated pets. Also considered are the anticipated durations (short-, intermediate- or long-term) and routes of exposure (oral, inhalation, or skin contact). In addition, an assessment of health risks must consider available information on aggregate exposure and cumulative effects.

ii) Assessing risks to the environment

With respect to the evaluation of environmental risks, Health Canada's environmental risk assessments follow a structured, tiered approach to determine the likelihood that exposure to a pesticide can cause adverse effects on individual organisms, populations, or ecological systems. This involves screening assessments starting with simple methods, conservative exposure scenarios and sensitive toxicity effects metrics, then moving on, where required, to more refined assessments that can include exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods.

The environmental assessment considers both the exposure (environmental fate, chemistry, and behaviour, along with the application rates and methods) and hazard (toxic effects on organisms) of a pesticide. The exposure assessment examines the movement of the pesticide in soil, water, sediments and air, as well as the potential for uptake by plants or animals and transfer through the food web. The possibility for the pesticide to move into sensitive environmental compartments such as groundwater or lakes and rivers, as well as the potential for atmospheric transport, is also examined. The hazard assessment examines effects on a large number of internationally recognized indicator species of plants and animals (terrestrial organisms include invertebrates such as bees, beneficial arthropods, and earthworms, birds, mammals, plants; aquatic organisms include invertebrates, amphibians, fish, plants and algae), and includes considering effects on biodiversity and the food chain. Acute and chronic effects endpoints are derived from laboratory and field studies that characterize the toxic response and the dose–effect relationship of the pesticide.

The characterization of environmental risk requires the integration of information on environmental exposure and effects to identify which, if any, organisms or environmental compartments may be at risk, as well as any uncertainties in characterizing the risk.

iii) Value assessment

Value assessments consist of two components: an assessment of the performance of a pest control product and its benefits.

Assessing pesticide performance involves an evaluation of the pesticide’s efficacy in controlling the target pest and the potential for the pesticide to damage host crops or use sites. Where the efficacy of a pesticide is acceptable, the assessment serves to establish appropriate label claims and directions and an application rate (or rate range) that is effective without being excessive, and with no unacceptable damage to the use site or host organism/crop (and subsequent hosts or crops) under normal use conditions.

In many cases, proof of performance alone is sufficient to establish the value of the pesticide, so that an in-depth or extensive evaluation of benefits may not be required. However, a more thorough assessment of benefits may be undertaken in particular cases where performance alone does not sufficiently demonstrate value, or while developing risk management options.

Risk management

The outcomes of the assessments of risks to human health and the environment, and the assessment of value, form the basis for identifying risk management strategies. These include appropriate risk mitigation measures and are a key part of decision-making on whether health and environmental risks are acceptable. The development of risk management strategies take place within the context of the pesticide's conditions of registration. Conditions can relate to, among other things, the specific use (for example, application rates, timing and frequency of application, and method of application), personal protective equipment, pre-harvest intervals, restricted entry intervals, buffer zones, spray drift and runoff mitigation measures, handling, manufacture, storage or distribution of a pesticide. If feasible conditions of use that have acceptable risk and value cannot be identified, the pesticide use will not be eligible for registration.

The selected risk management strategy is then implemented as part of the registration decision. The pesticide registration conditions include legally-binding use directions on the label. Any use in contravention of the label or other specified conditions is illegal under the *Pest Control Products Act*. Implementation of post-market decisions follow the framework articulated in the Policy on Cancellations and Amendments Following Re-evaluation and Special Review.[9]

Following a decision, continuous oversight activities such as post-market assessments, monitoring and surveillance, including incident reporting, all play an essential role to help ensure the continued acceptability of risks and value of registered pesticides.

[9] PMRA Regulatory Directive DIR2018-01 *Policy on Cancellations and Amendments Following Re-evaluation and Special Review*.

References

Additional information considered

Published information

PMRA Document Number	Reference
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