UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM

Date: August 14, 2019

SUBJECT: **Saflufenacil**: Tier I (Scoping) Review of Human Incidents and Epidemiology

PC Code: 118203
Decision No.: 553780
Petition No.: NA
Risk Assessment Type: NA
TXR No.: NA
MRID No.: NA

DP Barcode: D453677
Registration No.: NA
Regulatory Action: NA
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Summary and Conclusions

Both the Incident Data System (IDS) and NIOSH Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides were reviewed for saflufenacil incidents. EPA reviewed the AHS publications listed on the AHS publication website. One published AHS study investigating the potential association between maternal exposure to saflufenacil and spontaneous preterm births was identified. The authors reported no evidence of a significant positive association between maternal exposure to saflufenacil during month 8 of pregnancy and spontaneous preterm births. The Agency will continue to monitor the incident and epidemiology information and, if a concern is triggered, additional analysis will be included in the risk assessment.

Detailed Review

I. ACTION REQUESTED

This review is intended to fulfill our requirement to docket summaries of incident data that were reported to the Agency, as well as to ensure human incident data and the Agricultural Health Study (AHS) are part of the problem formulation phase of registration review for saflufenacil. HED's RAB I has requested that TEB conduct a Tier I Scoping review summary of recent incident data from IDS and SENSOR as per standard protocol under the Agency's Registration Review Program. One component of the Agency's Registration Review Program is consideration of human incident data. In conjunction with a human health risk assessment based on other data sources, such human incident data can assist the Agency in better defining and characterizing the risk of pesticides/pesticide products.

It is important to remember that reports of adverse health effects allegedly due to a specific pesticide exposure (*i.e.*, an "incident") are largely self-reported and therefore, generally speaking, neither exposure to a pesticide or reported symptom (or the connection between the two) is validated or otherwise confirmed. Typically, causation cannot be determined based on incident data, and such data should be interpreted with caution. Nonetheless, incident information can be an important source of feedback to the Agency: incidents of severe outcome, or a suggested pattern or trend among less severe incidents, can signal the Agency to further investigate a particular saflufenacil or product. Epidemiology studies can also be useful and relate the risk of disease, *e.g.*, cancer, and exposure to an agent such as a pesticide product in the general population or specific sub-groups like pesticide applicators.

II. BACKGROUND

Saflufenacil is registered as a selective herbicide, developed for the control of broadleaf weeds by pre-plant and pre-emergence applications to cereal small grains, corn, chickpeas, cotton, edible beans, edible peas, lentils, lupine, sorghum, soybeans and sunflowers; post-emergence applications to fruit tree orchards, nut tree orchards, and vineyards; and fallow croplands and non-agricultural areas, including pine plantations, rights-of-way, and bare ground. Additionally, saflufenacil is used as a dessicant and/or defoliant on sunflowers.

For this evaluation, both the OPP Incident Data System (IDS) and the Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health (CDC/NIOSH) Sentinel Event Notification System for Occupational Risk-Pesticides (SENSOR) databases were consulted for pesticide incident data on the active ingredient saflufenacil (pc code: 118203). The purpose of the database search is to identify potential patterns in the frequency and severity of the health effects attributed to saflufenacil exposure. In addition, saflufenacil is included in the AHS and information from the AHS is provided in this report.

III. RESULTS/DISCUSSION

a. IDS (Incident Data System)

OPP's IDS includes reports of alleged human health incidents from various sources, including mandatory Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) Section 6(a)(2) reports from registrants, other federal and state health and environmental agencies, and individual consumers. Since 1992, OPP has compiled these reports in IDS. IDS contains reports from across the U.S. and most incidents have all relevant product information recorded. Reports submitted to the IDS represent anecdotal reports or allegations only, unless otherwise stated in the report.

IDS records incidents in one of two modules: Main IDS and Aggregate IDS:

- Main IDS generally contains incidents resulting in higher severity outcomes and provides more detail with regard to case specifics.[1] This system stores incident data for death, major and moderate incidents, and it includes information about the location, date and nature of the incident. Main IDS incidents involving only one pesticide are considered to provide more certain information about the potential effects of exposure from the pesticide.

- Aggregate IDS contains incidents resulting in less severe human incidents (minor, unknown, or no effects outcomes). These are reported by registrants only as counts in what are aggregate summaries.

