Bayer CropScience

Document Title

Tier 2 Summary of Further Information of the Active Substance for

Flupyradifurone
(BYI 02960)

Data Requirements

Regulation (EC) No 1107/2009

Regulatory Directive 2003-01/Canada/PMRA
OPPTS guidelines/US/EPA

Annex IIA
Section 1, Point 3
Document M

According to OECD format guidance for industry data submissions on plant protection products and their active substances

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Author(s)

Rauen, H.W.; van Waetermeulen, X.; Nauen, R.; Thielert, W., Haas, M.

Bayer CropScience

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OWNERSHIP STATEMENT

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IIA 3 Further Information on the active substance

IIA 3.1 Function e.g. fungicide

Flupyradifurone (BYI 02960) is an insecticide.

IIA 3.2 Effects on harmful organisms e.g. contact action

IIA 3.2.1 Nature of the effects on harmful organisms

Sivanto is a systemic insecticide for foliar spray use and intended mainly for controlling sucking pest such as aphids, hoppers and whiteflies. Sivanto can be applied curative and preventive but is most effective when applied at threshold level. It acts by contact or after ingestion, and has systemic properties. Flupyradifurone interacts with insect nicotinic acethylcholine receptors, a class of neurotransmitter-gated cation channels which are involved in excitatory neurotransmission, a target also known for neonicotinoid insecticides (CNIs).
Sivanto can control important CNI resistant pest populations such as Bemisia tabaci, Phorodon humuli and Empoasca sp. Spectrum extension to mealybugs, leafminer, weevils and (flea) beetles is under examination.

IIA 3.2.2 Translocation in plants

Flupyradifurone is taken up into leaves/stems after spray application and via roots, if applied to soil or alternative substrates. After uptake, flupyradifurone is translocated acropetally in the xylem, in direction of the transpiration stream and is translaminarily distributed into adjacent plant cells. There is virtually no relevant translocation of flupyradifurone in basipetal direction within the phloem.

IIA 3.3 Fields of use e.g. forestry

Flupyradifurone is intended to be used as an insecticide in agriculture on a range of crops such as pome and stone fruits, grape, fruiting and leafy vegetables (indoor and outdoor), and hops but also on ornamentals. It is also considered, to use the product as seed treatment on soybeans.

IIA 3.4 Harmful organisms controlled and crops / products protected or treated

Please refer to the Documents D-1 and D-3 for details on pets- and crop-combinations. In general, the harmful organisms controlled comprise aphids, hoppers and white flies.

IIA 3.4.1 Details of existing and intended uses

Please refer to the Documents D-1 and D-3.
Document D-1: M-421862-01-1
Document D-3: M-427337-01-1

Some examples are listed below:

Target Crops	Target Pests
Pome fruits (apple, pear)	Aphids, (psyllids)
Grapes	Leaf hoppers
Raspberry	Aphids
Strawberry	Aphids
Hop	Aphids
Ornamentals	Aphids, Whiteflies
Flower bulbs	Aphids
Tobacco	Aphids
Fruiting vegetables (tomatoes, eggplant, peppers)	Aphids, Whiteflies
Cucurbits (cucumbers, zucchini)	Aphids, Whiteflies
Watermelon	Aphids, Whiteflies
Lettuce	aphids
Peas (Field and Garden)	Aphids, seed beetles
Potatoes	aphids

IIA 3.4.2 Details of harmful organisms against which protection is afforded

Flupyradifurone contained in formulated product Sivanto™ SL 200 provides excellent control of a broad number of sucking pests such as aphids, whiteflies and hoppers, and is under evaluation in a broad range of other pests (i.e. lafminer, mealybugs, psyllids and mired bugs). These pests have generally a high reproduction potential and a lack of control of them can lead to considerable losses of crop value. Their short life cycle can contribute to the development of resistance to insecticides, as for example whiteflies and aphids.

Sap-sucking pests are responsible for three types of damage: direct damage (feeding on sap, which can weaken the plants; cause deformations and reduce the yield); indirect damage (accumulation of honeydew produced by the insects, which serves as a substrate for the growth of black sooty mold on leaves and fruit), transmission of viruses.

