Registration Decision RD2026-16

Spiropidion, A20262 Insecticide

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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 section of Evaluation Approach of this document.

Registration Decision Statement[2] for Spiropidion, A20262 Insecticide

Health Canada's Pesticides Regulatory Directorate (PRD), pursuant to subsection 8(1) of the *Pest Control Products Act*, is granting registration for the sale and use of Spiropidion Technical Insecticide, and A20262 Insecticide containing the active ingredient spiropidion, to control or suppress aphids, whiteflies, mealybugs, and two-spotted spider mites on terrestrial food and feed crops, and greenhouse food crops.

This decision is consistent with the Proposed Registration Decision PRD2026-09, *Spiropidion, A20262 Insecticide,* containing the detailed evaluation of the information submitted in support of this registration, which underwent a 30-day consultation period ending on 5 July 2026. The evaluation found that, under the approved conditions of use, the health and environmental risks and the value of the pest control product is acceptable. Health Canada received written comments relating to the health, environmental and value assessments during the public consultation period conducted in accordance with section 28 of the *Pest Control Products Act*. However, some of the comments were not directly related to the proposed decision in PRD2026-09, *Spiropidion, A20262 Insecticide*.

Comments and responses

1. Comment related to the interpretation of the NOAEL in the 1-year dog study

The commenter stated that the dog-study NOAEL was increased in PRD2026-09 from 3 to 10 mg/kg bw/day after reinterpreting a decrease in female body weight at 10 mg/kg bw/day as normal biological variation rather than treatment-related toxicity. The commenter argued that this change is significant because dogs appear to be the most sensitive species in the toxicology database and severe adverse effects, including deaths, were observed at higher doses in the same species. The commenter further stated the scientific basis for the reclassification is not adequately explained in PRD2026-09. The commenter also raised concerns about contamination of control animals in the same dog study based on the detection of spiropidion or its metabolites in plasma samples as reported by EFSA, arguing that this may affect the validity of the control-group comparisons relied upon to support the revised NOAEL.

[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:

Health Canada has considered the concern raised by the commenter that PRD2026-09 does not sufficiently explain the revision of the NOAEL from 3 mg/kg bw/day to 10 mg/kg bw/day in the 1-year oral dog toxicity study.

The concern arises because the previous Evaluation Report for Submission 2020-4760 identified a NOAEL of 3 mg/kg bw/day and a LOAEL of 10 mg/kg bw/day in the 1-year dog study based on decreases in female body weight and body weight gain observed at 10 mg/kg bw/day.

As outlined in PRD2026-09, the results of some toxicology studies were re-examined in the current assessment after the applicant provided scientific rationales supporting reconsideration of previous conclusions. As part of this re-examination, Health Canada conducted a more detailed analysis of the body weight data for individual animals in all test groups, including controls, in the 1-year dog study over the entire study duration. Based on this reassessment, it was determined that the individual female body weight values at 10 mg/kg bw/day fell within the variability observed in the concurrent control group throughout the study, and the apparent lower mean value was therefore considered to represent normal biological variation rather than a treatment-related adverse effect. Based on this reassessment, the NOAEL for the study was revised to 10 mg/kg bw/day and the LOAEL to 30 mg/kg bw/day. At 30 mg/kg bw/day, clear treatment-related adverse effects were observed, including mortality and severe clinical signs that resulted in animals being sacrificed in extremis and termination of dosing following adverse clinical observations. The revision to the NOAEL in the 1-year dog study was the only change to the toxicology assessment that resulted from reconsideration of previous conclusions and the review of the scientific rationales provided by the applicant.

With respect to the comment regarding potential contamination of control animals raised by EFSA, Health Canada did not identify any such deficiency that would invalidate the interpretation of the 1-year dog study or its use in the risk assessment. Although EFSA reported that JMPR identified an issue with spiropidion or its metabolites being detected in plasma samples in some control animals in the 1-year dog study, the JMPR monograph[3] (2021) in fact noted that spiropidion was not detected in any blood sample and that metabolite SYN547305 was detected at concentrations above the LOQ in all samples except in the control group in the 1-year dog study. The absence of spiropidion and its metabolite in plasma samples from control dogs is confirmed by Health Canada's assessment of the available study report (PMRA No. 3161321) for the 1-year dog study. The JMPR did note that in short-term toxicity studies in rodents and in the 90-day dog study (but not the 1-year dog study), a number of control blood samples subject to bioanalysis were contaminated, either with the parent compound spiropidion or metabolite SYN547305, and that the reason for the contamination was not clearly identified. The JMPR concluded that the contamination did not invalidate the results or interpretation of the toxicological findings in those studies. Health Canada reached this same conclusion.

[3] https://iris.who.int/server/api/core/bitstreams/c55b6983-c078-4e37-bd83-24a47d68b088/content

2. Comment related to the maternal NOAEL in the rabbit developmental toxicity study

The commenter stated that previously identified maternal toxicity findings in a rabbit developmental toxicity study were reclassified in PRD2026-09, treating decreased body weight gain and reduced food consumption at 30 mg/kg bw/day as non-adverse and thereby increasing the maternal NOAEL to 30 mg/kg bw/day. The commenter noted that this NOAEL is used as the point of departure for the general population acute reference dose (ARfD). The commenter further stated that this reclassification appears inconsistent with established developmental toxicity assessment practices, which generally consider decreased body weight gain and food consumption to be key indicators of maternal toxicity, and requested disclosure of the magnitude of the decreases in body weight gain and food consumption.

Health Canada response:

Health Canada has considered the comment regarding the maternal toxicity findings in the rabbit developmental toxicity study and the associated revision to the reporting of the maternal effects in the study.

The commenter notes that the Evaluation Report for Submission 2020-4760 identified a maternal NOAEL of 30 mg/kg bw/day and a maternal LOAEL of 60 mg/kg bw/day in the rabbit developmental toxicity study. A clarification is provided in PRD2026-09 to correct a minor error reported in the Evaluation Report for Submission 2020-4760 by explaining how the decrease in body weight gain and slight decrease in food consumption that were observed at 30 mg/kg bw/day are characterized as non-adverse, while maternal body weight loss, observed at 60 mg/kg bw/day, was considered adverse and served as the basis for the maternal LOAEL. There was no change to the maternal NOAEL or LOAEL in PRD2026-09, only clarification regarding the nature of the effects reported at the existing NOAEL and LOAEL. The maternal body weight gain at the dose level of 30 mg/kg bw/day was on average 100 g less than that of the control group, with no impact on maternal body weight (which was on the order of 3000 g), and the food consumption of these animals was only sporadically reduced, and not prolonged, resulting in a mean overall food consumption that was only 8% lower than that of the control group.

The commenter referenced a definition of toxicity based on a change in body weight gain or body weight loss of 7% in rabbits from a workshop on maternal toxicity. The specific information referenced by the commenter could not be located in the available summary of the cited workshop.[4] However, the basis for the information cited by the commenter appears to stem from studies demonstrating that a loss of net body weight, not a reduction in body weight gain relative to controls, of 7% can occur in feed-restricted maternal rabbits without impacting fetal development.[5] In the case of maternal animals in the rabbit developmental toxicity study with spiropidion, the decreased body weight gain relative to controls noted at 30 mg/kg bw/day was

[4] Beyer, B.K., Chernoff, N., Danielsson, B.R., Davis-Bruno, K., Harrouk, W., Hood, R.D., Janer, G., Liminga, U.W., Kim, J.H., Rocca, M., Rogers, J. and Scialli, A.R. (2011), ILSI/HESI maternal toxicity workshop summary: maternal toxicity and its impact on study design and data interpretation†. Birth Defects Research Part B: Developmental and Reproductive Toxicology, 92: 36-51. https://doi.org/10.1002/bdrb.20281

[5] Danielsson, B.R. (2013). Maternal Toxicity. In: Barrow, P. (eds) Teratogenicity Testing. Methods in Molecular Biology, vol 947. Humana Press, Totowa, NJ. https://doi.org/10.1007/978-1-62703-131-8_24

considered to be slight and non-adverse, whereas the loss of net body weight at 60 mg/kg bw/day, was considered adverse, consistent with the cited workshop findings.

Health Canada notes that the classification of adversity is based on a weight-of-evidence evaluation of the nature, magnitude, severity, and toxicological significance of the observed findings within the context of the entire study. In this case, body weight loss observed at 60 mg/kg bw/day was considered indicative of maternal toxicity and formed the basis of the maternal LOAEL, whereas the effects observed at lower dose levels were determined not to represent adverse maternal toxicity. Consequently, the maternal NOAEL remained at 30 mg/kg bw/day.

The commenter questioned the timing of the "Supplemental Data to Support SYN546330 – Oral (Gavage) Prenatal Developmental Toxicity Study in the Rabbit (PMRA No. 3161350)" and its role in the reclassification of previously reported findings. This supplemental information simply consisted of Microsoft Word renditions of report tables to aid in the review, and did not contain new data or information to influence Health Canada's conclusions from the review of the rabbit developmental toxicity study.

