REGULATION No 1107/2009

DECISION TO WITHDRAW APPROVAL OF THE ACTIVE SUBSTANCE INDOXCARB IN GB

DRAFT

Issue

This report sets out the proposed decision to withdraw approval of the active substance indoxacarb in Great Britain (GB). It explains the process for reviewing the approval and the reasons for the proposed decision. It summarises the information relevant to the decision and the grace periods that apply.

Background

Indoxacarb is an insecticide active substance used in plant protection products, which are regulated under the retained Regulation (EC) No 1107/2009 ("the Regulation"). The Regulation requires that active substances must be approved for such use. Approval is given if, in the light of current scientific and technical knowledge, the active substance satisfies the approval criteria provided for in Art. 4 of the Regulation.

Regulatory Process

Approval of the active substance indoxacarb in the European Union (EU) was non-renewed by Regulation (EU) 2021/2081 following routine EU review. The Regulation entered into force on 19 December 2021 and applies direct in Northern Ireland. Although this decision had no legal effect in GB, the approval criteria in GB are the same as in the EU. In light of new scientific and technical knowledge, HSE considered that this decision indicated that indoxacarb may no longer satisfy the criteria for approval provided for in Art. 4 of the Regulation. Therefore, HSE proposed a review of the GB approval of indoxacarb under Art. 21(1) of the Regulation and GB competent authorities agreed for HSE to carry out this function. The review was a phased review considering first human health concerns arising from the EU review. The review first considered the impact of the new toxicological reference values adopted by the EU, and considered reliable by HSE, on dietary and non-dietary risks to human health (i.e., Art 4(2)(a) and Art. 4(3)(b) of the Regulation). Ecotoxicological aspects would have been reviewed if representative uses had shown an acceptable risk for human health.

At the time of the initiation of the review, HSE considered that the authorisation holders Sharda and FMC Agro Limited to be producers of indoxacarb. HSE informed them of the initiation of the review and the reasons for it. They were given the opportunity to submit comments for consideration as part of the review. Further comments were submitted to HSE in response to the initial assessment conducted by HSE and included in the proposed conclusion published in August 2022.

HSE accepted the submission of further comments on an exceptional basis that information with greater relevance to GB situations were available, which were not previously submitted by the producers due to misinterpretation of the process. HSE agreed that the submission of further information would be acceptable in this case according to the provision under Art. 21(5) of the Regulation. The comments received are summarised in Annex 1 of this report.

Following the submission of comments and additional supporting studies, HSE undertook an independent, objective, and focused assessment of indoxacarb considering current scientific and technical knowledge. This included a review of the aforementioned scientific evidence that supported the EU non-renewal decision and the comments received from the indoxacarb producers. HSE concluded that indoxacarb failed to meet the approval criteria provided for in Art. 4 of the Regulation and so should be withdrawn in GB. A summary of the HSE scientific review is provided in Annex 2.

HSE concluded that the failure to meet the approval criteria as regards Art. 4(3)(b) of the Regulation was sufficiently clear that it was unnecessary to obtain independent scientific advice. Moreover, a detailed assessment of any further areas of the risk assessment, such as the ecotoxicology area, was unnecessary. Given the concerns identified, it would be inappropriate to delay a GB decision whilst further detailed assessment of those other areas was carried out.

In accordance with the agency agreements, HSE notified the GB competent authorities of its proposed decision that approval of indoxacarb should be withdrawn, the reasons for that decision and the details of the grace period it proposed to set. The GB competent authorities gave their consent to HSE exercising that function and HSE notified producers of the decision, the reasons for it and the grace period set on [dd mm yyyy].

Decision

HSE referred its conclusion and intended decision to GB competent authorities as required under the terms of legal delegations of functions via the Agency Agreements between HSE and the individual competent authorities.

The decision reflects the overall conclusion from the HSE assessment and consideration of the scope to manage the risks arising from the use of plant protection products containing the active substance.

Consequently, plant protection products containing indoxacarb cannot be authorised in GB and existing authorisations must be withdrawn in accordance with the requirements of the Regulation.

Statement of Reasons

The reasons for the decision to withdraw indoxacarb in GB are:

- Unacceptable risk to operators, workers, residents, and bystanders from the authorised GB uses of indoxacarb in plant protection products

Grace Period

In accordance with Art. 21(7) of the Regulation, authorisations of existing products should be phased out so that:

- advertisement, sale, and supply of each product is allowed until dd mm yyyy;
- storage, disposal, and use is allowed until dd mm yyyy.

Further Information

The GB Approvals register will be updated to reflect this decision.

