April 26, 2023

William R. Reeves, Ph.D.
Regulatory Scientific Affairs
Bayer U.S. LLC Crop Science Division
700 Chesterfield Parkway West
Chesterfield, MO 63017

Re: Proposed Amendments to Rules Governing Health Risk Limits for Groundwater, Minnesota Rules, Chapter 4717, Part 7500, Part 7850, and Part 7860; Revisor's ID Number RD4587, OAH Docket No. 5-9000-38941

Dear William Reeves:

In an April 26, 2023 post-hearing comment to MDH, Bayer Crop Sciences reiterates that the Minnesota Department of Health (MDH) relied on an immunotoxicity study (Badgujar 2013[1]) that is missing key information that would allow it to inform a quantitative risk assessment for imidacloprid. They promote the use of a different registrant-sponsored study (Kennel 2010[2]) as the appropriate immunotoxicity study for imidacloprid. Bayer argues that the Kennel 2010 study did not show any immune response in animals after imidacloprid exposure. MDH respectfully disagrees with Bayer's conclusions.

MDH selected a peer-reviewed immunotoxicity study (Badgujar 2013) that reported reduced delayed-type hypersensitivity in female mice. There was a strong dose-response alongside the correct controls. MDH was able to conduct an appropriate risk analysis based on this study. MDH also analyzed the data in Kennel 2010, supplied by Bayer Crop Sciences. Kennel focused on a different arm of the immune system (IgM titers in the serum after antigen challenge) in a different species (rat) that produced data with high standard deviations. Despite this high variability, MDH believes that there is, in fact, evidence of a reduction in IgM after imidacloprid treatment in treated animals, but because of the study limitations, statistical significance was not achieved.

MDH thanks Bayer Crop Sciences for sharing Kennel 2010 with MDH. Although Kennel 2010 was conducted under Good Laboratory Practices (GLP), it was not available to the public or public agencies prior to MDH's proposed imidacloprid guidance. MDH agrees with Bayer Crop Sciences that GLP regulations and peer review are not equivalent. Bayer writes in their comments that "GLP regulations enable thorough reviews not only of the data but also the qualifications of the people who conducted the study, the full chemical identity of the test

material, calibration records for all laboratory equipment, and rigorous documentation of study conditions". Much of GLP is directives for excellent record keeping. Peer review is scrutiny of the data and the conclusions of a study, once the study is completed. MDH's 2008 SONAR[3] requires peer-reviewed studies as the basis for developing guidance as spelled out in Minnesota Statute section 144.0751[4]. There is not a requirement for GLP.

There is also no requirement for other states to approve a chemical in order for MDH to calculate health-based water guidance values. The citation and link provided by Bayer that claims the Wisconsin DNR disproving of their imidacloprid value is dubious, at best. When you search the article, the word imidacloprid is not found. Perhaps there was some action, but it is not clear from documentation shown. Additionally, it is not actually the Wisconsin DNR, it is the Wisconsin Natural Resources Board, a policy group. There isn't a single toxicologist or risk assessor on the board, rather it is led by people with administrative and business backgrounds. Some of the members have a science background that is appropriate for natural resources management such as deer culls. Health-based values are derived using toxicological and risk assessment principles, very specific knowledge that is difficult to critique for those who are not trained. In addition, California's Office of Environmental Health Hazard Assessment (OEHHA), is still reviewing imidacloprid. There is no mention of imidacloprid in the citation or link supplied by Bayer Crop Sciences.

Lastly, MDH would like to emphasize that HRLs are developed to protect the health of all Minnesotans. MDH conducted a thorough analysis of the imidacloprid database including documents produced by EPA. MDH maintains that the purpose of MDH and EPA are different. While MDH produces HRLs that are health-based, EPA reviews pesticides through a registration lens. In EPA's website, "Why We Review Pesticides" EPA states that "EPA…reviews pesticides to ensure they can be used safely, without unreasonable risks to human health and the environment[5]." *Unreasonable risk*. This is the purpose: to register pesticides for use. It is not specifically to protect human health, as MDH risk assessments are. It follows that the "reasonable certainty of no harm" is a different standard than protecting all Minnesotans, including those most sensitive or most highly exposed. Every risk assessment at MDH begins with the aim of protecting every Minnesotan. That is a different approach than a 'reasonable certainty.

In conclusion, MDH is confident in the selection of Badgujar 2013 as the critical study for imidacloprid. This selection provides protection of imidacloprid exposure to the most highly sensitive or most highly exposed Minnesotans.

Sincerely,

/s/Sarah Johnson

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References

[1]Badgujar, PC et al. (2013). Immunotoxic Effects of Imidacloprid Following 28 Days of Oral Exposure in BALB/c mice. Environmental Toxicology and Pharmacology. 35(3):408-418.

[2]Kennel. (2010). Unpublished. Imidacloprid 28-day Immunotoxicity Study in the Male Wistar Rat by Dietary Administration. Bayer Crop Science, Study No. Sa 09406; MRID 48298701

[3]Minnesota Department of Health Statement of Need and Reasonableness (SONAR). (2008). https://www.leg.mn.gov/archive/sonar/SONAR-03733.pdf#page=2

[4]Minnesota Statutes. (2022). Health Standards. 144.0751. https://www.revisor.mn.gov/statutes/cite/144.0751

[5]EPA. (Accessed 2023). https://www.epa.gov/pesticide-reevaluation/why-we-review-pesticides