Re-evaluation Note REV2016-14

Special Review Decision: Fluazifop-P-butyl

(publié aussi en français)

30 September 2016

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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ISSN: 1925-0630 (print)
1925-0649 (online)

Catalogue number: H113-5/2016-14E (print version)
H113-5/2016-14E-PDF (PDF version)

Special Review Decision

Pursuant to subsection 17(2) of the *Pest Control Products Act*, the Pest Management Regulatory Agency (PMRA) initiated a special review of pest control products containing fluazifop-P-butyl based on a decision taken by Norway in 2001. The PMRA evaluated the aspects of concern that prompted the special review in accordance with the subsection 18(4) of the *Pest Control Products Act*. The proposed special review decision was published for consultation in the Re-evaluation Note REV2015-09, *Special Review of Fluazifop-P-butyl: Proposed Decision for Consultation* and it outlines the Agency's proposed decision and the reasons for it.

Comments received during the consultation process were taken into consideration in making this special review decision and they did not result in changes to the proposed continued acceptability of pest control products containing fluazifop-P-butyl as described in REV2015-09. Appendix I summarizes the comments received during the consultation period and provides the PMRA's response to these comments. Following publication of REV2015-09, the PMRA has updated the human health risk assessment of fluazifop-P-butyl and additional label statements are now required (Appendix II). The PMRA, under the authority of the *Pest Control Products Act*, is confirming the current registration of technical grade active ingredient products containing fluazifop-P-butyl in Canada with the additional label statements outlined in Appendix II.

Regulatory Directive DIR2014-01, *Approach to Special Reviews*, presents the details of the PMRA's special review approach.

To comply with this decision, the required mitigation measures must be implemented on all products labels sold by registrants no later than 24 months after the publication date of this document. Registrants of the products containing fluazifop-P-butyl will be informed of the specific requirements affecting their product registration(s) and of the regulatory options available to them.

Other Information

Any person may file a notice of objection[1] regarding this decision on fluazifop-P-butyl within 60 days from the date of publication of this special review decision. 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 Health Canada's website, Request a Reconsideration of Decision, or contact the PMRA's Pest Management Information Service.

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

Appendix I Comments and Responses

The PMRA received comments from stakeholders in response to Re-evaluation Note REV2015-09, *Special Review of Fluazifop-P-butyl: Proposed Decision for Consultation*. The PMRA consolidated and summarized the comments related to this special review and provides responses below.

1.1 Comment on the requirement for an extra margin of safety

Based on the available information regarding potential health concerns from a pre- and post-natal exposure perspective and the completeness of the toxicology database, the commenter questioned the selection of a 1-fold *Pest Control Products Act* factor and whether it would provide an appropriate margin of safety for PMRA's human health risk assessment

PMRA Response

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects unless it is determined on the basis of reliable scientific data that a different margin of safety would be appropriate. This factor takes into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, as well as potential pre- and post-natal toxicity.

As summarized in REV2015-09, with respect to the completeness of the database, the fluazifop-P-butyl developmental and reproductive database contains the full complement of required studies including developmental toxicity studies in rats and rabbits, as well, a reproductive toxicity study in rats.

With respect to sensitivity of the young, REV2015-09 considered evidence of developmental delay in the database including delayed ossification, increased incidences of hydronephrosis and decreased body weight gain during lactation. These effects were considered by the PMRA to be of low concern because they are not malformations and, therefore, the *Pest Control Products Act* factor was reduced to 1-fold. Since publication of REV2015-09, the PMRA completed the review of additional developmental studies that were recently submitted as part of a new use application, resulting in a reconsideration of the full toxicology database (Canada, 2016). Evidence of malformations including diaphragmatic hernia, microphthalmia and lens abnormalities were observed in developmental and reproductive toxicity studies, which represented serious effects and were observed in the presence and absence of maternal toxicity in different studies in the rat.

Based on the reconsidered database, the PMRA has selected for acute dietary and occupational human health risk assessment a NOAEL of 7.1 mg/kg bw/day for developmental toxicity from the rat reproductive toxicity study. The selected endpoint is the lowest NOAEL for malformations in the database. The *Pest Control Products Act* factor has been retained at 3-fold when this developmental NOAEL is used for risk assessment (Canada, 2016). For chronic dietary exposure, a NOAEL of 0.51 mg/kg bw/day from a 2-year chronic toxicity study

continues to be the most appropriate endpoint for risk assessment (consistent with REV2015-09), and the *Pest Control Products Act* factor was reduced to 1-fold for this scenario (Canada, 2016). Selection of this chronic endpoint is protective of all developmental effects observed in the database, including malformations, as it provides a margin of 1420 to the NOAEL for malformations established in the three generation reproductive toxicity study in rats, which is the lowest NOAEL for malformations in the database. It also provides a margin of 400 to the NOAEL in the rat developmental toxicity study, and is therefore considered protective.