3. Comment related to the magnitude of the *Pest Control Products Act* factor

The commenter stated that PRD2026-09 does not provide the reliable scientific data required under the *Pest Control Products Act* to justify reducing the default 10-fold PCPA factor to 3-fold. The commenter noted that, although the document identifies evidence of sensitivity in the young in the developmental toxicity studies, it provides only a brief qualitative statement that these effects were not serious and does not present supporting data or analyses to substantiate that conclusion.

The commenter further stated that PRD2026-09 does not explain the scientific or methodological basis for selecting a 3-fold factor specifically.

Health Canada response:

Health Canada has considered the comment related to the reduction of the *Pest Control Products Act* factor (PCPA factor) from the presumptive 10-fold value to 3-fold for developmental toxicity endpoints, and herein provides additional clarification and justification for this approach.
As described in both the Evaluation Report for Submission 2020-4760 and PRD2026-09, Health Canada conducted an assessment of the available toxicology database to determine whether there was evidence of increased sensitivity of the young and whether the database was complete and adequate for characterizing that sensitivity. This assessment also considered the nature of the findings. The assessment concluded that the database was adequate for determining potential sensitivity of the young and that sensitivity was observed in the rat and rabbit developmental toxicity studies based on increased incidences of skeletal variations occurring in the absence of maternal toxicity. However, these developmental findings were not considered serious in nature (as further discussed below) and were not associated with serious effects such as malformations or effects on fetal survival.

The reduction of the PCPA factor to 3-fold is consistent with the framework described in SPN2008-01. This Science Policy Note indicates that a different factor than the default 10-fold PCPA factor may be determined where reliable scientific data support such a decision. Several

lines of evidence are considered to characterize the level of concern for effects in the young. The principal components in determining this level of concern are sensitivity of the young noted in the database and seriousness of the prenatal or postnatal effects. In addition to the nature and severity of the developmental findings, other factors that are taken into account include the dose-response relationship, confidence in the endpoint, and the overall completeness of the database.

While increased incidences of skeletal variations were identified in the rat and rabbit developmental toxicity studies at dose levels that did not result in maternal toxicity, these developmental effects were not considered serious in nature. As outlined in SPN2008-01, a serious endpoint is defined as causing congenital malformations, resulting in persistent or significant disability or incapacity, life-threatening or resulting in death. Variations are classified as structural changes that do not impact viability, development, or function, which can be reversible and are found in the normal population under investigation.[6]

Overall, the available database was considered adequate for characterizing the sensitivity of the young and the level of concern was reduced by the fact that the effects consisted of skeletal variations rather than malformations, occurred only at dose levels above the selected point of departure, and were supported by a complete and reliable toxicology database. Accordingly, a 3-fold PCPA factor was retained for risk assessments based on the developmental toxicity endpoints. Health Canada considers this approach to be consistent with SPN2008-01 and protective of sensitive populations, including pregnant women, infants, and children, while reflecting the weight of scientific evidence available for spiropidion.

4. Comment related to how revising the magnitude of the PCPA factor would require an updated human health risk assessment

The commenter stated that applying the default 10-fold PCPA factor would result in substantially more conservative reference values and significantly reduce the reported safety margins, materially affecting the risk assessment. The commenter provided recalculations of the risk assessment using the 10-fold PCPA factor for the toxicology reference values. They further stated that acute dietary exposure for females aged 13–49 years could exceed the more conservative ARfD, chronic dietary exposure for children aged 1–2 years would substantially reduce the available margin below the more conservative ADI, and the current 12-hour restricted-entry interval for pome fruit hand thinning may be insufficient, potentially requiring a much longer interval to meet the higher margin-of-exposure target.

Health Canada response

Health Canada has considered the comment that should the default 10-fold PCPA factor be retained, this would materially change the dietary and occupational risk assessment conclusions presented in PRD2026-09 and therefore necessitate recalculation of the associated reference values and risk estimates.

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[6] Green, M. L., Kluever, A., Chen, C., Dobreniecki, S., Halpern, W., Hannas, B., Hoberman, A., McNerney, M. E., Mitchell-Ryan, S., Shafer, T. J., Van Cruchten, S., & White, T. (2024). HESI workshop summary: Interpretation of developmental and reproductive toxicity endpoints and the impact on data interpretation of adverse events. Birth Defects Research, 116(2), e2311. https://doi.org/10.1002/bdr2.2311

As discussed in the response to Comment 3, Health Canada determined that application of a 3-fold PCPA factor for risk assessments based on the developmental toxicity endpoints is scientifically justified and consistent with the framework described in SPN2008-01. The decision was based on a weight-of-evidence evaluation of the available toxicology database, including the completeness of the database, the nature and toxicological significance of the developmental findings, the absence of treatment-related malformations or other serious effects in the young, and the conclusion that the observed skeletal variations were not considered serious in nature. The available data therefore supported reducing the default 10-fold PCPA factor while retaining an additional 3-fold margin of protection for sensitive subpopulations.

Because Health Canada has concluded that the 3-fold PCPA factor remains appropriate, the commenter's recalculations are based on an alternative regulatory assumption that was not adopted in the risk assessment. Consequently, the risk assessment conclusions presented in PRD2026-09 remain health protective and are based on the assessment factors that Health Canada determined to be scientifically appropriate under the *Pest Control Products Act* and consistent with the principles outlined in SPN2008-01.

5. Comment related to the separate consultation processes for the review of the toxicology assessment and the proposed MRLs.

The commenter stated that the consultation process creates a timing and scope issue because the toxicological reference values underpinning the proposed MRLs can only be challenged through PRD2026-09, which closes before the related PMRL2026-07 consultation and after which those issues are explicitly excluded from consideration in the MRL process. As a result, there is no stage in the combined consultation framework where changes to the toxicology assessment could directly influence the residue limit decision that relies on it.

Health Canada response:

Health Canada has considered the comment that the toxicology assessment in PRD2026-09 and the associated proposed maximum residue limit (PMRL) document should be combined into a single consultation process.

Health Canada will consider this feedback for exploring ways to improve the consultation process for how Proposed Registration Decisions (PRDs) and PMRLs are consulted. However, a potential change in the consultation process would only be implemented after careful consideration and would not be implemented retroactively for previously published proposed decisions. As such, this comment is appreciated and will be considered for improving future process but does not impact the current decision.

6. Comment related to the confirmation of the WTO Notification

The commenter stated that they were unable to locate a WTO notification specifically corresponding to PMRL2026-07 and requested confirmation that a WTO notification has been filed for this consultation, along with the associated WTO notification reference number.

Health Canada response:

Health Canada has considered the comment regarding the accessibility of information related to the proposed maximum residue limits (MRLs) and the WTO Notification.

The proposed MRLs were notified internationally through the World Trade Organization (WTO) Sanitary and Phytosanitary (SPS) notification process. WTO/SPS notifications are publicly available through online notification portals, including the WTO ePing SPS&TBT Platform (https://eping.wto.org/en/Search/AllInformation), which can be searched using the active ingredient name. For example, a search for "spiropidion" (in the Free text search box) and "Canada" (in the Member(s) box) in the ePing database identifies WTO/SPS notification **G/SPS/N/CAN/1643**, which contains the information required under the WTO/SPS notification process and provides a link to Health Canada's proposed MRL consultation document, PMRL2026-07.

7. Comment related to the literature review

The commenter stated that PRD2026-09 discloses only a single literature search—a PubMed search for the keyword "spiropidion" focused on toxicology—and provides no evidence of literature searches covering exposure, dietary assessment, or environmental fate. The commenter also raises concerns about the data underlying its dietary exposure assessment. Although it states that residue trials were conducted in Canada and/or the United States, the cited bibliography appears to identify only U.S. trials for domestically registered crops. In addition, the dietary risk assessment relies on U.S. food consumption data (NHANES/WWEIA, 2005–2010), meaning the assessment is based on older American dietary patterns rather than current Canadian data. Finally, while the consultation confirms that complete residue datasets exist in order to run the OECD MRL calculator, those data are not publicly disclosed, preventing independent evaluation of the assessment's statistical basis.

Health Canada response:

Health Canada has considered the comment that the literature search described in PRD2026-09 was limited to hazard-related information, that the dietary risk assessment relies on food consumption data that are foreign and not recent, and the request for disclosure of the crop field trial data and residue datasets supporting the proposed MRLs.

