Registration Decision RD2026-12

Acynonapyr and Kodama Miticide

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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 written comments directly related to the proposed decision, such as comments directed to the Science evaluation, 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 Evaluation approach of this document.

Registration decision statement[2] for acynonapyr

Health Canada, pursuant to subsection 8(1) of the *Pest Control Products Act*, is granting registration for the sale and use of Acynonapyr Technical and Kodama Miticide, containing the active ingredient acynonapyr, to control Tetranychid mites on Crop Group 11-09: Pome Fruits.

The Proposed Registration Decision PRD2026-03, *Acynonapyr and Kodama Miticide*, containing the detailed evaluation of the information submitted in support of this registration, underwent a 30-day consultation period ending on 12 March 2026. 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 written comments relating to the health assessment of acynonapyr and Kodama Miticide, as well as a written comment in support of their registration, during the public consultation period conducted in accordance with section 28 of the *Pest Control Products Act*. Health Canada also received a comment that was not directly related to the proposed decision in PRD2026-03, *Acynonapyr and Kodama Miticide.*

Additional written comments relating to the health, environmental, and value assessments of acynonapyr and Kodama Miticide were received after the consultation period had closed. Although these comments were submitted late, they were exceptionally reviewed by Health Canada because the pilot established under NOI2025-02[3] to adjust the consultation period for Category A applications has not yet been finalized.

Comments and responses

Health Canada received comments from the registrant on the health assessments of acynonapyr and Kodama Miticide. The responses are provided below.

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.*
3 Health Canada Notice of Intent NOI2025-02, *Adjusted consultation period for Proposed Registration Decision for Category A applications (Registration of new active ingredients or major new uses of pesticides) (15 July 2025).*

1. Comment related to the developmental neurotoxicity (DNT) study requirements and uncertainty factor (UF)

The registrant commented that a DNT study is not included in the standard data requirements and that the existing toxicological database does not provide evidence of developmental neurotoxicity or developmental effects in the young in the absence of maternal or systemic toxicity. They stated that there were no indicators in the available studies that would trigger concern for specific neurodevelopmental effects at dose levels below those causing general systemic toxicity. Considering the weight of evidence, the registrant stated that the application of an additional threefold UF to account for potential developmental neurotoxicity is not scientifically warranted.

Health Canada response:

In Health Canada's Guidance for Developing Datasets for Conventional Pest Control Product Applications,[4] it is stated that neurotoxicity testing may be appropriate for pest control products known or suspected to be neurotoxicants. As outlined in the PRD2026-03, the concern for the potential for acynonapyr to impair neurodevelopment was based in part on the fact that acynonapyr exerts its pesticidal activity by interfering with the nervous system of insects. The guidance further recommends that testing specifically for DNT should be considered if the test substance is hormonally active in vivo. In the acynonapyr database, effects on thyroid gland pathology and thyroid hormonal regulation were observed in several toxicity studies. Concern for potential DNT was therefore raised based on the knowledge that acynonapyr is capable of targeting the nervous system of insects and evidence for hormone changes in vivo. Without studies assessing DNT potential in the available mammalian toxicity database, it is unknown if effects on neurodevelopment would occur at the same dose levels causing generalized systemic toxicity, thus necessitating the application of a database UF to ensure adequate protection for potential DNT effects at lower dose levels than those selected for assessing risks to human health.

2. Comment related to No Observed Adverse Effect Levels (NOAELs) and Lowest Observed Adverse Effect Levels (LOAELs) differences and dose spacing

The registrant commented that the differences in NOAELs and LOAELs across the mammalian toxicology database are mainly attributable to dose spacing variations rather than inherent species-specific sensitivities. The registrant therefore recommended that the highest NOAEL, which remains below the lowest LOAEL across all studies, be selected for assessing risks to human health, as opposed to the lowest NOAEL in the database. As such, the registrant proposed utilizing the NOAEL of 10 mg/kg bw/day from the 90-day dog study (PMRA No. 3328862) as the basis for deriving toxicology reference values for both subchronic and chronic (non-cancer) risk assessments.

[4] Health Canada Guidance for Developing Datasets for Conventional Pest Control Product Applications: Data Codes for Parts 1, 2, 3, 4, 5, 6, 7 & 10 (12 February 2021).