[DATE]

Annex 1 – List of information submitted in response to GB Article 21 review, with brief HSE action

Specialist Area	Company	Description	HSE comment
Dietary Exposure (Residues)	Sharda	Position paper: Potential impact of the new EU toxicological endpoints on the consumer risk and GB MRLs in Great Britain.	Evaluated as part of HSE assessment of dietary exposure
Non-dietary Exposure	Sharda	Position paper non-dietary exposure: Potential impact of the new EU toxicological endpoints on non-dietary exposure.	Evaluated as part of HSE assessment of non-dietary exposure
Toxicology	FMC	Communication letter to EU on the toxicological endpoints in support of expert meeting.	Considered as supplementary to EU assessment of toxicological endpoints
Toxicology	FMC	*In vitro* metabolism of 14C-indoxacarb in human, rat, mouse, dog and rabbit hepatocytes.	Considered in HSE assessment of toxicological endpoints
Toxicology	FMC	Subchronic oral neurotoxicity study.	Considered in HSE assessment of toxicological endpoints
Toxicology	FMC	Subchronic Toxicity study.	Considered in HSE assessment of toxicological endpoints
Toxicology	FMC	Repeated dose dermal toxicity study.	Considered in HSE assessment of toxicological endpoints
Toxicology	FMC	Developmental toxicity study.	Considered in HSE assessment of toxicological endpoints
Toxicology	FMC	Oral (Gavage) Developmental Neurotoxicity study.	Considered in HSE assessment of toxicological endpoints

Toxicology	Sharda	Dermal absorption study.	Evaluated as part of HSE assessment of toxicology
Toxicology	FMC	Dermal absorption study.	Evaluated as part of HSE assessment of toxicology
General	FMC	Position paper included toxicology, dietary and non-dietary risk assessments.	Evaluated as part of HSE assessment
General	FMC	Reporting table containing comments from the applicant for the EU renewal.	Considered as supplementary to EU assessment of toxicological endpoints
General	FMC	Comments on EU EFSA Conclusion.	Considered as supplementary to EU assessment of toxicological endpoints

Annex 2 – Summary Assessment by HSE Supporting the Recommendation

The HSE review took account of the information that supported the EU decision to non-renew indoxacarb. HSE considered the comments provided by indoxacarb authorisation holders and producers.

Toxicology (Human Health)

Toxicological endpoint for assessment of risk following acute dietary exposure - ARfD (acute reference dose):

For the EU renewal evaluation of indoxacarb, the applicant submitted a new rat developmental toxicity study. The study report was also submitted to HSE by FMC during the commenting period. HSE concluded that the NOAEL of 0.5 mg/kg bw/day from the rat developmental toxicity study was robust and applying a safety factor of 100 to this NOAEL, the **ARfD was 0.005 mg/kg bw**.

Toxicological endpoint for assessment of risk following long-term dietary exposure – ADI (acceptable dietary intake):

The NOAEL of 0.5 mg/kg bw/day from the same developmental study was used to derive the ADI. HSE concluded the **ADI was 0.005 mg/kg bw/day.**

Toxicological endpoint for assessment of risk following long-term non-dietary exposure – AOEL (acceptable operator exposure level):

The NOAEL of 0.5 mg/kg bw/d from the same developmental study was used to derive the AOEL. The AOEL was set applying a safety factor of 100 and the oral absorption value of 60% to the NOAEL of 0.5 mg/kg bw/day. HSE concluded the **AOEL was 0.003 mg/kg bw/day**.

Toxicological endpoint for assessment of risk following acute non-dietary exposure – AAOEL (acute acceptable operator exposure level):

The NOAEL of 0.5 mg/kg bw/day from the same developmental study was used to derive the AAOEL. The AAOEL was set applying a safety factor of 100 and the oral absorption value of 60% to the NOAEL of 0.5 mg/kg bw/day. HSE concluded the **AAOEL was 0.003 mg/kg bw/day**.

Dermal absorption

In the UK, the majority of authorised indoxacarb-containing products are water-dispersible granules (WG) containing up to 30% indoxacarb. A new *in vitro* human dermal absorption study was submitted by Sharda to determine more appropriate dermal absorption values than those established at EU level for the representative product. Based on the new data from Sharda, dermal absorption values of 0.064% for the concentrated product and 35% for the in-use dilution (0.05 g/L) were determined by HSE in accordance with the EFSA (2017) dermal absorption guidance. Further information was submitted by FMC concerning the dermal absorption of plant protection products authorised in GB. HSE notes the information was submitted and considered at EU level during the first review of indoxacarb for the representative product; a wettable granule (WG) formulation containing 300 g/kg indoxacarb. Since the representative product is identical to the WG indoxacarb-containing products authorised in the GB, HSE considered these studies to be relevant for the review. HSE has re-evaluated the studies in line with the EFSA (2017) guidance and concluded dermal absorption values of 1.2% for the concentrated product and 50% (default value) for the in-use dilution (0.4 g/L).