For the Main IDS for the five years from January 1, 2014 to July 18, 2019, there were four incidents reported that involved the active ingredient saflufenacil. Of these four incidents, two incidents involved the single active ingredient saflufenacil (only). These two incidents were classified as moderate severity. The other three saflufenacil incidents reported involved multiple active ingredients. These incidents were also classified as moderate severity.
For Aggregate IDS for the five years from January 1, 2014 to July 18, 2019, there were 12 incidents reported involving saflufenacil. These incidents were classified as minor severity.

b. SENSOR-Pesticides

The Center for Disease Control's National Institute for Occupational Safety and Health (CDC/NIOSH) manages a pesticide surveillance program and database entitled the Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides.[2] All cases must report at least two adverse health effects. Evidence for each case is evaluated for its causal relationship between exposure and illness based on the NIOSH case classification index.[3] Using standardized protocol and case definitions, SENSOR-Pesticides state coordinators, operating out of the state's department of health, receive state pesticide incident reports from local sources, then follow up with case sources to get incident scenario to obtain medical records and verify

[1] Occasionally, low severity incidents are self-reported by the consumer directly to Main IDS.
[2] SENSOR-Pesticides webpage: http://www.cdc.gov/niosh/topics/pesticides/overview.html.
[3] https://www.cdc.gov/niosh/topics/pesticides/pdfs/casedef.pdf

exposure scenario information.[4] This database includes pesticide illness case reports from multiple states from 1998-2015.[5]

A query of SENSOR-Pesticides from 2010-2015 identified two cases involving saflufenacil. These cases were low in severity. One case was an agricultural worker experienced an ocular exposure to glyphosate and saflufenacil while handling the pesticides. This case was treated in the hospital for corneal abrasion and eye pain/irritation.

The second case was non-occupational; this case was drifted on by a neighboring farmer who was making an application despite high winds; the farmer did not see the case. The case experienced altered taste, upset stomach, and upper respiratory irritation. The case did not seek medical treatment. The farmer who made the application was cited for the following violations: application not consistent with the label, weather conditions favored drift, and not identifying sensitive areas on adjacent properties.

c. Agricultural Health Study (AHS)

The AHS is a federally-funded study that evaluates associations between pesticide exposures and cancer and other health outcomes and represents a collaborative effort between the US National Cancer Institute (NCI), National Institute of Environmental Health Sciences (NIEHS), CDC's National Institute of Occupational Safety and Health (NIOSH), and the US EPA. The AHS participant cohort includes more than 89,000 licensed commercial and private pesticide applicators and their spouses from Iowa and North Carolina. Enrollment occurred from 1993 – 1997, and data collection is ongoing. The AHS maintains a list of publications resulting from AHS studies[6]. If there are AHS findings in the published literature relevant to a pesticide undergoing registration review, the Agency will ensure these findings are considered in the problem formulation/scoping phase of the registration review process and, if appropriate, fully reviewed in the risk assessment phase of the process. Saflufenacil is included in the AHS.

In creating this Scoping Memorandum, EPA reviewed the AHS publications listed on the AHS publication website. As of July 2019, one AHS publication, Shaw et al. (2018) investigated the association betweenmaternal exposure to saflufenacil and spontaneous preterm births. We summarize this study below:[7]

> Shaw et al. (2018) conducted a case-control study to evaluate the association between maternal pesticide exposures including saflufenacil and spontaneous preterm births. The study population consisted of pregnant women who lived in San Joaquin Valley, California, and who gave birth between 1998 – 2011 in California. Cases included pregnant women (gestational ages 20 – 41 weeks), who had a singleton birth, and the birth weight was

[4] https://www.cdc.gov/niosh/topics/pesticides/pdfs/pest-sevindexv6.pdf
[5] Currently participating states are: California, Florida, Illinois, Louisiana, Michigan, Nebraska, New Mexico, North Carolina, Oregon, Texas and Washington. The participating states for a given year vary depending on state and federal funding for pesticide surveillance.
[6] Agricultural Health Study: Publications https://aghealth.nih.gov/news/publications.html
[7] In evaluating and reporting on the AHS studies, for odds ratios (ORs), risk ratios (RRs), and hazard ratios (HRs), the confidence interval (CI) acted as a proxy for significance testing, with CIs that do not contain the null value (OR / RR / HR = 1.00) considered significant.

between 500 – 5000 grams. Controls were frequency matched to the cases (3:1 ratio) and selected at random. Multivariable analyses were conducted to determine odds ratios and 95% CIs, adjusting for maternal age (years), race/ethnicity (non-Hispanic white, U.S.-born Hispanic, foreign-born Hispanic, other), education (less than high school, high school, more than high school), parity (1 or ≥2), prenatal care initiated by fifth month (yes vs no), and payer source for care (Medi-Cal, private, or other). For saflufenacil, the authors reported no evidence of a significant positive association between maternal exposure during month 8 of pregnancy and spontaneous preterm births (delivery during gestational weeks 32 – 36) (OR: 1.11, 95% CI: 0.72 – 1.70; Cases (exp/not exp): 25/22,483; Controls (exp/not exp): 205/197,256).

IV. CONCLUSION

Both the Incident Data System (IDS) and NIOSH Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides were reviewed for saflufenacil incidents. EPA reviewed the AHS publications listed on the AHS publication website. One published AHS study investigating the potential association between maternal exposure to saflufenacil and spontaneous preterm births was identified. The authors reported no evidence of a significant positive association between maternal exposure to saflufenacil during month 8 of pregnancy and spontaneous preterm births. The Agency will continue to monitor the incident and epidemiology information and, if a concern is triggered, additional analysis will be included in the risk assessment.