Health Canada response:

When deriving toxicology reference values for use in human health risk assessments, selecting the lowest NOAEL in the available toxicology database is consistent with Health Canada's Guidance Document, A Framework for Risk Assessment and Risk Management of Pest Control Products.[5] Additional considerations that are critical to selecting the appropriate point of departure (POD) for assessing human health risks include human relevance of the observed effects, as well as the pertinence of the animal exposure conditions to the route, frequency and duration of human exposure. As such, the offspring NOAEL of 5.9 mg/kg bw/day from the 2-generation reproductive toxicity study (PMRA No. 3328878) and the NOAEL of 4 mg/kg bw/day from the 1-year oral toxicity study in the dog (PMRA No. 3328864) were selected as the PODs for assessing risks following short- to intermediate term and long-term exposures, respectively. While the NOAEL of 10 mg/kg bw/day in the 90-day dog study falls below the LOAELs of 30 mg/kg bw/day and 20 mg/kg bw/day in the reproductive toxicity and 1-year dog studies, respectively, the LOAEL in the 90-day dog study of 50 mg/kg bw/day is in exceedance of these LOAELs. The higher NOAEL of several studies may be appropriate to select provided that the conditions of those studies are comparable. However, the conditions in the 90-day dog, 1-year dog, and 2-generation reproductive toxicity studies differ in terms of species, exposure duration, and developmental stage of the test animals. In contrast to the 90-day dog study, the 1-year dog study provides a longer duration of exposure, making it more appropriate for assessing long-term human health risks, particularly those related to systemic toxicity. Furthermore, the 2-generation reproductive toxicity study is specifically designed to assess reproductive and developmental outcomes, which are not assessed in the 90-day dog study. Therefore, selecting the lowest NOAEL values for the relevant human exposure scenarios ensures appropriate human health protection against the adverse effects noted in those specific studies.

3. Comment related to the rat 2-generation reproductive toxicity study

The registrant commented that the decreased pup weights noted at 30 mg/kg bw/day in the 2-generation reproductive toxicity study in rats (PMRA No. 3328878) were observed exclusively in the F1 generation and were not reproduced in the F2 generation. They further stated that statistically significant reductions in pup weights were noted at 30 mg/kg bw/day through postnatal day 28. However, the registrant asserted that these reductions should not be considered treatment-related as they correlate with the moderately larger mean litter size in this dose group (14.2 pups) compared to controls (13.3 pups). It is well-established that larger litter sizes are typically associated with lower individual pup weights due to increased intra-uterine competition and reduced maternal resources per pup. The registrant therefore concluded that the threshold for adversity was not reached at this dose level.

Health Canada response:

In general, the absence of a treatment-related finding in one generation of offspring in a 2-generation reproductive toxicity study does not invalidate the potential for treatment-related findings in the other generation. Effects may manifest differently across generations due to exposure timing, differences in sensitivity, impact of developmental windows, and influence of parental toxicity. In addition to the decreased body weight noted in F1 pups, an increased

[5] Health Canada Guidance Document, *A Framework for Risk Assessment and Risk Management of Pest Control Products (12 April 2024)*.

incidence of clinical signs, such as dehydration and cold to touch, was noted in F1 offspring only, starting at the mid-dose level. It is acknowledged that larger litter sizes can result in lower individual pup body weight. In the F1 offspring of the 2-generation reproductive toxicity study with acynonapyr, the mean live litter size at the mid-dose level of 30 mg/kg bw/day was slightly higher than the control mean, but did not reach statistical significance. Additionally, the mean F1 litter size at the next highest dose level was statistically significantly smaller than the control mean, yet significant reductions in mean offspring body weight of even greater magnitude were noted at this dose level. In the F2 generation, there were comparable differences in the mean live litter size in the control, low-dose and mid-dose groups yet there were no downstream effects on litter weight in these groups. Overall, there were statistically significant decreases in pup body weight of 7–10% compared to the control in the F1 offspring starting at 30 mg/kg bw/day that followed a dose-responsive trend up to the high dose and could not be solely attributed to the slightly larger mean litter size. As such, Health Canada has concluded that the threshold for adversity was achieved for this endpoint at the 30 mg/kg bw/day dose level, and when combined with other treatment-related findings noted at this dose level, including the clinical signs of toxicity noted above, support the establishment of the offspring NOAEL in the 2-generation reproductive toxicity study at 30 mg/kg bw/day.