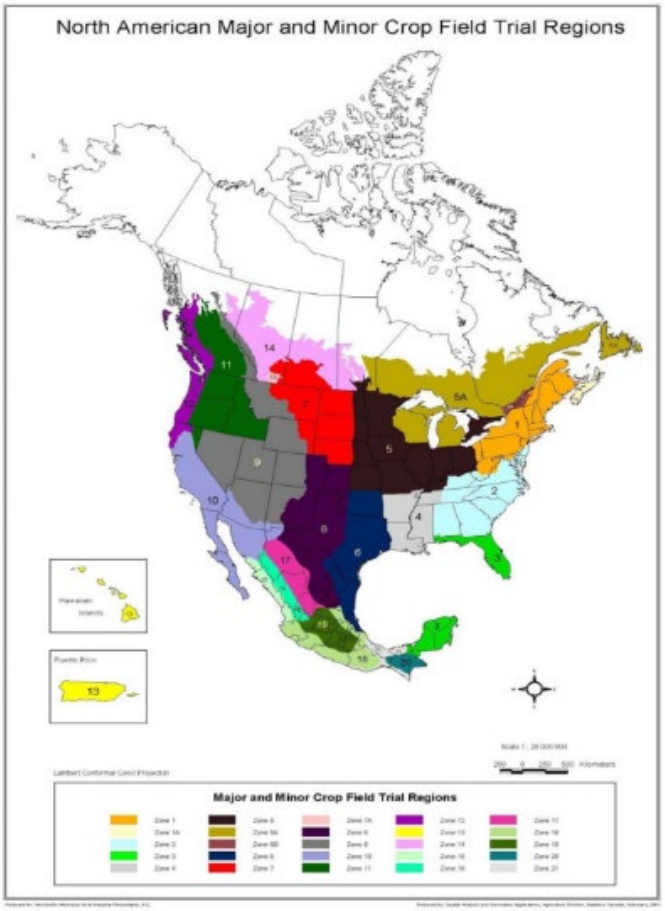
The literature search described in PRD2026-09 was conducted to identify published information relevant to the toxicological assessment of spiropidion and therefore formed one component of the hazard assessment. The dietary risk assessment integrates the hazard assessment and the dietary exposure assessment. The dietary exposure assessment is based on application-specific residue chemistry data submitted in support of the proposed uses together with food consumption data and established dietary exposure methodologies.

With respect to dietary exposure assessment, Health Canada uses established and internationally recognized methodologies and data sources that have been developed for pesticide dietary risk assessment and are accepted by regulatory authorities.

As pesticide residue data for each proposed spiropidion food use were required to calculate MRLs and to assess dietary exposure, crop field trial data were submitted and reviewed. A

literature review for dietary exposure data was not conducted, as crop trials are conducted in accordance with Health Canada's residue chemistry requirements and are designed to reflect pesticide use patterns that lead to the highest possible residues. The resulting residue data are used to calculate MRLs and conduct dietary risk assessments.

As per the Updated Residue Chemistry Guidelines (19 October 2022), the total number of crop field trials required for a given crop is determined by the total production area and the dietary share and the specific locations of the field trials are distributed according to the share of total crop area reported in each region. A map of North American Major and Minor Crop Field Trial Regions is presented below:



There are fourteen major and four minor field trial regions in Canada and the USA. Each of these regions recognizes physical characteristics, such as soils, and crops and climate, that make the region unique. The subzones address differences within a region, generally reflected in the types of crops grown in that region. Some of the Canadian growing regions correspond to equivalent American growing regions, for example, Zones 1, 5, 5A, 5B (Zones 5, 5A and 5B are now collectively referred to as Zone 5), 7, 11 and 12.

Field trials conducted in the United States, in the equivalent growing region, can be used to fulfill Canadian requirements provided the use pattern is the same as the one proposed in Canada. Residue data generated from outside of North America may be accepted on a case-by-case basis.

As outlined in Science Policy Note SPN2017-02, *Joint Canada/United States Field Trial Requirements*, in the context of joint residue trial projects intended to support simultaneous domestic registration applications in both the United States and Canada (as is the case with spiropidion), the USEPA and Health Canada have agreed to the trial requirements for the representative crops in the NAFTA Residue Chemistry Crop Groups (see section 40 CFR 180.41 of the eCFR website and Health Canada website [Residue Chemistry Crop Groups - Pesticides and Food - Health Canada]). As such, as long as field trials provided for a given crop or for a representative crop of the subject crop have been conducted in growing regions according to SPN2017-02, the location of these trials are acceptable to support registrations in both the US and in Canada. The submitted field trial data met these criteria.

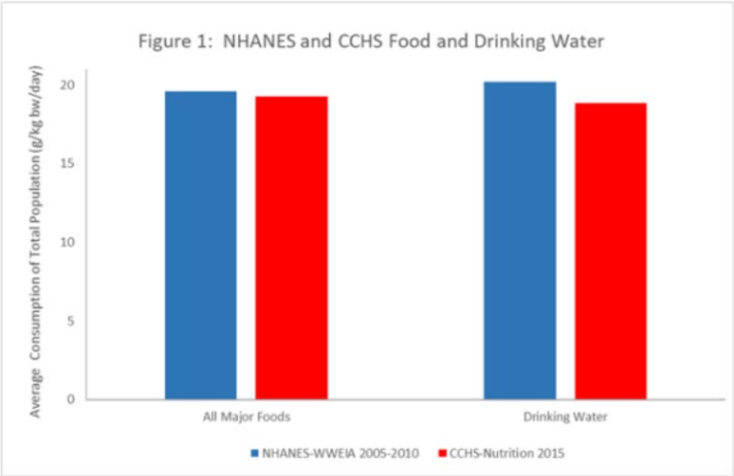
In regards to the request for disclosure of detailed information about the crop field trials and the full residue data set used to run the OECD MRL Calculator, Health Canada notes that residue field trial studies submitted in support of a pesticide registration application, constitute confidential test data (CTD) under the *Pest Control Products Act*. The Act provides a mechanism through which members of the public may inspect such data. As described in Health Canada's guidance document, Inspection of Confidential Test Data supporting registration decisions may be inspected upon application to Health Canada after a final registration decision has been made. The guidance further explains the application process and inspection procedures, including options for in-person inspection in the Reading Room at Health Canada's National Head Office in Ottawa or remote inspection arrangements. Accordingly, while PRD2026-09 summarizes the scientific basis for the proposed decision, stakeholders seeking access to the underlying scientific studies and datasets may do so through the CTD inspection process established under the *Pest Control Products Act*.

Food consumption data

As mentioned in PRD2026-09, acute and chronic dietary risk assessments for spiropidion were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 4.02, 05-10-c), which incorporates consumption data from the National Health and Nutrition Examination Survey/What We Eat in America (NHANES/WWEIA) for the years 2005-2010.

Health Canada conducted a detailed analysis of the consumption datasets available for North America (i.e., 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 to explain why Health Canada uses NHANES data.

Amongst others, comparison of the total consumption levels determined for NHANES and CCHS shows a very similar pattern between the USA and Canada (Figure 1). The average food consumption level for NHANES is 2% higher compared to the CCHS, while drinking water consumption is 7% higher.



Health Canada has selected NHANES data for use in dietary risk assessments for pesticides over the CCHS after carefully considering several factors (refer to SPN2014-01, *General Exposure Factor Inputs for Dietary, Occupational, and Residential Exposure Assessments*) including:

Quality and accessibility of the data: Both the NHANES and the CCHS are high quality databases that are accessible to the public. However, by virtue of the greater population size, NHANES collects more survey data, thereby providing more accuracy inherent with a larger dataset.

Relevance for people in Canada: As noted in Figure 1 above, the consumption levels of food and drinking water for each dataset are similar, making the data from both surveys applicable to people in both Canada and the U.S. In fact, in some cases, the U.S. consumption data are slightly higher, rendering them more protective of the population as a whole.

Conversion of foods "as eaten" to the raw agricultural commodity (RAC): Both NHANES and the CCHS collect consumption data "as eaten" foods, but only NHANES data is broken down further to RACs within the Dietary Exposure Evaluation Model – Food Commodity Intake Database™ program (DEEM-FCID™, Version 4.02, 05-10-c) using the FCID recipe list (available online as a website developed by the University of Maryland in collaboration with the USEPA Office of Pesticide Programs). This is extremely important because both the consumption data and pesticide residue concentration must be based on RACs to most accurately estimate dietary exposure for a pesticide; the DEEM-FCIDTM program multiplies the consumption amount of a RAC, such as wheat flour, with the pesticide residue concentration for this RAC.

Inclusion of vulnerable population groups: Both NHANES and CCHS collect data from populations for varying ages, sex, regions and ethnic origin. However, NHANES has the added advantage of also collecting data for infants less than 1 year of age, which is often the most sensitive age group for identifying dietary risks for pesticides. The CCHS does not collect data for this age group.

Time frame: The 2015 CCHS consumption data is more recent than the NHANES 2005-2010 data. However, the NHANES data provides greater confidence because it has more data points: it covers multiple years and captures consumption patterns over a longer period of time. More

recent NHANES consumption data are available (up to March 2020). This will replace the current version once converted to RACs and Health Canada has determined that it continues to meet the requirements for dietary exposure and risk assessments for pesticides.

Based on the above factors, Health Canada has determined that using the NHANES dataset which is a component of DEEM-FCID, is most appropriate for determining exposure levels to pesticides in the diets of Canadians.

It should be noted that Health Canada continually monitors and incorporates revisions to both NHANES and CCHS consumption data and will continue to ensure that the data used in dietary exposure and risk assessments for pesticides are appropriate and protective of people in Canada. Accordingly, Health Canada concludes that the dietary risk assessment was based on an integrated evaluation of the available hazard and exposure information using established risk assessment methodologies. The scope of the published literature search conducted for the toxicology assessment does not invalidate the exposure assessment, nor does it affect Health Canada's conclusion that dietary risks associated with the proposed uses of spiropidion are acceptable when assessed against the applicable health-based reference values. Furthermore, the scientific studies and datasets underlying the assessment are available through the legislated confidential test data inspection process described above.

