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INDOXACARB

Volume 3 – B.3 (AS)

Rapporteur Member State: France
Co-Rapporteur Member State: Spain

Version History

When	What
2016-12	Initial RAR

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B.3. <u>DATA ON APPLICATION</u>

B.3.1. USE OF THE ACTIVE SUBSTANCE

Plant protection products containing indoxacarb (DPX-KN128) are to be used in agriculture situations under field and greenhouse conditions, as an insecticide for control of a broad spectrum of lepidopteran in a large range of crops and of some pests belonging to other orders such as homopteran pests (leafhoppers and planthoppers).

More specifically, the claimed representative uses for indoxacarb (DPX-KN128) concern the control of lepidopteran insect pests in the representative crops; lettuce, maize (grain and silage) and sweet corn and for the control of the coleopteran insect pest *Diabrotica virgifera* in maize and sweet corn.

Application is by tractor-mounted hydraulic field sprayers with ground-directed booms. For maize (grain and silage) and sweet corn the application must be made from above the crop.

B.3.2. FUNCTION

Insecticide.

B.3.3. EFFECTS ON HARMFUL ORGANISMS

Indoxacarb (=DPX-KN128) is active as a larvicide by stomach and contact routes of entry into the insect. The importance of stomach versus contact action varies with the species and the crop situation. Data from laboratory and field indicates that the product is active on all larval stages of Lepidoptera, together with some activity on some other orders. For certain species the active has ovicidal effect. Paralysis occurs within a few hours of exposure and results in cessation of movement and feeding. Final control takes 1-3 days. The metabolite IN-JT333 also shows insecticidal effects.

Study about the lack of insecticidal activity of R enantiomer (IN-KN127), Study submitted to the EU for the first time in this submission and listed under reference lists “Documents Submitted”.

The active substance indoxacarb (DPX-KN128) was discovered by DuPont in 1991 as a racemic mixture (DPX-JW062), where the S-enantiomer is the active insecticidal enantiomer (DPX-KN128) and the R-enantiomer is the non-active insecticidal enantiomer (IN-KN127). The lack of insecticidal activity of IN-KN127 was investigated in DuPont-21517.

Report: Andaloro, J.T., (2006); Insecticidal activity of technical grade DPX-KN128 and DPX-KN127
DuPont Report No.: DuPont-21517
Guidelines: None cited **Deviations:** None
Test Facility: DuPont Stine-Haskell Research Center, Newark, Delaware, USA
Test Facility Report No.: DuPont-21517
GLP: No
Certifying Authority: Not applicable.

Summary
The level of biological activity of DPX-KN128 and IN-KN127 on key Lepidopteran pests was investigated. Larval mortality and feeding damage was investigated and the following laboratory reared species were tested: diamondback moth, *Plutella xylostella*, cabbage looper, *Trichoplusia ni*, cotton bollworm, *Helicoverpa zea*, and cotton budworm, *Heliothis virescens*, beet armyworm, *Spodoptera exigua*, and fall armyworm, *Spodoptera frugiperda*. Technical DPX-KN128 and IN-KN127 were applied at 1, 5, 10 and 50 ppm.

DPX-KN128 showed high activity on all species tested. IN-K127 only showed a side effect when used at 50 ppm on diamondback moth (*Plutella xylostella*) and beet armyworm (*Spodoptera exigua*) larvae, but no

noticeable effect on cotton budworm (*Heliothis virescens*), cotton bollworm (*Helicoverpa zea*), cabbage looper (*Trichoplusia ni*) and fall armyworm (*Spodoptera frugiperda*) was observed in terms of mortality.

The level of insecticidal activity expected from IN-KN127 would be negligible.

Efficacy of KN127 and KN128 technical on 2nd instar of *Plutella xylostella* and *Trichoplusia ni* on collards in the laboratory

Treatment	Rate ppm ai	% Mortality 96 h after exposure		% Feeding damage 96 h after exposure (% reduction vs UNT)	
		P. xylostella	*T. ni*	*P. xylostella*	*T. ni*
KN127	1	8	0	50 (0)	90 (0)
	5	0	8	50 (0)	80 (0)
	10	26	0	50 (0)	80 (0)
	20	34	0	40 (20)	90 (0)
	50	26	6	30 (40)	70 (13)
KN128	1	66	100	10 (80)	10 (88)
	5	84	100	10 (80)	10 (88)
	10	100	100	0 (100)	10 (88)
	20	100	100	10 (80)	10 (88)
	50	100	100	0 (100)	10 (88)
X-77 alone (non-ionic surfactant)	500	8	0	50	100
Untreated	----	8	0	50	80

Efficacy of KN127 and KN128 technical on 2nd instar of *Helicoverpa zea* and *Heliothis virescens* on cotton in the laboratory

Treatment	Rate ppm ai	% Mortality 96 h after exposure		% Feeding damage 96 h after exposure (% reduction vs UNT)	
		H. zea	*H. virescens*	*H. zea*	*H. virescens*
KN127	1	0	0	100 (0)	100 (0)
	5	0	0	100 (0)	90 (10)
	10	0	---	100 (0)	---
	20	0	0	100 (0)	90 (10)
	50	0	0	100 (0)	80 (20)
KN128	1	8	4	60 (40)	50 (50)
	5	92	46	30 (70)	30 (70)
	10	100	---	30 (70)	---
	20	100	88	20 (80)	20 (80)
	50	100	96	10 (90)	10 (90)
X-77 alone (non-ionic surfactant)	500	0	0	100	100
Untreated	----	0	0	100	100