For indoor fruiting vegetables, whiteflies, and among them *Bemisia tabaci*, are major pests especially for Southern Europe countries. They have developed resistance to insecticides from different chemical classes. Sivanto with 112,5 g Flupyradifurone /ha provides a very high level of control of *B. tabaci* (including resistant populations) offering at least 3 weeks of residual efficacy after the last application. These applications will also be able to control aphid’s populations which could infest the crop at the same time.

On apple *Dysaphis plantaginea* can cause direct feeding damage leaves (leaf curling) and on fruits. These aphid species can be effectively controlled by Sivanto from 40-60 g a.i/ha/m c.h (*D. plantaginea and A. pomi*).

Psylla piri on pear is the major sucking pest on pear; high populations of adults and nymphs feeding on new shoots can have a direct effect on the growth of trees; they also produce a vast amount of honeydew, damaging the leaves and the fruits. In the majority of situations, one application of Sivanto at 67,5 g a.i/ha/ m canopy height , targeted against the first generation is sufficient to provide a good level of control of the pear sucker populations for at least 3 weeks.

Flupyradifurone containing Sivanto is recommended to be used at 125 g a.i/ha against *Nasonovia ribisnigri* in lettuce, and 150 g a.i/ha against *Phorodon humuli* in hops.
In lettuce, 11 field trials carried out in different climatic zones support that Flupyradifurone foliar applied at 125 g a.i/ha provides a more stable control of aphids in lettuce than a lower application rate, 75 g a.i/ha. The efficacy provided by Sivanto at 125 g a.i/ha, as assessed in 25 field trials, implemented in field or protected conditions, turns out to be at same or better level than various reference products (neonicotinoids, feeding blocker, inhibitor of lipid biosynthesis). Sivanto SL 200 is plant safe to a wide range of lettuce varieties and types.
Results from 18 trials carried out in hops in Czech Republic, Germany, Poland, demonstrate that Sivanto at 150 g a.i/ha delivers a high control of *Phorodon humuli*, similar or better than Flonicamid. Lower application rates (100 and 120 g a.i/ha) provide lower initial control than 150 g a.i/ha, and lower control of aphids in cones. Sivanto SL 200 is plant safe to all the hop varieties tested in the efficacy trials.

IIA 3.4.3 Effects achieved e.g. sprout suppression

After ingestion of Flupyrydifurone, the active substance interacts with insect nicotinic acetylcholine receptors, a class of neurotransmitter-gated cation channels which are involved in excitatory neurotransmission. Flupyradifurone acts as an agonist, i.e., and induces a depolarising ion current and causing excitation of the nerve cell which can be measured by electrophysiological methods. The lasting effect of the product results in a disorder of the nervous system of the insect and subsequently death of the treated insects.

IIA 3.5 Mode of action

IIA 3.5.1 Mode of action, mechanism(s) and pathway(s) involved

Flupyradifurone interacts with insect nicotinic acetylcholine receptors, a class of neurotransmitter-gated cation channels which are involved in excitatory neurotransmission, a target also known for neonicotinoid insecticides. Like the naturally occurring neurotransmitter acetylcholine, flupyradifurone acts as an agonist, i.e., the binding of flupyradifurone to the receptor protein induces a depolarising ion current, causing excitation of the nerve cell which can be measured by electro-physiological methods. In contrast to acetylcholine, flupyradifurone cannot be inactivated by the acetylcholinesterase. The lasting effect of the product results in a disorder of the insect nervous system and subsequent death.

IIA 3.5.2 Details of active metabolites and degradation products

Not relevant. The metabolism of BYI 02960 (Flupyradifurone) does not yield any metabolite with biological activity.

IIA 3.5.3 Formation of active metabolites and degradation products

Please refer to AII 3.5.2

IIA 3.6 Possible development of resistance or cross-resistance

Report:	**KIIA 3.6/01, Nauen, R. 2012**
Title:	Possible development of resistance or cross-resistance Flupyradifurone (BYI 2960)
Report No & Document No	M-428792-01-1
Guidelines:	Regulation (EC) No 1107/2009, Regulatory Directive 2003-01/Canada/PMRA OPPTS guidelines/US/EPA
GLP	**n.a.**

The report provides resistance management information regarding key invertebrate pests targeted by flupyradifurone (BYI 2960), especially covering aphids and whiteflies.