The Continuous Oversight Policy applies to pesticides registered in Canada. Following registration of an active ingredient, PRD determines whether it would be subject to ongoing monitoring of scientific literature in accordance with the policy. Additional details are available in the Continuous Oversight Policy document.

At the time of the consultation on PRD2026-09, spiropidion was not registered in Canada and, therefore had not yet been considered for monitoring of scientific literature under the Continuous Oversight Policy, including the application of the search methodologies. Following publication of a registration decision, spiropidion would be considered for inclusion in ongoing monitoring activities in accordance with the Continuous Oversight Policy.

8. Comment related to the international conclusions regarding the 2-year carcinogenicity study in rats

The commenter stated that neither the Evaluation Report for Submission 2021-2460 nor PRD2026-09 includes information related to tumor incidence or other specific data from the 2-year rat carcinogenicity study. The commenter further stated that a more conservative characterization of the same study by the JPMR is not addressed in PRD2026-09, and questioned whether a human-relevance mode of action assessment was conducted for the tumors identified by the JMPR.

Health Canada response:

Health Canada has considered the comment regarding the interpretation of the 2-year rat carcinogenicity study and differences between Health Canada's assessment and those conducted by other regulatory authorities, including the Joint FAO/WHO Meeting on Pesticide Residues (JMPR).

Health Canada reviews and considers assessments undertaken by other regulatory authorities and international expert bodies, including JMPR, as part of its evaluation process. However, Health Canada's risk assessment is based on an independent review of the complete data package submitted in support of the registration application and is conducted in accordance with the requirements of the *Pest Control Products Act*, Health Canada's risk assessment policies, and a weight of evidence evaluation of the available scientific information. As a result, differences may arise among regulatory authorities in the interpretation of study findings, the selection of critical effects, the identification of points of departure, and the derivation of toxicological reference values, even where the same underlying study is considered.

With respect to the 2-year rat carcinogenicity study, the JMPR noted that Leydig cell adenomas were reported at 100 ppm (in two animals) and at 500 ppm (in two animals), with no obvious dose-response, and that no treatment-related preneoplastic lesions were reported. The JMPR established an ADI of 0–0.02 mg/kg bw, based on the NOAEL of 2.4 mg/kg bw per day for an equivocal increase in testicular interstitial cell adenomas at 100 ppm (equal to 4.7 mg/kg bw per day) in the 2-year rat study, and using a safety factor of 100. Health Canada reviewed the same study and the associated tumour findings as part of its assessment and considered the overall weight of evidence from the toxicology database when characterizing the carcinogenic potential of spiropidion. Health Canada concluded that there was no evidence of tumorigenicity in the 2-year rat study due to the low incidence of tumors and the lack of dose response; as such, a human relevance assessment was not necessary.

Health Canada's conclusions regarding the 2-year rat carcinogenicity study are supported by its independent evaluation of the complete database and the weight of evidence available at the time of the assessment. While Health Canada considered JMPR's review and other international assessments, the final characterization of hazard and risk reflect Health Canada's own scientific evaluation and regulatory framework.

Health Canada further notes that the underlying study reports and supporting scientific data, including the 2-year rat carcinogenicity study, constitute confidential test data under the *Pest Control Products Act*. The *Pest Control Products Act* provides a mechanism through which members of the public may inspect confidential test data supporting pesticide registration decisions. As described in Health Canada's Inspection of Confidential Test Data: Guidance Document, interested persons may apply to inspect these studies following a final registration decision. The guidance document describes the application process and inspection procedures, including options for inspection at Health Canada's Reading Room in Ottawa or through remote inspection arrangements. Accordingly, stakeholders seeking to review the underlying study reports and supporting data may do so through the legislated confidential test data inspection process.

9. Comment related to the consideration of international status of related pesticides in the cumulative assessment

The commenter stated that the international regulatory and litigation history, including the classification of spirodiclofen as carcinogenic by the United States Environmental Protection Agency (USEPA), were not taken into consideration in the determination of the cumulative assessment for spiropidion with other compounds included in the common mechanism group.

Health Canada response:

Health Canada has considered the comment that the cumulative assessment group (CAG) for spiropidion should account for the international regulatory and litigation history of other group members, including carcinogenicity classifications that have been assigned to spirodiclofen by other regulatory authorities.

As described in PRD2026-09, the cumulative assessment was conducted in accordance with Health Canada's cumulative risk assessment framework, which focuses on pesticides that share a common mechanism of toxicity or a pattern of common toxic effects relevant to human health risk assessment. Under Science Policy Note SPN2018-02, cumulative risk assessments are developed around common mechanisms of toxicity and common toxicological outcomes for which cumulative exposure and cumulative effects can reasonably be assessed. The international regulatory status, hazard classifications assigned by other jurisdictions, or litigation history are not relevant to the determination of a common mechanism group. Rather, the assessment focuses on whether there is sufficient scientific information to support a common mechanism group and to identify common effects appropriate for cumulative risk characterization.

Consistent with this framework, spiropidion, spirodiclofen, spiromesifen, and spirotetramat were considered a common mechanism group because they share the same pesticidal mode of action as well as structural similarities, and the available mammalian toxicology data identified common effects involving the thyroid and cholesterol metabolism. As it was not possible to rule out a shared mammalian mode of action related to these effects, Health Canada conducted a cumulative assessment based on these common toxic effects and the potential for co-occurring exposure through food, drinking water, and residential uses. The cumulative assessment focused on effects for which there was evidence of commonality across the group and which were relevant for repeated exposure scenarios.

Furthermore, in the Health Canada assessment of spirodiclofen,[7] treatment-related tumors were observed, consistent with the conclusion of the USEPA noted by the commenter. However, Health Canada did not identify carcinogenicity as a relevant endpoint for spiropidion, spiromesifen or spirotetramat. Since cancer was not identified as a common effect across the members of the cumulative assessment group, there was no evidence to support a conclusion that carcinogenicity represented a common toxic effect arising from a common mechanism of toxicity among spiropidion, spirodiclofen, spiromesifen, and spirotetramat, and thus a cumulative risk assessment was not required on the basis of carcinogenicity.

Accordingly, Health Canada concludes that the cumulative assessment presented in PRD2026-09 is consistent with the principles outlined in SPN2018-02. The assessment appropriately focused on the common thyroid and cholesterol-related effects identified across the group and did not identify scientific justification to include carcinogenicity as a common cumulative endpoint for the tetronic and tetramic acid derivative insecticides included in the cumulative assessment group.

[7] Health Canada Regulatory Note REG2006-06; https://publications.gc.ca/collections/Collection/H113-7-2006-6E.pdf

10. Comment related to the toxicology reference values established by international regulatory authorities

The commenter stated that the ADI established by the JPMR for spiropidion is lower than that established by Health Canada, and noted the EFSA's inability to confirm the dietary reference doses established by the JMPR. The commenter further noted the EFSA's position that the genotoxicity data summarized in the JMPR evaluation were insufficiently detailed. The commenter further stated that PRD2026-09 does not explain the basis for the discrepancy between the conclusions of Health Canada and those of EFSA and JMPR.

Health Canada response:

Health Canada recognizes that other regulatory authorities and international organizations may reach different conclusions regarding a pesticide's hazard characterization, critical endpoints, points of departure, or health-based reference values. As discussed in the response to Comment 8, Health Canada considers assessments conducted by international bodies and foreign regulators, including the JMPR, as part of its review process. However, Health Canada's assessments are based on an independent evaluation of the complete data package and are conducted in accordance with the requirements of the *Pest Control Products Act* and Health Canada's established science policies and risk assessment framework. Consequently, different regulatory authorities may derive different reference values or arrive at different conclusions from the same study or database. Such differences do not necessarily indicate an error in any assessment, but may reflect differences in scientific judgement, policy approaches, data availability, or statutory requirements.

Health Canada continues to work with international counterparts, including foreign regulatory agencies and international expert bodies, with the objective of promoting scientific collaboration and, where appropriate, greater alignment of risk assessment approaches. Nevertheless, some differences among regulatory outcomes will persist because regulatory decisions are ultimately made within the legislative and policy frameworks governing each organization. As a result, hazard classifications, toxicological reference values, and risk assessment conclusions adopted by other jurisdictions are considered as relevant information but do not determine Health Canada's regulatory conclusions under Canadian legislation.

11. Comment related to the immunotoxicity study waiver

The commenter noted that Health Canada's conclusion regarding a lack of consistent effects on immune-related parameters in the available toxicology database, which formed part of the basis for accepting the waiver for an immunotoxicity study, contradicted conclusions reached by EFSA.

Health Canada response:

Health Canada has considered the comment regarding immune-related findings in the database and the acceptance of the immunotoxicity study waiver.

