



## Sulfoxaflor and bees

Sulfoxaflor has recently come onto the market in China (Shao et al. 2013) and the USA (Dow Agro Sciences 2013; USEPA 2013), was reviewed by the EFSA in 2014 (EFSA 2014) and approved in the European Union in 2015.

Sulfoxaflor, an active substance of the family of sulfoximines, is a fourth-generation neonicotinoid based on its target receptors and binding sites, that exhibits a high insecticidal activity against a broad range of sap-feeding insects (Babcock et al. 2011, Cutler et al. 2013).

### Mode of action

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It acts on nAChRs, with a pharmacological profile similar to that of imidacloprid (Cutler et al. 2013). For this reason, sulfoxaflor may be considered as a neonicotinoid. However, the nature of the interactions with nAChRs differs between sulfoxaflor and the other neonicotinoids (Sparks et al. 2013). The action of sulfoxaflor and other sulfoximines, similar to that of imidacloprid, involves receptor desensitization, receptor selectivity, a differential action at low and high doses and, probably, receptor desensitization after a prolonged exposure (Oliveira et al. 2011, Watson et al. 2011, Cutler et al. 2013). This needs to be taken into account when considering possibilities for insecticide rotation in order to manage resistance toward neonicotinoids based on modification of the target site (Cutler et al. 2013).

Considering the pharmacology (binding sites at nACh receptors) of sulfoxaflor, insects belonging to the hemiptera order show the highest sensitivity. However, toxicity to non-hemiptera insects can be also expected at higher application rates (Cutler et al. 2013).

### Metabolism

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Compared to imidacloprid, acetamiprid, dinotefuran, thiamethoxam, and clothianidin for which the extents of metabolism are respectively 85.1, 95.5, 55.1, 46.8, and 45.6 % after 24 h, sulfoxaflor presents an almost undetectable metabolism (Sparks et al. 2012).

### Toxicity to bees

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Table in Annex 1 summarizes the LD<sub>50</sub> values included in the European dossier. The EFSA identified a high risk to bees and several data gaps were also pointed out, namely the effects on non-Apis bees or the risk of field uses when applying risk mitigation measures. Among others, potential adverse effects on bee brood could not be excluded together with toxicity following foliar application (EFSA 2014).

The USEPA determines that the acute oral toxicity (LD<sub>50</sub>) to be 0.052 µg of sulfoxaflor per bee and that the acute contact toxicity (LD<sub>50</sub>) to be 0.13 µg of active substance per bee. In parallel, the EFSA determines an oral LD<sub>50</sub> of 0.146 µg of sulfoxaflor per bee and a contact LD<sub>50</sub> of 0.379 µg of sulfoxaflor per bee. When sulfoxaflor is included into commercial formulations the oral LD<sub>50</sub> of

two products is 0.065 or 0.075 µg of sulfoxaflor per bee, respectively. This may indicate possible synergistic effects with some of the coformulants. Sulfoxaflor has proved to potentiate the herbicidal effects of pyridine carboxylic acid compounds (Satchivi and Schmitzer 2011), however it is not clear to what extent the insecticidal effect of sulfoxaflor is also enhanced by this combination.

The EFSA concluded a high toxicity to bees even considering the numerous limitations in the studies included into the dossier and a number of sub-lethal effects do not taken into account in the framework of risk assessment (Bee Life 2013 Annex II).

## **Residues using Good Agricultural Practices (GAPs)**

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Residues in fruits and other matrices following an application of sulfoxaflor under GAP are used for the estimation of MRLs. The FAO has summarised the residues in different crops collected from studies carried out worldwide. Highest residue (HR) values in citrus fruits was 0.44 mg kg<sup>-1</sup>, in pomme fruits 0.26 mg kg<sup>-1</sup>, in stone fruits 1.2 mg kg<sup>-1</sup>, in grapes 1.6 mg kg<sup>-1</sup>, and strawberries 0.21 mg kg<sup>-1</sup>. On fruiting vegetables and cucurbits the HR value is 0.27 mg kg<sup>-1</sup>. Leafy vegetables HR value is 2.9 mg kg<sup>-1</sup> sulfoxaflor. (FAO 2011)

## **Analytical sensibility**

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Currently there is the possibility to detect sulfoxaflor at a level of detection (LOD) of ranging from 0.2 to 0.6 µg kg<sup>-1</sup>, and LOQs from 0.7 to 2.0 µg kg<sup>-1</sup> (Xu et al. 2012). These are more than 100 times lower than the MRLs proposed by the European Commission in (MRL 0.05 mg kg<sup>-1</sup>).