4. Comments related to the findings of skin fibroma and fibrosarcoma and astrocytoma in the rat 2-year carcinogenicity study

The registrant provided arguments against Health Canada's determination that the increased incidences of skin fibroma and fibrosarcoma and brain astrocytoma in the 2-year carcinogenicity study in rats (PMRA No. 3328713) were treatment-related. The registrant stated that in a carcinogenicity study where a large number of comparisons are made, there is a greater potential to find statistically positive findings between control and treatment groups due to chance, or false positives, and cited appropriate methods to adjust for multiple comparisons. Specifically, the registrant cited appropriate p-values to use as criteria for statistical significance for rare and common neoplasms.

The registrant further stated that the skin neoplasms should not be considered rare tumours. To support this claim, the registrant provided tabulated historical control data from the literature for skin fibroma and fibrosarcoma in different rat strains and sources. Based on the historical incidence of skin fibroma and fibrosarcoma and the appropriate statistical considerations for common tumours, the registrant asserted that the two cases of fibroma and two cases of fibrosarcoma in the skin of high-dose male rats in the study with acynonapyr would not represent a reliable result. Finally, the registrant recommended that fibroma and fibrosarcoma not be combined as one neoplastic entity for statical analysis, noting that fibrosarcoma may develop from a primary malignant cell, or develop as a transition from a primary benign into a malignant neoplasia.

Similarly, the registrant stated that the astrocytoma in two males and one female in the high-dose group in the 2-year carcinogenicity study in rats with acynonapyr to not be rare neoplasms, and again cited historical control data for different strains and sources of rats from the literature (PMRA No. 3552792). The registrant also asserted that the number of observed cases of brain astrocytoma with acynonapyr is not considered suitable for statistical evaluation.

The registrant also stated that there is a potential misdiagnosis in the female rat identified with an astrocytoma as the affected female rat was also observed with a lymphoblastic lymphoma, which can mimic malignant reticulosis or present as an astrocytoma in the brain. Therefore, the registrant asserted that the astrocytoma observed in the female rat is not likely representative of a primary brain tumour and should not be considered in the risk assessment.

Health Canada response:

Statistical analysis is only one of many factors taken into consideration when determining the relevance of observed neoplasms in carcinogenicity studies. In the case of the skin and brain tumours observed in the 2-year rat study with acynonapyr, the incidences in the high-dose males were not statistically significantly different than controls. Hence, the concern about false positive results noted by the registrant is not relevant.

Historical control data specific to the laboratory that conducted the 2-year carcinogenicity study in rats were provided by the registrant during the review of the acynonapyr database. These laboratory-specific historical control data were already taken into consideration when determining the level of concern for the noted skin and brain tumours and are more relevant for comparison than data from the published literature. The incidence of the noted skin and brain tumours in males from the high-dose group exceeded the range of laboratory-specific historical incidences in control animals.

Based on recent guidance for combining tumours for statistical analysis (Keenan et al., 2024)[6], the combination of skin fibromas and fibrosarcomas was considered appropriate.

The astrocytoma in the high-dose female rat was not considered by Health Canada to be related to treatment.

It is important to note that although skin and brain tumours were noted in high-dose male rats, the cancer slope factor used for the human health risk assessment for acynonapyr was derived based on the combined incidence of mesenteric lymph node hemangioma and hemangiosarcoma in male rats treated with acynonapyr as it was determined to be the most health-protective.

5. Comment related to the dermal absorption study methodology

The registrant noted that the Organisation for Economic Co-operation and Development (OECD) Test Guidelines 427[7] and 428[8] do not impose specific limitations on skin wash methodologies and that the submitted dermal absorption "triple pack" study (PMRA No. 3630579) was conducted using a skin washing procedure intended to mimic standard human practices, with the Geiger counter (a radiation monitor) serving solely as a process control. The registrant concluded that the resulting dermal absorption values of 1.02% for the field dilution and 0.14% for the concentrate are accurate and not underestimated under the study conditions.