Efficacy of KN127 and KN128 technical on 2nd instar of *Spodoptera exigua* and *Spodoptera frugiperda* on soybeans in the laboratory

Treatment	Rate ppm ai	% Mortality 96 h after exposure		% Feeding damage 96 h after exposure (% reduction vs UNT)	
		S. exigua	*S. frugiperda*	*S. exigua*	*S. frugiperda*
KN127	1	---	4	---	70 (30)
	5	0	4	70 (22)	80 (20)
	20	0	0	70 (22)	80 (20)
	50	21	0	50 (44)	70 (30)
KN128	1	---	25	---	30 (70)
	5	54	100	20 (78)	20 (80)
	20	79	96	10 (89)	10 (90)
	50	100	100	10 (89)	10 (90)
X-77 alone (non-ionic surfactant)	500	0	0	90	100
Untreated	----	0	0	90	100

B.3.4. Field of use envisaged

Indoxacarb (DPX-KN128) is to be used in agriculture.

B.3.5. Harmful organisms controlled and crops or products protected or treated

As regards to the representatives uses (lettuce, maize, sweet corn), indoxacarb (DPX-KN128) in Indoxacarb 150 g/L EC is used for the control of the chewing insects, *Helicoverpa armigera, Spodoptera littoralis, Spodoptera exigua, Chrysodeixis chalcites, Autographa gamma,* and *Mythimna unipuncta* in lettuce*; Ostrinia nubilalis* and *Diabrotica virgifera* in maize and sweet corn.

B.3.6. Mode of action

Biochemical pathway: The mode of action is the binding of the pure active substance DPX-KN128 (indoxacarb) to the sodium channel complex leading to blockage of ion flow. Indoxacarb (DPX-KN128) belongs to the oxadiazines insecticides and is classified under IRAC group 22A, as voltage-dependent sodium channel blocker.

Physiological mechanism: Insects exposed to indoxacarb exhibit symptoms of cessation of feeding, uncoordination, paralysis, and death in 24-60 hours. These data are consistent with the conclusion that indoxacarb acts through an effect on the insect nervous system.

B.3.7. Information on the occurrence or possible of the development of resistance and appropriate management strategies

Possible occurrence of resistance: Indoxacarb (DPX-KN128) acts as “voltage-dependant sodium channel blocker” according to the IRAC International Mode of Action classification, also coded as MoA group 22. Indoxacarb is the only member of the MoA subgroup 22 A and belongs to the oxadiazine chemical class. It has to be noted that metaflumizone also belongs to MoA group 22, but to the subgroup 22 B. The pyrethroids, which also act on the neuronal sodium channel, act on a different “gate” which has the effect of stopping the sodium channel from closing. This is the opposite of the mechanism of indoxacarb (=DPX-KN128).

The Insecticide Resistance Action Committee (IRAC) continuously monitors globally for cases of resistance and according to the database, some cases of resistance have been noted in the literature.

Cases of indoxacarb resistance indicated on the IRAC database for agricultural pests – February 2016 (http://www.pesticideresistance.org/search.php)

Genus Species	Common Name(s)	Cases
Choristoneura rosaceana	oblique banded leafroller	4
Earias vittella	the spotted bollworm	5
Helicoverpa armigera	cotton bollworm	6
Heliothis virescens	tobacco budworm	2
Lobesia botrana	european grapevine moth	1
Plutella xylostella	diamond-back moth	49

Sitophilus zeamais	maize weevil, rice weevil	7
Spodoptera exigua	beet army worm, lesser army worm	38
Spodoptera litura	mediterranean climbing cutworm	34
Tuta absoluta	tomato leafminer	3

Preventive actions are proposed. Indeed, repeated and exclusive use of indoxacarb may lead to the build-up of resistant strains of insects in some crops. Some insect species are known for their propensity to develop resistance to products used repeatedly for control. Since the development of resistance cannot be predicted, this product should be used as part of the resistance management strategies established for the use area (IRM programmes). These strategies should include incorporation of cultural and biological control practices, alternation of the mode-of-action (MoA) group of insecticides on succeeding generations and targeting the most susceptible life stage.

A set of management strategies to reduce the risk of developing resistance are proposed. Modifiers applied to the use of the active substance and its products include the restriction on the maximum number of applications, minimum rate per application and primarily the alternation with different modes of action. It is considered that with these modifiers in place, the risk is reduced to a sustainable level.

Susceptibility monitoring methods for indoxacarb: Currently a wide range of bioassay and biochemical tests are employed to characterise the susceptibility of target pests to insecticides. There are currently several approved IRAC methods covering a wide range of pest species which can be found on the IRAC website and can apply to indoxacarb too. In the time period from 2002 to 2013, numerous field populations of *H. armigera, S. exigua, S. littoralis, P. xylostella, O. brumata, A. orana, C. pomonella, L. botrana, E. ambiguella*, *Tuta absoluta,* and *Meligethes aeneus* were tested in Europe for establishing their sensitivity to indoxacarb before and soon after commercial introduction (baseline monitoring). After the screening and validation of different laboratory assay methods, also a user-friendly kit (LFB) was optimized and adopted for extended semi-field sensitivity screening.

Management strategy: Indoxacarb is providing to growers a valuable resistance management option for insect pest control; however it is considered that the unrestricted use of indoxacarb would pose a significant resistance risk. It’s therefore indicated that below measures are adopted in order to reduce the potential risk connected to unrestricted use.

Indoxacarb should always be applied within spray programs involving the use of other effective insecticides with a different mode of action. Two consecutive pest generations should not be exposed to the same insecticidal MoA. Insecticide MoA alternation is the primary route to resistance avoidance.

B.3.8. References relied on

None.