## Annexe 1. Results of acute toxicity tests (laboratory)

| Test species | Test substance          | Test system / Duration                  | Endpoint   | Reference                              |
|--------------|-------------------------|---|--|--|
| Honey bee    | Sulfoxaflor (technical) | Lab. acute oral, 48h                    | LD <sub>50</sub> oral = 0.146 µg a.s./bee  | Bergfield, A. 2007a<br>IIA 8.7.1 /01   |
| Honey bee    | Sulfoxaflor (technical) | Lab. acute contact, 72h                 | LD <sub>50</sub> contact = 0.379 µg a.s./bee   | Bergfield, A. 2007b<br>IIA 8.7.2/01    |
| Honey bee    | GF-2626                 | Lab. acute oral, 48h                    | LD <sub>50</sub> oral = 0.539 µg GF-2626/bee<br>LD <sub>50</sub> oral = 0.065 µg Sulfoxaflor/bee   | Vinall, S. 2010a<br>IIIA1 10.4.2.1 /01 |
| Honey bee    | GF-2626                 | Lab. acute contact, 48h                 | LD <sub>50</sub> contact = 2.356 µg GF-2626/bee<br>LD <sub>50</sub> contact = 0.283 µg Sulfoxaflor/bee   | Vinall, S. 2010b<br>IIIA1 10.4.2.2 /01 |
| Honey bee    | GF-2372                 | Lab. acute oral, 48h                    | LD <sub>50</sub> oral = 0.153 µg GF-2372/bee<br>LD <sub>50</sub> oral = 0.075 µg Sulfoxaflor/bee   | Vinall, S. 2010<br>IIIA2 10.4.2.1 /01  |
| Honey bee    | GF-2372                 | Lab. acute contact, 48h                 | LD <sub>50</sub> contact = 0.224 µg Sulfoxaflor/bee  | Vinall, S. 2009<br>IIIA2 10.4.2.2 /01  |
| Bumble bee   | GF-2032                 | Lab. acute oral and contact, 72h        | LD <sub>50</sub> oral = 0.027 µg XDE/208/bee<br>LD <sub>50</sub> contact = 7.554 µg Sulfoxaflor/bee  | Vinall, S. 2009<br>IIIA1 10.4.2.1 /02  |
| Honey bee    | X11719474               | Lab. acute oral, 48h                    | LD <sub>50</sub> oral >100 µg./bee*  | Vinall, S. 2009<br>IIA 8.7.1 /02       |
| Honey bee    | X11519540               | Lab. acute oral, 48h                    | LD <sub>50</sub> oral >91.2 µg./bee*   | Vinall, S. 2010a<br>IIA 8.7.1 /03      |
| Honey bee    | X11579457               | Lab. acute oral, 48h                    | LD <sub>50</sub> oral = 45.7 µg./bee   | Vinall, S. 2010b<br>IIA 8.7.1 /04      |
| Honey bee    | X11721061               | Lab. acute oral, 48h                    | LD <sub>50</sub> oral >103.5 µg./bee*  | Vinall, S. 2010c<br>IIA 8.7.1 /05      |
| Honey bee    | GF-2032                 | Laboratory foliar residue toxicity test | No significant adverse effects to bees when exposed to foliar residues of GF-2032 treated 3, 6 or 24 hours previously at 200 g Sulfoxaflor/ha.         | Lee, B. 2008<br>IIIA1 10.4.3/01        |
| Honey bee    | GF-2372                 | Laboratory foliar residue toxicity test | No significant adverse effects to bees when exposed to foliar residues of GF-2372 treated 3, 6 or 24 hours previously at 100 and 200 g Sulfoxaflor/ha. | Bergfield, A. 2009<br>IIIA2 10.4.3/01  |

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