Flupyradifurone interacts with insect nicotinic acetylcholine receptors (nAChRs), a class of neurotransmitter-gated cation channels which are involved in excitatory neurotransmission, a target also known for neonicotinoid insecticides, nicotine, sulfoxaflor and spinosyns. However flupyradifurone is a butenolide insecticide and chemically different from neonicotinoids, but it binds as an agonist to the same receptor site. Therefore flupyradifurone can be assigned to IRAC (Insecticide Resistance Action Committee) mode of action Group 4, which includes all insecticidal agonists of the nAChR.

Flupyradifurone specifically controls a number of sucking pests in vegetables and other crops. Baseline studies were conducted with different aphid species including *Nasonovia ribis-nigri* (lettuce aphid), *Phorodon humuli* (damson-hop aphid) and *Myzus persicae* (green peach aphid). Furthermore baseline data for the most important whitefly species, *Bemisia tabaci* (sweet-potato whitefly) and *Trialeurodes vaporariorum* (greehouse whitefly) are presented.

Flupyradifurone does show good activity against all species mentioned above and baseline susceptibility is usually in the low mg/L range. No resistance to field-recommended rates was detected in any of the sucking pests investigated. Slight cross-resistance was observed in neonicotinoid-resistant *B. tabaci* strains, but the low resistance ratios calculated would not affect field efficacy of flupyradifurone. Very recently *M. persicae* was shown to have locally developed resistance to neonicotinoid insecticide sprays in peaches in southern France, northern Spain and northern Italy, but no reports are known from any secondary host species yet. All *M. persicae* strains collected from secondary hosts were completely susceptible to flupyradifurone with little variation in response between populations.

General resistance management guidelines for flupyradifurone are given and are based on recommendations given by the Insecticide Resistance Action Committee for mode of action Group 4 insecticides.

IIA 3.7 A material safety data sheet for the active substance

Report:	**KIIA 3.7/01, Anonymus; YYYY**
Title:	Bayer CropScience Safety Data Sheet for Flupyradifurone techn. (Spec. No.: 102000025488)
Report No & Document No	M-424153-01-1 M-424153-01-1
Guidelines:	**Regulation (EC) No. 1907/2006**
GLP	**n.a.**

IIA 3.8 Procedures for destruction and decontamination

IIA 3.8.1 Pyrolytic behaviour under controlled conditions at 800 °C

Report:	**KIIA 3.8.1/01, Nuesslein, F., 2012**
Title:	Flupyradifurone, Incineration as a safe means of disposal and pyrolytic behaviour under controlled conditions
Report No & Document No	M-422993-01-1 M-422993-01-1
Guidelines:	EU Directive 1107/EEC Annex II, Point 3.8.1
GLP	**n.a.**

Incineration of Flupyradifurone is recommended as the way of safe disposal by controlled incineration at an approved chemical waste facility. Since the halogen content of Flupyradifurone (13 % w/w halogens) is higher than 1%, the standard process are: temperature higher than 1100°C, residence time higher than 2 seconds, oxygen excess higher than 6% (according to European Directive EC/94/67; Article 6).
Moreover, hydrofluoric acid exhaust gases should not exceed 1 mg.m-3 as an average on 24 hours (according to European Directive EC/94/67; Article 7).

IIA 3.8.2 Detailed instructions for safe disposal

Leftover quantities of the product have to be burned in an authorised special waste incineration plant. Comply with local legislation.
As containers are combustible (HDPE): Burn these emptied containers in an authorised special waste incineration plant. Comply with local legislation.
Otherwise, they should be rendered unusable after cleaning, e.g. by puncturing, and disposed of in accordance with local regulations.
Note that empty containers can be land filled after cleaning, when in compliance with local regulations.

IIA 3.8.3 Methods other than controlled incineration for disposal

No methods other than controlled incineration are recommended for disposal.

IIA 3.9 Procedures for decontamination of water in case of an accident

In case of contamination of water with Flupyradifurone accidental spillage, always try to isolate and protect the contaminated area. Water should be used as sparingly as possible to clean up the area. Where feasible, the contaminated water should be pumped out and isolated for further appropriate treatment. The collected contaminated water must be burnt in a commercial incinerator. If incineration facilities are inadequate, obtain advice from the manufacturer on other decontamination methods. In any case, the contaminated water must not come in contact with surface water. If accidentally contaminated water is used to produce drinking water, ensure with the competent authorities that the level of contamination does not reach the parametric value for drinking water.

IIA 3.10 Other/special studies

No other / special studies have been conducted.