



Department of Pesticide Regulation



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MEMORANDUM

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DATE: May 3, 2016

SUBJECT: REVIEW OF THE PROPOSED FIELD TRIAL FOR THE BIOPESTICIDES MON104559, MON104551, MON104550, AND MON104553: DOUBLE STRANDED RNA-BASED MITICIDES FOR THE CONTROL OF *VARROA DESTRUCTOR* IN COLONIES OF *APIS MELLIFERA*

Overview

The Human Health Assessment Branch (HHAB) reviewed the proposal for field trials of the experimental biopesticides MON104549, MON104551, MON104550, and MON104553 by Rohan Liu on behalf of the Monsanto Company (Chesterfield, MO). The goal of the field trials is to ascertain their individual efficacies as miticides against *Varroa destructor* mites. *V. destructor* can cause varroosis in honeybees (*Apis mellifera*). It does this by attaching to honeybees and weakening them by feeding on their hemolymph. In doing so, *V. destructor* can also serve as a vector for pathogenic RNA viruses (e.g. the deformed wing virus). A *V. destructor* infestation can cause the death of an infected honeybee colony. As such, *V. destructor* infestations have the potential to significantly impact agricultural industries that are dependent on the health of honeybees. The proposed field trials will be conducted in Placer and Imperial Counties between May 1 and October 31, 2016 with the possibility of commercial, university, and/or government cooperation. The trials will involve the treatment of up to 80 hives per treatment arm (2 trials with 40 hives per trial; 480 hives total) with monitoring by Monsanto's representatives. The complete testing protocol will include treatments with experimental dsRNA miticides MON104549, MON104551, MON104550, and MON104553, a "commercial standard" treatment, and a blank control. Treatments will be applied as sucrose-based feeding solutions to honeybee hives at a rate of 3.2 g/hive. Treated hives will not be moved, used for pollination, or for the harvest of any hive products, including honey.



HHAB Summary

The active ingredients in MON104549, MON104551, MON104550, and MON104553 are double-stranded ribonucleic acid (dsRNA) biopolymers designed to target and interfere with messenger RNA transcripts presumably necessary for *V. destructor* to cause varroosis and facilitate colony death. No specific dsRNA sequence or target information were provided for review, so general aspects of RNA interference technologies were used to bridge knowledge gaps in order to complete the HHAB review required for this memo. The function of dsRNA-mitocides is based on their specific sequences of nucleotides, conformations and chemical modifications. As such, their introductions into the environment represent the potential for novel human health hazards and exposure risks. Presently, there are insufficient data to evaluate the human health risk from the use of dsRNA as mitocides. Human dietary exposure to MON104549, MON104551, MON104550 and MON104553 following their experimental use in the proposed trials is expected to be minimal as no hive products will be harvested for commercial use. Occupational exposure risks to apiculturists and other on-site research personnel are more difficult to assess since detailed information on specific dsRNA sequences and targets, product formulation additives that may affect dsRNA stability, apiculture practices, formulation handling, and personal protective equipment requirements were not provided to HHAB for review.

Background of dsRNA-Based Biopesticides

In 2014, US Environmental Protection Agency (USEPA) charged a scientific advisory panel (SAP) with the problem formulation phase for human health and ecological risk assessments of biopesticides based on technologies with a mode of action dependent on RNA interference (RNAi). The SAP panel and the USEPA agreed that the primary route of exposure to dsRNAs would be from oral ingestion. The SAP further concluded that any ingested dsRNAs would likely be broken down to single nucleotides by the digestive process and that the absorption of physiologically relevant levels of dsRNA with any potential for “off-target” interference would be unlikely. It should be noted that there was not a consensus amongst experts on the lack of risks posed by dsRNA to human health as evidenced by the review submitted as a comment by Heinemann, et al. The SAP acknowledged that more and better data were needed to address critical uncertainties that will come up when comprehensive human health risk assessments are conducted. Issues concerning dermal and inhalation exposures were not covered by this SAP.

Svetlana Koshlukova
May 3, 2016
Page 3

References

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Liu, R. Pesticide Research Authorization (DPR-REG-027a) for MON104549, MON104551, and MON 104553. 06 April 2016

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Heinemann JA1, Agapito-Tenfen SZ, Carman JA. A comparative evaluation of the regulation of GM crops or products containing dsRNA and suggested improvements to risk assessments. *Environ Int.* 2013 May; 55:43-55.