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6 Keenan, C. et al. (2024). Guide for Combining Primary Tumors for Statistical Analysis in Rodent Carcinogenicity Studies. Toxicologic Pathology, 52(1), 13-20. doi:10.1177/01926233241230553.

7 OECD Test Guideline 427, *Skin Absorption: In Vivo Method* (Adopted: 13 April 2004).

8 OECD Test Guideline 428, *Skin Absorption: In Vitro Method* (Adopted: 13 April 2004).

Health Canada response:

In OECD Guidance Document 28[9] and OECD Test Guidelines 427 and 428, there is limited guidance on skin wash methodologies and only specifies that it should mimic human washing and reflect normal practices. There is no discussion of the use of a radiation monitor as part of the skin wash and it is unclear how relying on a radiation monitor to determine the end of the skin wash would reflect a standard shower process. There is concern that the use of the radiation monitor could result in use of a greater number of swabs in the washing step and be more excessive compared to a standard wash, and may underestimate dermal absorption. This is described in more detail below and in the recently published SPN2026-01.[10] Although this science policy note was published after PRD2026-03, SPN2026-01 reflects the policy applied to the selection of the acynonapyr dermal absorption value.

In order to validate the use of in vitro studies to determine dermal absorption values for exposure assessments, a retrospective analysis of the "triple pack" studies was conducted (Allen, et al., 2021;[11] SPN2026-01). The outcome of this analysis generally validated the use of in vitro dermal absorption methodologies, as absorption from rat in vitro studies was close to or overestimated absorption from rat in vivo studies for the majority of the "triple pack" studies that were included. However, there were a few "triple pack" studies that reported lower in vitro dermal absorption compared to in vivo dermal absorption. For some of these, the skin wash in the in vitro study included the use of a radiation monitor (in other words, a Geiger counter) to determine when the skin wash was complete, while the rat in vivo study had a normal guideline wash. While it is unknown if the different washing procedures were a major contributor of the lower absorption in the in vitro study, there is concern that a skin wash using a Geiger counter may be more excessive in comparison to what is specified in the test guidelines and may underestimate absorption.

This limitation is primarily noted for human in vitro studies, as dermal absorption values selected from these studies are considered to be more refined compared to dermal absorption values selected from rat studies, as rat skin is more permeable than human skin. Therefore, in vitro human dermal absorption studies, where the skin wash is more excessive than what is specified in the guidelines, may not be acceptable to directly determine a dermal absorption value (SPN2026-01).

For acynonapyr, a dermal absorption value of 9% was determined from the human in vitro component of the "triple pack" study (PMRA No. 3630579) based on the low dose group. This dermal absorption value includes all tape strips as absorbed, which is consistent with standard practice for in vitro studies (SPN2026-01). However, there was uncertainty with this value, given the use of the Geiger counter to determine the end of the skin wash and that it may potentially underestimate absorption. As such, a dermal absorption value was determined from the rat in vivo component of the "triple pack" study (PMRA No. 3630579). A dermal absorption value of 10% was determined from the low dose group, 120 hour exposure duration. While a Geiger

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9 OECD Guidance Document for the Conduct of Skin Absorption Studies. OECD Series on Testing and Assessment Number 28. ENV/JM/MONO(2004)2 (5 March 2004).

10 Health Canada Science Policy Note SPN20206-01, *Updated Policy on the Use of In Vitro Dermal Absorption Studies in Risk Assessment (11 March 2026).*

11 Allen, D. G. et al. (2021). Retrospective Analysis of Dermal Absorption Triple Pack Data, ALTEX. 38(3), 463-476. doi: 10.14573/altex.2101121.

counter was also used in this study for the skin wash, rat skin is more permeable to acynonapyr than human skin (at least fourfold). Therefore, there was confidence that the 10% dermal absorption value from the rat in vivo data would not underestimate absorption of acynonapyr through human skin. In addition, as the dermal absorption value is from rat in vivo data, it can be applied to a wider range of formulation types and products containing acynonapyr, compared to a dermal absorption value selected from human in vitro data (SPN2026-01).

