



National Honey Bee Advisory Board

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Effects on non target organisms not understood

The National Honey Bee Advisory Board and beekeeping industry has greatly benefited from independent scientific input. Beekeepers and farmers hope, and yet have concerns about RNA technology, as described in the recent New York Times article, “*Genetic weapon against insects raises hope and fear in farming,*” (1-27-14). We agree with the findings of the EPA Scientific Advisory Panel (SAP) concerning RNAi technology that “not all aspects of the fate of dsRNA in the environment and potential effects on nontarget organisms are necessarily understood.” EPA asked this panel of scientists to provide them with their expertise concerning this new pesticide technology. The scientists stated in their White Paper of Sept. 30, 2013, “Better understanding of the mechanisms influencing uptake, particularly if they can be extrapolated to other organisms, would reduce uncertainty in exposure assumptions and help to focus risk assessments on the most appropriate organisms.”

The SAP includes scientists working in entomological fields to human studies from acclaimed universities across the United States.

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The FIFRA SAP concluded in their report, “The new categories of dsRNA products, however, will present additional hazard and risk assessment challenges due to their unique modes of action and other toxicological endpoints that cannot be measured using the traditional testing paradigm.”

The EPA welcomed public comment concerning the White Paper and the National Honey Bee Advisory Board was pleased to provide input. Honey bees, as the Scientific Advisory Panel stated, could be greatly impacted by the RNAi pesticide technology. They expressed their concerns that “not all aspects of the fate of dsRNA in the environment and potential effects on nontarget organisms are necessarily understood.” They advised that it is unclear how RNAi technology can translocate throughout the environment, but possible transmission may include dust from degraded plant material, soil, plant pollen taken to bee hives, and even mammals consuming the plants and depositing the digested food far from the initial treatment area. The nontarget exposure opportunities present many concerns. For honey bees specifically, “The factors influencing the possibility of exposure by this pathway (e.g. longevity of dsRNA once consumed, concentration resulting within the herbivorous insect) are not known.”

The National Honey Bee Advisory Board supports the findings of these noted researchers. We agree with EPA’s Scientific Advisory Panel, that “the unique nature of dsRNA and RNAi raise several issues of concern with respect to the typical data set submitted for nontarget effects:”

“1) The potential influence of latent effects on results of nontarget testing.” “Some studies, such as nontarget insect studies, are carried out for sufficient time to observe effects on reproduction, and latent effects would more likely be observed.”

“2) The appropriate life stage for testing.” “However, given the range of possible unexpected effects, it is conceivable that an effect could occur in the field that would not be observed in the lab.”

“3) The possibility of chronic effects.” “Suppression of genes without overt signs of toxicity may be considered insignificant following a single exposure; however, long-term exposure and continuous or repeated knockdown could result in chronic effects.”

The SAP’s White Paper sums up their concerns succinctly, exclaiming EPA “has not, to date, assessed the hazards or risks of dsRNA applied directly to the environment as components of end-use products intended for pest control under Section 3 of FIFRA.” The “screening level assessments currently used for traditional chemical pesticides may not be applicable due to the unique modes of action of dsRNA active ingredients.”

The FIFRA SAP and the National Honey Bee Advisory Board (NHBAB) acknowledge EPA’s goal is to “ensure that unreasonable effects do not occur to nontarget populations.” The SAP White Paper references sixty-four RNA/DNA/RNAi/gene studies which made it clear this new

technology “will present additional hazard and risk assessment challenges due to their unique modes of action and other toxicological endpoints that cannot be measured using the traditional testing paradigm.” The NHBAB agrees with the EPA’s Scientific Advisory Panel and the review of research by Lundgren and Duan (2013) observing “that the current tiered hazard assessment approach used by the Agency, is inappropriate to address the following unique hazards potentially posed by dsRNA products:

- Off target gene silencing
- Silencing the target gene in unintended organisms
- Immune stimulation
- Saturation of the RNAi machinery in cells.”

The NHBAB agrees with the FIFRA SAP “that accurate, standardized methods for measuring and assessing the aforementioned hazards will be necessary to conduct robust nontarget species risk assessments on dsRNA products.”

However, we express our concern that EPA granted an experimental use permit in 2013 for a 20,000 acre field study of RNAi corn to study the *Snf7* gene directed at the corn root worm before “standardized methods for measuring and assessing the aforementioned hazards” were developed. The FIFRA Scientific Advisory Panel White Paper appears to have been ignored when EPA approved a field test, without applicable testing protocols for this technology. EPA’s goal is to “ensure that unreasonable effects do not occur to nontarget populations.” This experimental use permit puts nontarget organisms at risk. The Scientific Advisory Panel White Paper defined some of those risks:

“. . .double stranded RNA (dsRNA) was 10 times or more potent in its effect on gene expression.”

“Why some miRNAs trigger transitivity and some do not is not well understood at this time.”

“. . . the silencing of a gene targeted in one cell can lead to the silencing of a second gene in a distinct cell type.”

“Although the details of the RNAi pathways and their outcomes may differ among organisms, what is clear is that the influence of small RNAs on growth, development, defense and even transient heritability of traits is substantial.”

“It is unclear at this point whether a dsRNA PIP also would be incidentally present in root exudates, guttation droplets, or nectar, providing additional on-field sources of nontarget exposure.”

While RNAi technology may be a useful tool, “uncertainties clearly exist with respect to a complete understanding of all current and future applications of this technology.” “. . . The

current testing paradigm for nontarget species characterizations, which emphasized limited dose testing and use of mortality as an endpoint, likely will not be adequate to assess adverse effects resulting from off-target gene silencing, silencing of the target gene in unintended organisms, immune stimulation, and saturation of the RNAi machinery in cells.”

This RNAi technology is thought to be a possible control of Varroa, an insidious pest of honey bees. However, as the Varroa is basically a virus-filled-syringe in the guise of an arachnid, using RNAi upon Varroa or in bees to get at Varroa will subject honey bees to unknown gene silencing. As the FIFRA SAP committee succinctly stated RNAI “uncertainties clearly exist with respect to a complete understanding of all current and future applications of this technology.” RNAi technology must be researched fully to protect bees, to protect human health, and to protect the environment.

The National Honey Bee Advisory Board supports the findings of the EPA Scientific Advisory Panel, and expresses concern the EPA would ignore the recommendations of their own panel of scientific experts. The experimental use permit for RNAi technology on 20,000 acres clearly violates EPA’s mandate to “ensure that unreasonable effects do not occur to nontarget populations.”