Key Issues for RNAi Pesticides Identified in the OECD Working Document - *Considerations for the Environmental Risk Assessment of the Application of Sprayed or Externally Applied ds-RNA-Based Pesticides* Series On Pesticides No. 104 ENV/JM/MONO(2020)26

iPlanta Webinars: RNAi Based Pesticides

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The Organization for Economic Co-operation and Development (OECD) is an intergovernmental organization in which representatives of 37 industrialized countries in North and South America, Europe and the Asia and Pacific region, as well as the European Commission, meet to co-ordinate and harmonize policies, discuss issues of mutual concern, and work together to respond to international problems.

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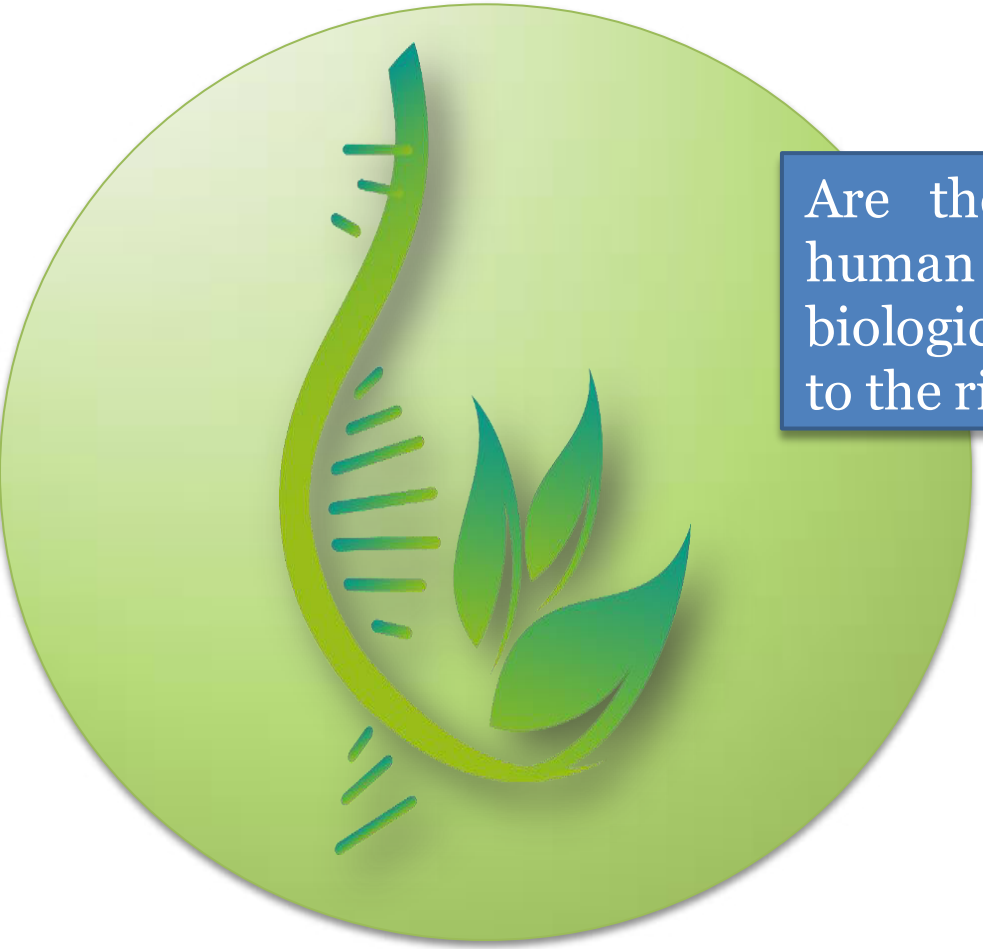
Risk Assessment for Externally Applied dsRNA-Based Pesticides



Are the current approaches to environmental and human health risk assessment of conventional and biological pesticides and or GM technologies applicable to the risk assessment of dsRNA-based pesticides?

Are additional data needed to be developed for dsRNA-based pesticides?

2015: OECD Ad Hoc Expert Group on RNAi-based pesticides (EG RNAi)

Background - dsRNA Pesticides Working Document

- OECD effort to develop a broad set of recommendations relating to environmental risk assessment considerations for exogenously-applied double-stranded RNA (dsRNA)-based products.

- Developed by the OECD Ad Hoc Expert Group on RNAi-based pesticides, a sub-group of the OECD Working Group on Pesticides, that helps member countries to harmonise the methods and approaches used to assess exogenously-applied dsRNA-based products.

- Does not address issues related to the risk assessment of genetically-modified crop plants, which incorporate the machinery to synthesize RNAi molecules specifically directed against a pest species feeding on the crop.