As noted in the Evaluation Report for Submission 2020-4760, the request to waive the conditional requirement for a short-term immunotoxicity study was granted based on the absence of consistent effects on immune-related parameters in the available repeat-dose toxicity studies

with spiropidion and the lack of immunotoxicity with other insecticidal compounds in the same class of chemistry as spiropidion. The EFSA 2024 report concluded that specific immunotoxicity tests were not performed and the potential for immunotoxicity of spiropidion was not fully addressed in the JMPR monograph, considering that findings on the immune system were identified in the available toxicity studies. However, it is stated in the JMPR monograph that there was no evidence of immunotoxicity reported in routine toxicological studies with spiropidion, and JMPR concluded that spiropidion is unlikely to be immunotoxic. It is not clear as to what effects on the immune system the EFSA 2024 report is referring.

12. Comment related to the status of regulatory approval in Europe

The commenter stated that the lack of formal approval of spiropidion in the European Union does not equate to an absence of international reviews, and highlighted the EFSA 2024 review as an independent review worth considering.

Health Canada response:

Health Canada has considered the comment that a lack of a formal assessment under the European Union's formal active substance approval process does not mean that there are no international records on spiropidion. Health Canada routinely monitors the international status of pest control products as part of its regulatory oversight activities. This includes consideration of scientific reviews, regulatory decisions, hazard assessments, risk assessments, and risk management actions undertaken by foreign regulatory authorities and international organizations, where relevant information is available. Such information may be considered during the review of new active ingredients, registration amendments, re-evaluations, and special reviews. Consequently, Health Canada was aware of and considered relevant international information pertaining to spiropidion as part of its assessment.

Although Health Canada considers assessments conducted by international organizations and foreign regulators, including the JMPR, EFSA, USEPA, and other regulatory authorities, where appropriate, Health Canada's assessments are based on an independent evaluation of the complete scientific database and are conducted in accordance with the requirements of the PCPA, Health Canada's science policies, and its established risk assessment framework. As a result, different regulatory authorities and international organizations may arrive at different hazard characterizations, points of departure, reference values, study interpretations, or overall regulatory conclusions, even when evaluating the same underlying studies. Such differences do not necessarily indicate a deficiency in any assessment, but may reflect differences in scientific judgement, available information, policy approaches, or the legislative and regulatory frameworks governing each organization.

With respect to the findings of the EFSA 2024[8] review, it is important to note the purpose of that review was to evaluate the available toxicological information provided in the JMPR monograph to confirm whether they are sufficient to confirm the JMPR toxicology reference values (TRVs) for spiropidion. EFSA noted that the level of detail in the JMPR monograph is not fully comparable to that usually available in the reports drafted for the EU peer review, and EFSA does not have access to the original background studies. They further noted that the results of genotoxicity studies are not presented in a sufficiently detailed way that would allow a critical

[8] https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2024.8693

review. As such, EFSA was not in a position to conclude on the TRVs derived by JMPR for spiropidion and did not recommend to use the JMPR TRVs for EU risk assessments. Health Canada, on the other hand, had full access to the study reports and underlying data for spiropidion which allowed for a comprehensive evaluation to be conducted.

As noted in the responses provided to the previous comments, Health Canada continues to work collaboratively with international counterparts to promote scientific cooperation, information sharing, and, where appropriate, greater alignment of science policies and risk assessment approaches. Nevertheless, some differences in regulatory outcomes are expected because decisions must ultimately be made within the statutory authorities and regulatory frameworks applicable to each organization. Accordingly, while international reviews are an important source of information, Health Canada does not rely solely on the conclusions of another authority when determining whether a pest control product meets the requirements of Canadian legislation.

13. Comment related to the lack of toxicological characterization of the primary metabolite

The commenter stated that there was a lack of information on the mammalian toxicity of the primary metabolite SYN547305 in PRD2026-09, while information on its environmental impact suggested a higher chronic toxicity to bees than spiropidion.

Health Canada response:

Health Canada has considered the comment that PRD2026-09 does not provide a separate mammalian toxicological characterization for the metabolite SYN547305, despite its inclusion in the residue definitions used for dietary exposure and its role as a major metabolite of spiropidion.

Health Canada notes that SYN547305 was considered in the overall human health assessment of spiropidion, and additional information is located in the Evaluation Report for Submission 2020-4760. Toxicokinetic studies demonstrated that spiropidion is rapidly metabolized following administration and that unchanged spiropidion was generally not quantifiable in blood, while SYN547305 was the predominant circulating metabolite. In repeat-dose toxicity studies conducted in rats, mice, and dogs, systemic exposure was primarily associated with SYN547305, with blood concentrations of SYN547305 generally exceeding those of the parent compound. The available information therefore indicates that the toxicology database for spiropidion inherently assessed substantial exposure to SYN547305 and that the toxicity findings observed following administration of spiropidion reflected exposure to both the parent compound and its principal metabolite SYN547305.

The inclusion of SYN547305 in the residue definitions for drinking water and dietary risk assessment was not based on its biological activity in insects. Rather, the environmental fate of spiropidion and its metabolites, the metabolism and residue chemistry data demonstrating that SYN547305 is a major residue component relevant to potential dietary exposure, as well as the available mammalian metabolism, toxicokinetic, and toxicology data on spiropidion and its metabolites were considered in establishing the residue definitions for the human health risk assessment.

Health Canada further notes that the comment references observations in the environmental assessment indicating that SYN547305 exhibited higher chronic toxicity to certain bee life stages than the parent compound. However, ecotoxicological findings in non-target organisms such as insects do not necessarily predict mammalian toxicity and are not, by themselves, sufficient to conclude that a separate mammalian hazard characterization is required. Human health assessments are based on the mammalian toxicology database and the available information regarding metabolism, toxicokinetics, and exposure. The fact that SYN547305 may exhibit different toxicity characteristics in certain environmental organisms does not establish that its mammalian toxicity exceeds that of spiropidion.

SYN547305 was considered by Health Canada within the broader mammalian toxicology, metabolism, and toxicokinetic database for spiropidion, which indicated that this metabolite is a major product of metabolism in mammals and a significant contributor to systemic exposure following administration of the parent compound, spiropidion. Based on the available evidence, the toxicology database was considered adequate to characterize the human health risks associated with dietary exposure to residues of spiropidion and SYN547305.

14. Comment related to the inhalation toxicity study waiver

The commenter stated that the results of the in vitro human airway epithelium model were inconsistent, in that cell death, or necrosis, of airway tissue was noted upon histological examination, but the standard tests that would normally detect the consequences of cell death were all negative. The commenter further stated that the orally-derived point of departure used in the human health risk assessment is not an adequate substitute for the direct characterization of repeated-exposure local respiratory effects based on the reported route-specific effects reflective of inhalation toxicity.

Health Canada response:

Health Canada has considered the comment that some findings in the available information related to inhalation toxicity are inconsistent. The apparent discrepancy in the results of the different parameters assessed in the in vitro human airway epithelium model is not necessarily evidence that one of those results is incorrect. The histopathology assessment may have detected localized or early epithelial injury that was insufficient in extent or severity to measurably affect other parameters tested, such as tissue-wide barrier integrity (TEER), membrane leakage (LDH release), or overall metabolic activity (resazurin assay). Regardless, the lack of cytotoxicity, as measured by the TEER and LDH tests, did not negate consideration of the histological findings of necrosis in the weight of evidence assessment of the request to waive the repeat-exposure inhalation toxicity study.

In evaluating the waiver request, Health Canada considered the entire toxicology database, including the available inhalation-specific studies. However, Health Canada determined that the most sensitive and risk-driving effects within the spiropidion toxicology database were developmental effects observed in the rat and rabbit developmental toxicity studies. These developmental skeletal variations formed the basis for the toxicological reference values used in dietary, occupational, residential, aggregate, and inhalation risk assessments. PRD2026-09 specifically notes that a standard repeat-exposure inhalation toxicity study would not evaluate these developmental endpoints and therefore would not be expected to address the critical effects

that drive the risk assessment. Health Canada further noted that the developmental NOAEL of 10 mg/kg bw/day selected for risk assessment corresponds, through route-to-route extrapolation, to an inhalation exposure concentration of approximately 0.04 mg/L. Based on the available route-specific findings from the 5-day dose range-finding study, the lowest exposure concentration recommended for a subchronic inhalation toxicity study in rats (0.03 mg/L) is very similar to this extrapolated equivalent concentration. Consequently, the available point of departure was considered protective of potential inhalation toxicity without requiring an additional repeat-exposure inhalation study.

Health Canada therefore concluded that a repeat-exposure inhalation toxicity study was unlikely to provide information critical to the assessment of human health risk.

15. Comment related to ground nesting bees and the pollinator risk assessment

The commenter stated that PRD2026-09 assessed pollinator risk using only honey bees and bumblebees and did not consider ground-nesting or other solitary bees. This reflected a recognized limitation of current regulatory frameworks, including those of the U.S. EPA and EFSA, which do not address soil exposure because honey bees do not nest in soil. The 2014 *Guidance for Assessing Pesticide Risks to Bees* (U.S. EPA, PMRA, and California DPR), on which PRD2026-09 is based, stated that honey bee colony studies were representative of honey bees and other social bees, while acknowledging that methods for non-*Apis* bees remained to be developed.