As part of the special review, the PMRA has re-assessed the human health risk assessment described in REV2015-09 to reflect the updated toxicology endpoints. This assessment takes into account all potential human health exposure scenarios (workers, non-workers, food and drinking water) and the updated toxicity information for fluazifop-P-butyl. For certain large field crops, additional label directions are required to ensure use of closed cab application equipment when more than 33 kg of active ingredient are handled in a single day and to limit the total amount handled per day to 50 kg (See Appendix II for label revisions).

1.2 Comment on the PMRA's review of aspects of concern

PMRA acknowledges evidence of reproductive and developmental (teratogenic) effects. However, in contrast to Norway's conclusion, the PMRA considers that risks to workers are not a concern because of precautionary statements required on the label of products containing fluazifop-P-butyl. REV2015-09 does not explain how a label statement for personal protective equipment is considered adequate protection for Canadian workers, when Norway concluded that risks to workers (and potential risks to consumers) were unacceptable, and banned fluazifop-P-butyl. REV2015-09 also does not discuss risks of exposure to the general population or other workers (including vulnerable individuals) from residues when protective clothing is removed, transported and laundered, or from drift at the time of application.

PMRA Response

The PMRA follows a risk-based scientific approach in determining the risk to human health from pesticides. This approach takes into consideration both the estimated level of exposure based on the directions for use on the Canadian label as well as the toxicity of the pesticide.

The PMRA has assessed the complete human health exposure scenario including risk to workers and non-workers as well as risk from food and drinking water. The risk assessment takes into account all potential exposure scenarios and the updated toxicity information for fluazifop-P-butyl.

The PMRA occupational risk assessment takes into account information from the fluazifop-P-butyl label including the listed personal protective equipment, application rates and directions for use. The health risk assessment concluded that exposure and risk to workers mixing/loading and applying fluazifop-P-butyl, as well as re-entering treated sites following application, was not of concern when label directions are followed, as the level of exposure is well below the amount that caused adverse effects in animal studies.

To further reduce exposure, additional label statements will be required to ensure use of enclosed-cab application equipment when more than 33 kg of active ingredient are used in a single day and to limit the total amount handled per day to 50 kg (See Appendix II for label revisions).

There are no residential uses of fluazifop-P-butyl and any exposure from drift to residential areas, or from handling or laundering contaminated clothing, is expected to be significantly less than occupational mixer/loaded/applicator exposure and therefore also not of concern.

The PMRA dietary risk assessment has considered total exposure to fluazifop-P-butyl from both domestically produced and imported foods, as well as from drinking water, and concluded that exposure is not of concern based on the current label directions for use and levels of fluazifop-P-butyl in imported commodities.

Therefore, based on the risk assessment, human health exposure to workers and non-workers, as well as exposure from food and drinking water, is not of concern when used according to the label.

Appendix II: Label Amendments

The following label statements must be added to the product label (Venture L Herbicide, Registration Number. 21209):

DO NOT handle more than 50 kg active ingredient/day (400 L Venture L of product).

A closed cab tractor is required when applying more than 33 kg active ingredient/day (264 L of Venture L product).

References

Published Information

PMRA Number	Reference
2530509	Rotterdam Convention. 2001. Interim Secretariat for the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade, PIC Circular XIII - June 2001
2149292	Canada. 2011. Pest Management Regulatory Agency. Proposed Re-evaluation Decision PRVD2011-11
2192467	Canada. 2012. Pest Management Regulatory Agency. Re-evaluation Decision RVD2012-05
2530508	United States. 2005. Environmental Protection Agency. Fluazifop-P-butyl: Revised HED Chapter of the Tolerance Reassessment Eligibility Document (TRED)
2530504	United States. 2008. Environmental Protection Agency. Fluazifop-P-butyl. Amended Human Health Risk Assessment to Support Use on Dry Beans, Peanuts and Post-bloom Application to Soybeans.
2530507	United States. 2014. Environmental Protection Agency. Fluazifop-P-butyl. Human Health Risk Assessment Scoping Document in Support of Registration Review
2530505	EFSA. 2012. Conclusion on the peer review of the pesticide risk assessment of the active substance fluazifop-P (evaluated variant fluazifop-P-butyl), EFSA Journal 2012;10(11): 2945
2556817	Canada, 2016. Evaluation Report for Category B, Subcategory 5.0 Application. New Maximum residue limit for previously assessed technical grade active ingredient. Fluazifop-P-butyl

Unpublished Information

PMRA Number	Reference
2530506	Norway. Form For Notification of Final Regulatory Action to Ban or Severely Restrict a Chemical *Fluazifop-P-butyl.* Norwegian Agricultural Inspection Service