As discussed in SPN2026-01, a scientific rationale or retrospective analysis of data could be submitted to address this current position regarding the use of radiation monitors to determine skin wash completion. As the primary concern with the use of a radiation monitor in the skin wash is that it might be more excessive than a standard/guideline wash, a rationale, validating study and/or retrospective analysis would need to confirm that this is not the case and a skin wash with a radiation monitor would not result in the underestimation of dermal absorption.

Comment in support of this registration

A Canadian grower group expressed support for the registration of acynonapyr and Kodama Miticide, noting that it will provide Canadian pome fruit growers with a new mode of action to control mites and contribute to resistance management.

Comments received after the consultation period had closed

Health Canada received additional comments from a non-governmental organization (noted as "commenter") after the consultation period had closed. Although these comments were submitted late, they were exceptionally reviewed by Health Canada because the pilot established under NOI2025-02 to adjust the consultation period for Category A applications has not yet been finalized. The information submitted was reviewed, and a high-level summary of the comments (grouped by themes) and the responses are provided below.

6. Comment on per- and polyfluoroalkyl substances (PFAS) classification and trifluoroacetic acid (TFA) concerns

The commenter referenced proposed European Union PFAS restrictions and questioned alignment with global sustainability goals. In addition, the commenter raised that acynonapyr may degrade into TFA, a persistent PFAS, and that this was not adequately addressed in the dietary risk assessment.

Health Canada response:

It is noted that acynonapyr contains a trifluoromethyl group. However, Health Canada has undertaken a thorough and complex scientific risk assessment of this new active ingredient in order to determine whether there is any risk to human health and the environment, and if that risk is acceptable. The health and environmental effects of an active ingredient in a pest control product are well characterized and form part of the risk assessment. A pest control product would not be registered for use in Canada unless it was determined that that there is no unacceptable risk to human health or the environment when the product is used according to label directions.

7. Comment on cumulative exposure

The commenter urged Health Canada to consider cumulative PFAS exposure from all sources.

Health Canada response:

As stated in SPN2018-02,[12] "cumulative assessment is aimed at identifying the human health risks associated with co-exposures to two or more pesticides that cause a common toxic effect(s) by the same, or essentially the same, sequence of major biochemical events (that is, a common mechanism of toxicity)." As cumulative assessments are only required for substances with a common mechanism of toxicity, it was not required here. In addition, aggregate exposure from all routes was assessed, and residential use was prohibited due to lifetime cancer risk. More details are available on page 26 of PRD2026-03.

8. Comment on the protection of infants and children

The commenter questioned whether Canadian-specific consumption data were used and whether the 10-fold children's safety factor was applied.

Health Canada response:

Health Canada has conducted a detailed analysis of the consumption datasets available for North America (in other words, the United States National Health and Nutrition Examination Survey – NHANES and the Canadian Community Health Survey – CCHS) and published Information Note on comparing food and drink consumption data from Canada and the United States[13] to explain why Health Canada uses NHANES data. Additional factors beyond the standard 100-fold uncertainty factor were applied in the calculation of the acceptable daily intake and the acute reference dose to afford additional protection for infants and children. More details are available on pages 19–20 and in Appendix I, Table 3 of PRD2026-03.

9. Comment on formulants and contaminants

The commenter raised concerns about preservatives like benzisothiazolinone (BIT) and dichlorooctylisothiazolinone (DCOIT), which may contain dioxins/furans and cause skin sensitization.

Health Canada response:

Health Canada confirms that all formulants were reviewed. Trace contaminants were below acceptable limits, and the products are labelled as potential skin sensitizers with appropriate personal protective equipment and restricted-entry interval requirements. More details are available on page 35 of PRD2026-03.

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12 Health Canada Science Policy Note SPN2018-02, *Cumulative Health Risk Assessment Framework* (17 April 2018).

13 Health Canada Information Note on comparing food and drink consumption data from Canada and the United States (19 April 2024).

10. Comment on environmental fate and risks to non-target organisms

The commenter expressed concerns about persistence, leaching, aquatic toxicity, and pollinator impacts.