The commenter further describes that this gap is relevant to spiropidion because it is registered on cucurbit crops, whose specialist pollinator, the ground-nesting hoary squash bee (*Peponapis pruinosa*), may be exposed to soil residues. Canadian research has shown soil concentrations exceeding solitary bee effect thresholds, while PRD2026-09 also reported exceedances of the honey bee larval level of concern (maximum RQ = 32 for SYN547305).

Health Canada response:

Health Canada has considered, as noted in the 2014 Guidance for Assessing Pesticide Risks to Bees, that there are limitations in the estimation of exposure for solitary bees in soil, including the lack of a defined and reliable exposure estimate or acceptable toxicity study protocols to be used in the risk assessment. Health Canada has been working with other stakeholders in study guideline development in order to address these issues.

The current risk assessment framework for pollinators uses a tiered approach. Tier I of the framework relies on laboratory data for individual honey bees that are representative of different life stages (larval/pupal and adults) and castes (e.g., worker bees). When data are available for additional bee species, they are used as an additional line of evidence. At the higher tiers of the framework, semi-field and full-field studies using honey bee colonies are relied upon. The honey bee data are used as a surrogate for both *Apis* and non-*Apis* bees, including other social and solitary species. The advantage of using honey bees is that the husbandry and life cycle of the species and its significance in pollination services is well known and test protocols are available.

Health Canada's protection goals relative to all bees include the maintenance of pollination services, hive product production and biodiversity. These goals are considered protective for social and solitary bees.

The commenter notes that recent Canadian research that sampled soil in Ontario cucurbit fields found that systemic insecticide residues reached concentrations exceeding solitary-bee-relevant effect thresholds, even where they remained below the honey bee benchmarks. This appears to be in reference to a study used in the special review of the soil and seed treatment uses of neonicotinoids on cucurbits and the potential risks to squash bees (PSRD2021-02/SRD2022-02). For more information on the neonicotinoid special review for squash bees, and the mitigation measures that were implemented in 2019, please see: https://www.canada.ca/en/health-canada/news/2021/06/backgrounder-proposed-special-review-decisions-for-squash-bee-exposure-to-neonicotinoids.html.

The conclusions from the cited research in Ontario cucurbit fields are specific to neonicotinoids and do not represent the risk profile for spiropidion. Exposure of ground-nesting bees to spiropidion and its transformation product, SYN547305, is expected to be limited because both are non-persistent in soil. Spiropidion and SYN547305 are rapidly transformed by soil microorganisms, with DT_{50} values ≤ 1.1 days.

The commenter inferred risk to larval ground-nesting bees based on the screening-level risk quotient of 32 for larvae exposed to SYN547305 reported in PRD2026-09, and the neonicotinoid soil data from Ontario cucurbit fields. It is acknowledged the screening-level risk quotient of 32 exceeds the level of concern of 1; however, the risk assessment was further refined using the results of semi-field and colony feeding studies, and risk mitigation measures were implemented. Brood and pupal effects observed at the highest dose in the colony feeding study are addressed through the pollinator risk mitigation measures outlined in PRD2026-09. As an additional line of evidence for the pollinator risk assessment and acceptability of risks to ground-nesting bees, it should be noted that risks to other ground-dwelling soil organisms (such as earthworms, collembolan and predatory mites) are acceptable based on highest application rate.

16. Comment related to colony feeding study

The commenter stated that PRD2026-09's 6-week colony feeding study reports that all control hives survived overwintering, while only 75%, 83%, and 75% of hives survived in the 12.5, 25, and 50 ppm treatment groups respectively. The document's conclusion is that "it is unclear if exposure to spiropidion played a role in the colony deaths since statistically significant effects were not observed." The commenter notes that a consistent reduction in survival across every treatment concentration tested, relative to 100% control survival, is not self-evidently a null result because it did not reach statistical significance. The commenter indicated that PRD2026-09 does not address the statistical power of the colony feeding study, nor does it explain why a consistent, dose-independent reduction across all three treatment groups should be treated as unrelated to treatment rather than as a signal the study lacked the power to confirm.

Health Canada response:

Health Canada considered the strength of the large-scale colony feeding study design. The Large-Scale Colony Feeding Study (LSCFS) design was developed in collaboration with the United States Environmental Protection Agency (USEPA) and Health Canada, and was worked on internationally under the International Commission for Plant-Pollinator Relationships (ICP-PR) to provide a Tier 2 refinement. The LSCFS was designed to evaluate effects on free-foraging honey bee colonies following chronic exposure to treated sucrose solution, and includes multiple

treatment levels, extended exposure periods, and increased replication (n = 4) to characterize dose-response relationships and determine colony-level No Observed Adverse Effect Concentrations (NOAECs). These results are then directly compared to pesticide residues measured in pollen and nectar from treated crops, improving the interpretation of field-relevant exposure.

The LSCFS addresses the protection goals of Health Canada's Pesticides Regulatory Directorate and the USEPA (maintenance of bee diversity, pollination services and hive product production), as well as those of the European Union (European Food Safety Authority, 2023; preventing colony- and population-level effects that exceed acceptable thresholds). The study provides information on population-level effects, colony survival and strength, overwinter survival, pollen storage area and area with nectar/honey. It also enables comparisons between control and treated colonies, and allows observed effects, or the absence of effects, in treated colonies to be interpreted in the context of pesticide residues detected in pollen and nectar collected from treated crops. An additional advantage of the LSCFS design over tunnel and field studies is the reduced uncertainty in exposure, as colonies are directly dosed rather than relying on exposure through treated crops. Furthermore, colonies can be observed for extended periods, including overwintering, allowing assessment of longer-term effects that cannot be evaluated in shorter-duration tunnel studies.

The statistical analyses conducted by the study author were considered acceptable for regulatory review, and independent recalculation was not warranted given the adequacy of the reported statistical methodology, the consistency of the results with the observed data, and the absence of biologically significant treatment-related effects. The statistical analyses were conducted by the study author as follows: The software "SAS®", version 9.4 and Microsoft Excel were used for the statistical analysis of the data. First, a comparison between the two control groups UTC1 (untreated control) and UTC2 (untreated control with solvent) was made. Since only two and only slightly statistically significant differences between the control groups were detected after start of feeding (CCA3: pupal cells, $p = 0.0477$; CCA5: bees, $p = 0.0472$), the control groups were pooled for further statistical comparison with the test item treatment groups to improve statistical power of the tests. Data from the test item treatments (T1, T2, T3) and the pooled control were checked for normality using Shapiro-Wilks test (p-value above 0.05 regarded as normally distributed). If the data were determined to be normally distributed, then Bartlett's test was used to check for homoscedasticity of data; if not, Levene's test was used. If data were not normally distributed or homoscedastic, they were logarithmically transformed. If the log-transformed data were normal and homoscedastic, transformed data were used for analysis to enable use of tests with higher statistical power, using the Dunnett's t-test. If data were normal but not homoscedastic, the Bonferroni-Holms corrected Welch test was used. If data were not normal, the Bonferroni-Holms corrected U-test was used ($p \leq 0.05$). There were 4 replicates per dose.

For the pre-application period, all tests were conducted in a two-sided approach whereas for the data assessed after application, one-sided tests ("upper" for empty cells, "lower" for food consumption, colony assessment data and colony strength) were conducted.

The survival rate observed in the test item treatment groups was comparable or lower than the average survival rates in the US (https://americanbeejournal.com/bee-informed-partnership-colony-loss-survey-2022-2023-results/). The similarity of the test data to the historical USDA

colony data indicates lack of biological significance. No effect of the test item treatment on survival rate could be observed.

Regardless of statistical power, as reported in PRD2026-09, Health Canada used the colony NOAEC of 25 ppm to compare with field pollen and nectar residues. This NOAEC was based on a comparison of treatment and control hives. The commenter is incorrect in stating "a consistent reduction in survival across every treatment concentration tested", as there was a limited dose response observed (i.e., 75, 83 and 75% survival at 12.5, 25 and 50 ppm, respectively). The identification of residue exceedances, together with other lines of evidence, supported the determination that chronic exposure to spiropidion could pose unacceptable risks to bee colonies in the absence of mitigation, which resulted in the implementation of pollinator protection measures, including bloom application restrictions and label statements. Even if a lower effect level had been used (i.e., <12.5 ppm), the overall risk conclusion and mitigation measures would not have changed.

17. Comment related to Occupational Exposure for Pick-Your-Own Patrons

The commenter stated that the postapplication occupational risk assessment is not protective of the risk associated with dermal exposure to patrons in pick-your-own (PYO) facilities by comparing the difference between the postapplication occupational and residential risk assessments of spiropidion. As such, the commenter requested Health Canada to conduct a quantitative dermal exposure assessment for children at PYO facilities.

Health Canada response:

Health Canada has considered the comment that a separate quantitative dermal exposure assessment should have been conducted for children at pick-your-own (PYO) facilities and that the postapplication occupational risk assessment is not representative of PYO exposure.

The commenter's comparison of the postapplication worker exposure assessments presented in Table 8 (in PRD2026-09) and the residential exposure assessments presented in Table 9 (in PRD2026-09) does not account for the fact that these tables evaluate different exposure scenarios using different assessment methodologies and exposure assumptions.