OECD Conference on Externally Applied dsRNA-Based Pesticides - Supported Working Document

- OECD, **10-12 April 2019**
- **Focus** on regulatory needs and aspects of risk assessment for dsRNA-based pesticides sprayed on crops and ingested by pests
- **Background document:** Environmental and Ecological Risk from the Topical Application of dsRNA-Based Pesticides Draft

OECD Conference on Externally Applied dsRNA Based Pesticides – Supported Working Document

Dedicated webpage

Programme, speakers, abstracts, presentation files and other related material from the conference

http://www.oecd.org//chemicalsafety/pesticides-biocides/conference-on-rnai-based-pesticides.htm

Proceedings of the conference including participants' discussions have been published online at the Frontiers Research Topic RNAi Based Pesticides https://www.frontiersin.org/research-topics/11066/rnai-based-pesticides#articles.

dsRNA Pesticides Working Document Key Conclusions

- dsRNA molecules developed for topical application to crops for pest control will be assessed by relevant government agencies using a similar set of considerations to those applied to chemical and biological pesticides.

- Pesticide use pattern and application method (e.g., greenhouse, outdoor, bait, sprayable) require consideration.

- Additional issues need to be considered such as the potential to silence genes with significant sequence identity with the target gene in the intended pest and the fate of RNA in the environment, treated crop or animal.

dsRNA Pesticides Working Document Key Conclusions

- Exposure is expected to be limited because of low application rates in comparison to many conventional chemical pesticides and the anticipated rapid degradation and dissipation of dsRNA in the environment.

- The potential for exposure of non-target organisms as well as responsiveness to environmental RNAi are the first parameters to consider in the risk assessment of external dsRNA applications.

dsRNA Pesticides Working Document Key Conclusions

- Sequence information alone should not and cannot be used as a stand-alone predictor of off-target effects.

- Bioinformatics can inform the selection and prioritization of non-target species for toxicity and effects testing.

- Bioinformatics can be augmented by an empirical approach – to introduce dsRNA (that is perfectly complementary to the target gene in a target organism) to a range of other organisms, starting with close relatives and then moving outwards, to see how more phylogenetically-distant organisms respond.

dsRNA Pesticides Working Document Key Conclusions

- Available evidence suggests that dsRNAs have a long record of safe consumption by humans and other vertebrates.

- Nucleic acids are naturally-occurring components of plant- and animal-derived foods and feed and are routinely consumed by humans and animals.

dsRNA Pesticides Working Document Key Conclusions

- Significant physiological and biochemical barriers exist in humans and other vertebrates to limit the uptake and distribution of exogenous RNAs.

- These barriers include nucleases in saliva, denaturation and depurination in the acid pH of the stomach, nucleases in the digestive tract, pancreatic secretions of bile salts and degradative enzymes, cellular membrane barriers, the polysaccharide coating of the intestinal epithelium, and intracellular degradation in endosomes and lysosomes.

dsRNA Pesticides Working Document Key Conclusions

- The barriers to dsRNA uptake identified in mammals applies to other vertebrates.

- Responsiveness across invertebrate taxa to environmental dsRNA cannot currently be predicted.

dsRNA Pesticides Working Document Key Conclusions

- In some cases, specific product formulations may be designed to overcome barriers to uptake for the target organism.

- Special attention should be paid to how barriers to uptake are proposed to be overcome for the target organism and the impact this could have on environmental persistence of dsRNA as well as to barriers to and uptake of the dsRNA by non-target organisms.

- Information and/or studies on the impact to uptake and environmental persistence that the formulation presents are important to characterize exposure to the dsRNA.

dsRNA Pesticides Working Document Key Conclusions

- Where specific product formulations impact barriers to and uptake of the dsRNA, product-specific formulation toxicology testing on organisms or test surrogates would help better characterize the potential for hazard.

- The necessity of such testing depends on the legal requirements in the different OECD member countries as well as the characterization of the product.

dsRNA Pesticides Working Document Key Conclusions

- Protocols for addressing risk with dsRNA-based products require some revisions compared to how they are carried out for conventional pesticides because dsRNA-based pesticides often take longer to display efficacy. Any evaluation needs to account for this time lag by extending the study observation period.

- For organisms that have been demonstrated to be responsive to environmental RNA, consideration of life cycle studies (growth, development and reproduction) and studies on other non-lethal effects could be considered.

- Additionally, any evaluation of a dsRNA-based pesticide should include monitoring for degradation of the dsRNA over time.

Future activities

- Working paper Human Health Risks from the Application of sprayed or externally applied dsRNA-Based Pesticides expected to start in 2021.