Health Canada response:

Health Canada conducted long-term water modelling (50–100 years), including multiple transformation products in exposure estimates, and required spray buffer zones, best management practices, and label precautions to mitigate risks to the environment. Section 4.0, Impact on the environment, of PRD2026-03 contains the details of this assessment.

11. Comment on the value assessment

The commenter claimed the product's value was not adequately demonstrated.

Health Canada response:

The *Pest Control Products Act* recognizes a pest control product's actual or potential contribution to pest management in its definition of value. The detrimental socio-economic impact of the subject pest on Canadian growers was characterized and the expected contribution to the management of these pests from the new active ingredient formed the basis for the finding of acceptable value. Evidence from 27 efficacy trials was used in the assessment. Data also confirmed crop safety, highlighted the novel mode of action for resistance management, and outlined economic and integrated pest management benefits.

12. Comment related to the Toxic Substances Management Policy (TSMP) evaluation

The commenter found that the TSMP assessment was inadequate.

Health Canada response:

A comprehensive TSMP evaluation was conducted and is reflected in PRD2026-03 (Appendix I, Table 35). Health Canada's strategy for implementing the Toxic Substances Management Policy (TSMP) is published under DIR99-03.[14] Details of the TSMP key management objectives are in Appendix I on page 9. For a substance to be deemed Track 1, all four TSMP Track 1 criteria must be met. When less than four of the criteria are met, the substance is not classified as TSMP Track 1. Acynonapyr and transformation products (AP, AY) do not meet all Track 1 criteria.

Other information

The relevant confidential test data on which the decision is based (as referenced in PRD2026-03, *Acynonapyr and Kodama Miticide*) are available for public inspection, upon application, in Pesticides Regulatory Directorate's Reading Room. For more information, please contact the Pesticides Information Service.

[14] Health Canada Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy* (12 March 1999).

Any person may file a notice of objection,[15] which must be based on scientific grounds, regarding this registration decision on acynonapyr and Kodama Miticide within 60 days from the date of publication of this Registration Decision through the Public Engagement Portal (Public Engagement Portal forms – Notice of Objection). The request for reconsideration must include the Notice of Objection form, the scientific explanation of the objection and the supporting scientific evidence in possession of the requestor that would not already be in Health Canada's possession or cite specific Health Canada documentation they wish to rely on as supporting evidence (for example, scientific reports) in the form of electronic copies of cited references. Each of the references provided or cited must be clearly associated with the objection it supports. Failure to provide a complete package may result in the Notice of Objection being considered ineligible for further consideration by Health Canada. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Canada.ca website or contact the Pesticides Information Service.

[15] 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 there is acceptable risk to human health and the environment, taking into account the conditions of registration.

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.[16]

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. 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.[17]

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.[18]

Assessments estimate potential health risks to defined populations[19] 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 the pesticide in occupational or residential settings, food and drinking water exposure, or exposure when interacting with treated pets.

16 Information Note – *Determining Study Acceptability for use in Pesticide Risk Assessments.*
17 Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks – August 1, 2000.
18 Science Policy Note: *The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides*.
19 Consideration of Sex and Gender in Pesticide Risk Assessment.

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*.

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.

List of abbreviations

AP	3-*endo*-[2-propoxy-4(trifluoromethyl)phenoxy]-9-azabicyclo[3.3.1]nonane
AY	2-hydroxy-5-(trifluoromethyl)pyridine
BIT	benzisothiazolinone
bw	body weight
CCHS	Canadian Community Health Survey
DCOIT	dichlorooctylisothiazolinone
DIR	Regulatory Directive
DNT	developmental neurotoxicity
F1	first filial generation
F2	second filial generation
kg	kilogram
LOAEL	lowest observed adverse effect level
mg	milligram
NHANES	National Health and Nutrition Examination Survey
NOAEL	no observed adverse effect level
NOI	Notice of Intent
OECD	Organisation for Economic Co-operation and Development
PFAS	per- and polyfluoroalkyl substances
PMRA	Pest Management Regulatory Agency
POD	point of departure
PRD	Proposed Registration Decision
SPN	Science Policy Note
TFA	trifluoroacetic acid
TSMP	Toxic Substances Management Policy
UF	uncertainty factor