For pome fruits, the postapplication worker exposure scenario assessed is for an adult hand thinning 8 hours per day, using a transfer coefficient (TC) of 3000 cm^2/hr on the day of application. It is noted that hand thinning involves greater contact with treated foliage than hand harvesting pome fruits (TC of 1400 cm^2/hr). In addition, harvesting would occur after the preharvest interval (PHI) of 21 days.

In comparison, the residential exposure scenario assessed is for adults and children conducting postapplication activities involving pome fruits commercially treated that are in their backyard for 1 and 0.5 hour/day, respectively. Activities would include harvesting, tree maintenance, and climbing trees, and could occur starting from the day of application. TCs of 1700 cm^2/hr (for adults) and 930 cm^2/hr (for children) are representative of all activities in residential trees.

A PYO scenario differs from both the occupational and residential scenarios evaluated in PRD2026-09. However, PYO activities involve harvesting fruit in a commercial orchard for approximately 2 hours and would occur only after the 21-day PHI, which is substantially longer

than the 12-hour restricted-entry interval considered in the occupational assessment. Consequently, dermal exposure for adults and children participating in PYO activities is expected to be lower than the postapplication occupational exposure assessed in PRD2026-09, including when considering children's climbing behaviour. Therefore, risks associated with dermal exposure to patrons at PYO facilities are not of concern. In 2016, after careful consideration of the existing PYO risk assessments and the related agricultural risk assessments, Health Canada determined that PYO dermal exposure is adequately addressed by the agricultural post-application occupational dermal risk assessment, primarily due to the higher exposure duration of occupational workers. As such, the approach taken to assess PYO exposure for spiropidion is consistent with this established policy.

18. Comment related to reliance on a foreign exposure model

The commenter questioned the use of the 2012 United States Environmental Protection Agency's Standard Operating Procedures for Residential Pesticide Exposure Assessment (USEPA Res SOP) to assess residential exposure and pick-your-own (PYO) exposure to Canadians from the use of spiropidion and requested confirmation that the exposure assumptions are appropriate for these scenarios.

Health Canada response:

Health Canada has considered the comment regarding the use of residential exposure assessment assumptions and models originating from the United States Environmental Protection Agency (USEPA), including the transfer coefficients and exposure scenarios used in the assessment.

Health Canada acknowledges that elements of the residential exposure assessment, including certain transfer coefficients and scenario assumptions, were derived from established exposure assessment methodologies described in the 2012 USEPA Res SOP. These methodologies have been developed using a substantial body of exposure science and have been widely applied by regulatory authorities for the assessment of residential pesticide exposure. Health Canada has evaluated these methodologies and determined that the resulting exposure scenarios are applicable for characterizing potential residential pesticide exposures in the Canadian context. Consequently, these exposure assessment approaches continue to be used where they are considered scientifically appropriate and protective of human health.

Health Canada's use of internationally recognized exposure assessment methodologies should not be interpreted as an assumption that Canadian and U.S. populations are identical. Rather, Health Canada evaluates the suitability of available models, exposure factors, and assessment approaches for Canadian regulatory purposes and applies them within the broader Canadian risk assessment framework established under the *Pest Control Products Act*. The resulting assessments are intended to be protective of Canadian populations, including infants, children, and other potentially sensitive subgroups.

It is noted that only the residential exposure scenario was assessed with parameters in the 2012 USEPA SOP. For more details about the assessments of the residential and PYO exposure scenarios, please refer to the response to comment 17.

19. Comment related to the Track 1 substance concentration in the end-use product

The commenter stated that A20262 Insecticide contains 0.035% of the preservative 1,2-benzisothiazolin-3-one, which contains low levels of polychlorinated dibenzodioxins and furans, identified as TSMP Track 1 substances. The document concludes that no further action is required because Health Canada's 2012 reassessment found the use of this preservative acceptable in pest control products at concentrations up to 0.1%, based on the view that dioxin and furan levels were low and being managed.

The commenter notes that the TSMP calls for the virtual elimination of Track 1 substances, a standard defined by Environment Canada as reducing releases to the lowest concentration that can be accurately measured. PRD2026-09 does not provide measured dioxin or furan concentrations for this specific product, relying instead on a 2012 class-wide assessment. As a result, the document does not demonstrate that releases from A20262 Insecticide meet the TSMP's stated virtual-elimination standard for Track 1 substances.

Health Canada response:

Health Canada has considered that A20262 Insecticide contains low levels of polychlorinated dibenzodioxins and furans, identified as TSMP Track 1 substances. As noted in PRD2026-09, the dioxin and furan levels in A20262 Insecticide are low/being managed as outlined in Regulatory Directive DIR99-03 for the implementation of TSMP. DIR99-03 notes that new pest control products containing a Track 1 substance as a microcontaminant may be registered where the level of the microcontaminant in the product is very low, the registrant has demonstrated that the level of the microcontaminant in the product is as low as can be achieved by the application of the best available technology from a manufacturing perspective, and that the use of the product in accordance with its proposed label is not expected to present unacceptable risks. Pesticides are not considered to be a major source of dioxins and furans that have chlorines in at least the 2, 3, 7 and 8 positions to the environment (Environment Canada and Health Canada, 1990).[9] Health Canada reviews levels of these contaminants in pest control products to ensure they do not increase.

A risk assessment for 1,2-benzisothiazolin-3-one, which considered the presence of dioxins and furans as microcontaminants, was conducted in 2012. It was determined that the use of this preservative in pest control products at a maximum of 0.1% is acceptable. The 2012 assessment continues to be scientifically relevant and sufficient to support the current regulatory position, as the underlying hazard considerations and exposure assumptions remain applicable. Accordingly, Health Canada maintains its policy of limiting this preservative to levels below 0.1%.

The concentration of 1,2-benzisothiazolin-3-one in A20262 Insecticide represents 35% of the allowable threshold of 0.1%, providing a 65% margin below the limit. Dioxins and furans are frequently present in complex mixtures of multiple compounds. As such, they are commonly

[9] Environment Canada and Health Canada, 1990. Polychlorinated Dibenzodioxins and Polychlorinated Dibenzofurans - PSL1. Ottawa, ON. ISBN: 0-662-17644-8. https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/canadian-environmental-protection-act-priority-substances-list-assessment-report-polychlorinated-dibenzodioxins-polychlorinated-dibenzofurans.html

represented by a toxic equivalency (TEQ) to describe the total toxicity of the mixture of the different dioxins and furans. The TEQ is calculated by multiplying the concentration of each dioxin and furan compound by its risk score compared to the most toxic dioxin, 2,3,7,8-tetrachlorodibenzodioxin (TCDD). The level of 1,2-benzisothiazolin-3-one in A20262 Insecticide corresponds to a TEQ of 0.0016 parts per trillion (ppt) for dioxins and furans, or 1.6×10^{-13}%.

20. Comment related to the drinking water modelling and spray buffer zones

The commenter inferred that the evidence for the conclusion that "leaching of spiropidion residues to groundwater may be a concern" is based on limited empirical evidence because 2 of the 3 TFD studies may have received insufficient water to adequately assessed leaching, and that new TFD studies should be required. The commenter thinks that because the Level 1 drinking water modelling considered the combined residue of spiropidion and its TPs to be stable (or half-life of 1000 days) water modelling for the water column metabolism and benthic metabolism pathways, that Level 1 modelling is not sufficient and that drinking water modelling should have been done at Level 2. The commenter objects to the use of the leaching statement as a mitigation measure, and notes that the leaching statement lacks enforceable measures, and it is believed that if a level 2 water modelling was conducted, the dietary exposure estimate would exceed the risk cup.

Health Canada response:

Health Canada has considered that Level 1 drinking water modelling uses worst-case scenario assumptions (maximum application rates, conservative application methods, the widest application dates, and fate parameters) to generate the most conservative estimated environmental concentrations (EECs) for drinking water. As noted by the commenter, the drinking water modelling assumed that the combined residue of spiropidion and its transformation products is stable for certain pathways (water column metabolism and hydrolysis). This is considered to be a worst-case scenario that is used in the absence of data to the contrary for every compound in the combined residue. That is, if the combined residue were assumed to be stable, the resulting EECs would be higher than those predicted if the combined residue were to dissipate. Additional data would be required only if refinements are needed to further characterize risk to human health.

The Level 2 drinking water modelling is a refinement in the risk assessment, and thus, less conservative than Level 1 (in other words, Level 2 would estimate lower EECs). Given that dietary risks based on the Level 1 drinking water modelling were determined to be acceptable in PRD2026-09, Level 2 drinking water modelling is not required.

The leaching potential of spiropidion and its transformation products was determined using a weight-of-evidence approach based on mobility information from laboratory soil adsorption/desorption studies, the leaching criteria of Cohen et al. (1984), groundwater ubiquity scores (GUS) and groundwater modelling. It was determined that leaching of spiropidion residues to groundwater could be a concern. No further information, such as additional terrestrial field dissipation studies, is required to make this determination.

