



Re-Assessment of the Plant Protection Product PROMAN – with the Active Ingredient Metobromuron [Edition 2]

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Authors' contributions

This work was carried out in collaboration among all authors. The opinion has been assessed and approved by the Panel on Plant Protection Products of VKM. All authors read and approved the final manuscript.

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Grey Literature

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ABSTRACT

Proman is a broad spectrum selective herbicide for potatoes grown outdoors, containing the active substance metobromuron. VKM's Panel on Plant Protection Products has previously discussed

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questions concerning Proman raised by The Norwegian Food Safety Authority, and stated its opinion in a report of 21. January 2015 (<http://www.vkm.no/dav/3c64afe035.pdf>).

Following this report, The Norwegian Food Safety Authority turned down the application to register Proman as a plant protection product in Norway. The applicant filed a complaint on this decision, and the VKM Panel has been asked to reassess its previous opinion in light of the information given by the applicant in the complaint.

The VKM Panel has discussed the arguments put forward in the complaint. The arguments did not change the Panel's main conclusions in the original assessment. Some changes in the wording of the conclusions were however done, in order to put more emphasis on areas of uncertainty.

These are the standing conclusions of VKM's Panel on Plant Protection Products:

On the relevance of the carcinogenic effects observed in the rat carcinogenicity study; fibrosarcomas in females and pheochromocytomas and Leydig cell tumours in males:

It is the opinion of VKM's Panel for Plant Protection Products that the relevance of the observed incidences of mammary gland tumours and Leydig cell tumours in the rat carcinogenicity study is strengthened by the fact that the increases in tumours associated with exposure to metobromuron are observed in hormone responsive tissues. The panel concludes that the carcinogenic effects observed in the rat carcinogenicity study could be relevant for tumour induction in humans.

Higher incidences of still dumbbell-shaped centres of thoracic vertebrae and nonossification of the 13th rib observed in the rat developmental toxicity study and whether these are considered to be malformations:

VKM's Panel on Plant Protection Products has discussed the classification of the different types of incomplete ossifications and concluded that incomplete ossification of sternbrae and non-ossification of the 13th rib in rats should by itself be considered to be variations, and not adverse developmental effects. On the other hand, the Panel agrees with ECHA that the "thoracic vertebral centres still dumbbell-shaped" should be considered as malformations, due to limited data and understanding of the mechanism underlying the observed slow reversal of these anomalies. Furthermore, it is the view of the Panel that the different types of retarded ossification induced by the exposure should be considered as a whole when assessing for developmental effects.

Establishment of the NOAEL for the developmental toxicity study in rats and the reference value (ARfD):

VKM's Panel on Plant Protection Products supports the proposal of an ADI value of 0.008 mg/kg bw/day based on a NOAEL of 0.8 mg/kg bw/day from the 2-year study in mouse, and AOEL of 0.016 mg/kg bw/day based on the NOAEL of 1.6 mg/kg bw/day from the 1-year feeding study in dog. The panel suggests an alternative ARfD value of 0.03 mg/kg bw based on a LOAEL of 10 mg/kg bw /day for the observations of incomplete ossification in the rat developmental study.

The anti-androgenic potential of metobromuron:

The rat carcinogenicity study indicates that metobromuron may interact with the endocrine system. The data from the Hershberger in vivo rat study, the in vitro studies, as well as the comparison with demonstrated effects and mechanisms for flutamide and linuron is suggestive of an anti-androgenic effect. Thus, it is the opinion of the VKM Panel on Plant Protection Products that an anti-androgenic effect of metobromuron cannot be excluded.

Keywords: VKM; assessment; Norwegian Scientific Committee for Food Safety; PROMAN.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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