

Evaluation Report for Category B, Subcategory 5.0 Application

Application Number: 2020-1238
Application: New Maximum Residue Limits (MRLs) for previously assessed Technical Grade Active Ingredient (TGAI)
Product: Sedaxane Technical
Registration Number: 30435
Active ingredient (a.i.): Sedaxane
PMRA Document Number : 3235662

Background

Sedaxane is a seed-treatment succinyl dehydrogenase inhibitor (SDHI) fungicide first registered in Canada in 2012. The detailed review of sedaxane can be found in Evaluation Report ERC2012-01, *Sedaxane* and in the Proposed Registration Decision PRD2015-03, *Sedaxane*.

Purpose of Application

The purpose of this application was to establish maximum residue limits (MRLs) for residues of sedaxane in/on imported cotton, peanut and rice. In addition, mode of action studies were submitted to conduct a cancer reassessment.

Health Assessments

Residue data from field trials conducted in the United States were submitted to support the importation of treated cotton, peanut, and rice into Canada. Sedaxane was applied to these crops at the registered foreign application rate, and harvested according to label directions. In addition, processing studies in treated cotton, peanuts, and rice were reviewed to determine the potential for concentration of residues of sedaxane into processed commodities.

Maximum Residue Limits

The recommendation for MRLs for sedaxane was based upon the submitted field trial data, and the guidance provided in the [OECD MRL Calculator](#). MRLs to cover residues of sedaxane in/on crops and processed commodities are proposed as shown in Table 1. Residues in processed commodities not listed in Table 1 are covered under the proposed MRLs for the raw agricultural commodities (RACs).

TABLE 1. Summary of Field Trial and Processing Data Used to Support Maximum Residue Limit(s) (MRLs)					
Commodity	Application Method/	Residues (ppm)	Experimental	Currently	Recommended

	Total Application Rate (g ai/100 kg seed)	LAFT	HAFT	Processing Factor	Established MRL (ppm)	MRL (ppm)
Cotton	Seed treatment / 15-19	<0.01	<0.01	No concentration of residues in refined oil	None	0.01
Peanut	Seed treatment / 15-18	<0.01	<0.01	No concentration of residues in peanut butter or in peanut oil	None	0.01
Rice	Seed Treatment / 18-20	<0.01	<0.01	No concentration of residues in rice bran or in polished rice	None	0.01

MRLs as proposed in Table 1 are recommended to cover residues of sedaxane. Residues in these crop commodities and their processed fractions at the proposed MRLs will not pose risks of concern to any segment of the population, including infants, children, adults and seniors.

Cancer Reassessment

The toxicology profile of this active ingredient can be found in PRD2015-03, *Sedaxane*. The Cancer Assessment in PRD2015-03 concluded that sedaxane exhibits oncogenic potential. There were treatment-related thyroid follicular cell tumours and hepatocellular tumours in male rats, uterine adenocarcinomas in female rats and hepatocellular tumours in male mice. No mode of action (MOA) information was provided for any of the tumour types in the original assessment. An adjusted unit risk value cancer potency factor (q_1^*) of 3.81×10^{-3} (mg/kg bw/day)⁻¹ for uterine adenocarcinomas in female rats was used for the cancer risk assessment as it was the highest value of the four tumour types.

Studies for the mode of action for the four types of treatment-related tumours were submitted. The MOA for uterine tumours in female rats based on an initiating key event of decreased body weight was not supported, as there were considerable data gaps and uncertainties in the studies provided. The proposed MOA for thyroid tumours in male rats was constitutive androstane receptor (CAR)/pregnane-X-receptor (PXR) induction. The key events were addressed with minor data gaps. Therefore the MOA for thyroid tumours in male rats was plausible and supported. The MOA for liver tumours in the mouse and rat was based of the CAR/PXR nuclear receptor pathway activation, leading to eventual liver tumour development. Studies to support the key events of this MOA were provided and considered adequate. The proposed MOA was considered plausible and supported a threshold approach to cancer risk assessment.

A review of the dietary combined chronic/carcinogenicity in rats revealed that the maximum tolerated dose (MTD) was exceeded in male and female rats at the highest dose tested, based on excessive decreases in body weight in males and females. As a result, the uterine tumours in

females and thyroid and liver tumours in male rats were not considered relevant for risk assessment, and the q₁* for uterine tumours in female rats is no longer applicable to the risk assessment.

Therefore, a threshold approach to cancer risk assessment is considered appropriate.

An occupational exposure assessment was not required for this application.

Chemistry, Value and Environmental Assessments

Chemistry, value and environmental assessments were not required for this application.

Conclusion

The Pest Management Regulatory Agency has completed an assessment of the information provided, and has found the information sufficient to establish MRLs for residues of sedaxane in/on imported cotton, peanuts and rice. In addition, a threshold approach to cancer risk assessment was considered appropriate for sedaxane.

References

PMRA Document Number	Reference
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