When leaching potential is determined to be a concern, Health Canada uses an advisory label statement to inform users of the conditions where leaching to groundwater is likely. The use of advisory label statements is a standard method used by Health Canada to inform users of the results of the scientific evaluation. The requirement for a leaching label statement is based on potential for exposure rather than risk. As determined in PRD2026-09, dietary risks including exposure to drinking water are acceptable with, or without, the leaching statement.

The commenter states that spray buffer zones are intended to mitigate risk from spray drift and surface runoff, and that the spray buffer zones do not mitigate risk from leaching. While the commenter is correct that spray buffer zones do not mitigate risks associated with leaching, they are only intended to mitigate risk from spray drift and are not intended to mitigate risks associated with runoff. For more information on spray buffer zones, please consult the Drift Mitigation portion of the Canada.ca website.

The conditions that could promote the runoff of a chemical (e.g., steep slope, heavy rain) may exist regardless of its attributes. As such, a label statement providing best management practices to reduce runoff is required on the labels of all products used outdoors in a manner where runoff could occur. This statement is required on the labels of spiropidion end-use products even though risks to aquatic organisms from runoff were determined to be acceptable.

In summary, regarding water, spiropidion end-use products require:

- An advisory statement to inform users of the potential of spiropidion residues to leach to groundwater.
- A label statement with best management practices to reduce runoff.
- Spray buffer zones of up to 1 metre to protect sensitive aquatic habitats from spray drift.

21. Comment related to a cumulative environmental assessment

The commenter stated that a cumulative environmental assessment should be conducted because the same co-occurrence rationale used to justify the human health cumulative assessment would appear to apply equally to non-target organism exposure.

Health Canada response:

A cumulative assessment is not currently part of Health Canada's environmental risk assessment framework. As such, a cumulative environmental assessment was not conducted for spiropidion.

At this time, there remains no consensus on international methodology for determining cumulative effects in the environment. Health Canada will continue to collaborate with provinces, other government departments, and domestic and international partners to advance scientific understanding towards the development of an approach to assess cumulative environmental effects of pesticides.

22. Comment related to the value assessment

The commenter stated that in PRD2026-09, the value section focused exclusively on efficacy, summarizing 84 trials across 14 countries and comparing A20262 Insecticide's pest-control performance with existing products. The commenter also stated that the PRD2026-09 document

does not provide an explicit assessment of spiropidion's health, safety, environmental, social, or economic benefits, as described in s. 2(1)(c) of the PCPA.

Health Canada response:

Health Canada has considered the comment regarding the value assessment and the focus on efficacy in PRD2026-09. As noted on page 1 of the proposed decision document, the *Pest Control Products Act* defines value as 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.

Health Canada's value approach is outlined in the published Guidance Document, *Value Assessment of Pest Control Products*. The value assessment for spiropidion took into account for example, the following information for health, safety and environmental benefits and social and economic impact:

A20262 Insecticide is for use in a wide range of crops, including many important fruit and vegetable crops. The economic value of some of these crops in Canada, according to Statistics Canada, include vegetable sales of $1.4 billion, fruit sales of $1.2 billion, and greenhouse vegetable and fruit sales of $2 billion in 2021.

The pests listed on the A20262 Insecticide label impact yield and crop value if not controlled. The listed crop groups and crops often require the use of insecticides to ensure that crops remain of value in the market, as infestation and even small blemishes make many of these crops unmarketable. In addition, the listed pests may also transmit diseases to crops. For example, mealybugs can transmit grapevine leafroll virus that can result in a 30% yield loss in grapes. Damage caused by, and presence of, many of the pests listed on the A20262 Insecticide label are not tolerated by the fresh market and can reduce the value of a crop if not controlled.

A20262 Insecticide is listed for use on five crop groups and five individual crops: Fruiting Vegetables (CG 8-09), Cucurbit Vegetables (CG 9), Leafy Vegetables (CG 4-13), Brassica Head and Stem Vegetables (CG 5-13), Pome Fruits (CG 11-09), grapes, greenhouse tomatoes, greenhouse peppers, greenhouse eggplant and greenhouse cucumber. These crop groups and crops are also being proposed for use for spiropidion in the United States of America. Additionally, the uses of A20262 Insecticide in greenhouse tomato, pepper, eggplant and cucumber have been developed under a joint PMC/IR-4 Minor Use project. Registration of A20262 Insecticide in Canada will help Canadian growers remain competitive and ensure food security.

23. Comment related to the resistance-management rotation claim and cumulative exposure assumption

The commenter stated that the value assessment in PRD2026-09 does not provide evidence for the claim that rotational use of spiropidion with spirotetramat provides a resistance-management benefit, especially since both actives share the same mode of action.

Health Canada response:

Health Canada has considered the comment regarding the claim that rotational use of spiropidion with spirotetramat provides a resistance-management benefit. Health Canada's approach to resistance management labelling is outlined in the document Regulatory Directive DIR2013-04*,* *Pesticide Resistance Management Labelling Based on Target Site/Mode of Action*. This document outlines a standard resistance management statement for inclusion on product labels.

In general, a new mode of action is considered to be a benefit to resistance management of other, older registered modes of action by providing an alternative mode of action for rotation to reduce selection for resistance. The standard resistance management label statement, as outlined in DIR2013-04 is to rotate with a different mode of action group (i.e., not another Group 23 insecticide). The label for A20262 will have the following standard statement for resistance management:

> "**Resistance Management Recommendation**:
>
> For resistance management, A20262 Insecticide contains a Group 23 insecticide. Any insect population may contain individuals naturally resistant to A20262 Insecticide and other Group 23 insecticides. The resistant individuals may dominate the insect population if this group of insecticides are used repeatedly in the same fields. Other resistance mechanisms that are not linked to site of action but are specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance-management strategies should be followed.
>
> **To delay insecticide resistance:**
>
> Where possible, rotate the use of A20262 Insecticide or other Group 23 insecticides with different groups that control the same pests in a field.
>
> Use tank mixtures with insecticides from a different group that is effective on the target pest when such use is permitted.
>
> Insecticide use should be based on an integrated pest management program that includes scouting and record keeping, and considers cultural, biological and other chemical control practices.
>
> Monitor treated pest populations for resistance development.
>
> Contact your local extension specialist or certified crop advisors for any additional pesticide resistance-management and/or IPM recommendations for the specific site and pest problems in your area."

The value assessment of the potential contribution of spiropidion to resistance management of labelled pests was discussed in PRD2026-09. The labelled pests, aphids, whitefly, and twospotted spider mites are common pests, and as a result, many products with a wide variety of active ingredients, including one other group 23 insecticide, spirotetramat, are registered for control of these pests on the listed crops. For mealybugs in grapes, registered active ingredients

are spirotetramat, potassium salts of fatty acids, canola oil, malathion and clothianidin. Spiropidion is a new active ingredient for use against these pests and may contribute to resistance management by providing a new alternative which can be used in rotation with existing products. As Group 23 insecticides are not known to have cross-resistance with other insecticide groups, there is a potential benefit with using spiropidion in rotation with other registered products with different modes of action to reduce the overall risk of resistance development.

Other information

Inspection of Confidential Test Data

The relevant confidential test data on which the decision is based (as referenced in PRD2026-09 *Spiropidion, A20262 Insecticide)* are available for public inspection, upon application, in the Pesticides Regulatory Directorate's Reading Room. For more information, please contact the Pesticides Information Service.

Notice of Objection

Any person may file a notice of objection,[10] which must be based on scientific grounds, regarding this registration decision on Spiropidion, A20262 Insecticide 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 wouldn't 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.

Proportional Effort

Active ingredients registered in Canada are categorized based on criteria in Health Canada's Policy on Proportional Effort. The categorization is used to inform Health Canada's allocation of resources related to pesticide reviews in alignment with the required level of regulatory effort. Spiropidion is categorized as higher proportional effort based on the environmental criteria. Information on the risk assessment conclusions that resulted in the categorization is included in the proposed regulatory decision PRD2026-09. The proportional effort categorization will be used to inform the scope and level of effort needed for future reviews.

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

Continuous Oversight

Health Canada's policy on continuous oversight of pesticides and the associated information note describe the process by which the Health Canada monitors published scientific literature for active ingredients registered in Canada, and the criteria used to determine which active ingredients will be monitored when a final regulatory decision is made. The criteria in the information note have been met, therefore, scientific literature and regulatory information will be monitored as part of continuous oversight for this active ingredient. Information found through continuous oversight will allow the Health Canada to keep pace with evolving science, and to identify emerging risks and take timely regulatory action as necessary.

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.[11]

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.[12] 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.[13]

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.[14]

Assessments estimate potential health risks to defined populations[15] 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. Also considered are the anticipated durations (short-, intermediate- or long-term) and routes of exposure (oral, inhalation, or skin contact). In

11 Information Note – Determining Study Acceptability for use in Pesticide Risk Assessments.
12 PRD Guidance Document, A Framework for Risk Assessment and Risk Management of Pest Control Products.
13 Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks - August 1, 2000.
14 Science Policy Note: The Application of Uncertainty Factors and the *Pest Control Products Act* Factor in the Human Health Risk Assessment of Pesticides.
15 Consideration of Sex and Gender in Pesticide Risk Assessment.

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.