Non-dietary Exposure

Non-dietary exposure to indoxacarb has been calculated to be **above** acceptable limits according to the EFSA (2014) non-dietary exposure guidance for the following situations:

- Acute operator exposure for application to oilseed rape, brassicas and pome fruit is above acceptable limits (exposure exceeds the threshold of 100% of AAOEL).

Crop	Application Method	Control Measures	Acute Systemic Exposure	
			% AAOEL	Acceptable?
Oilseed Rape & Brassicas (low crops)	Vehicle mounted boom sprayer	Gloves mixing/loading and application + RPE mixing/loading	293	**No**
Pome Fruit (high crops)	Broadcast air-assisted sprayer	Gloves mixing/loading and application + RPE mixing/loading + closed cab	257	**No**

- Longer term worker exposure for application to brassicas, pome fruit and protected fruiting vegetables is above acceptable limits (exposure exceeds the threshold of 100% of AOEL).

Crop	Worker Activity	Worker protection	Longer Term Systemic Exposure	
			% AOEL	Acceptable?
Brassicas	Hand harvesting	Workwear (arms, body and legs covered) and Splash Resistant Single Use (SRSU) gloves	250	**No**
Pome fruit	Hand harvesting and maintenance	Workwear (arms, body and legs covered) and Splash Resistant Single Use (SRSU) gloves	1007	**No**
Protected cucurbits	Hand harvesting	Workwear (arms, body and legs covered) and Splash Resistant Single Use (SRSU)	776	**No**

		gloves		

- Longer term resident exposure for application to pome fruit and brassicas is above acceptable limits (exposure exceeds the threshold of 100% of AOEL).

Crop	Application Method	Child / Adult	Pathway	Longer Term Systemic Exposure	
				% AOEL	Acceptable?
Pome Fruit	Broadcast air-assisted sprayer	Child	Sum (mean) of all pathways	514	**No**
		Adult	Sum (mean) of all pathways	276	**No**
Brassicas	Vehicle mounted boom sprayer	Child	Sum (mean) of all pathways	153	**No**
		Adult	Sum (mean) of all pathways	73	**Yes**

- Acute bystander exposure for application to pome fruit, brassicas and oilseed rape is above acceptable limits (exposure exceeds the threshold of 100% of AAOEL).

Crop	Application Method	Child / Adult	Pathway	Acute Systemic Exposure	
				% AAOEL	Acceptable?
Pome Fruit	Broadcast air-assisted sprayer	Child	Spray drift	795	**No**
			Vapour	<1	**Yes**
			Surface deposits	247	**No**
			Re-entry into treated crop	266	**No**
		Adult	Spray drift	441	**No**
			Vapour	<1	**Yes**
			Surface deposits	108	**No**
			Re-entry into treated crop	148	**No**
Brassicas	Vehicle mounted boom sprayer	Child	Spray drift	129	**No**
			Vapour	<1	**Yes**
			Surface deposits	39	**Yes**
			Re-entry into treated crop	140	**No**
		Adult	Spray drift	35	**Yes**
			Vapour	<1	**Yes**
			Surface deposits	17	**Yes**
			Re-entry into treated crop	78	**Yes**
Oilseed rape	Vehicle mounted boom sprayer	Child	Spray drift	129	**No**
			Vapour	<1	**Yes**

Crop	Application Method	Child / Adult	Pathway	Acute Systemic Exposure	
				% AAOEL	Acceptable?
			Surface deposits	20	**Yes**
			Re-entry into treated crop	72	**Yes**
		Adult	Spray drift	35	**Yes**
			Vapour	<1	**Yes**
			Surface deposits	9	**Yes**
			Re-entry into treated crop	40	**Yes**

Acceptable non-dietary exposure cannot be demonstrated for any uses of indoxacarb assessed for this Art. 21 Review of indoxacarb in GB. HSE concluded that indoxacarb fails to meet the approval criteria in regard to Art. 4(3)(b) of the Regulation.

Residues

Chronic intakes for all consumer groups (PRIMo v 3.1 and UK chronic model v 1.1) are below the ADI of 0.005 mg/kg bw/day therefore no chronic health effects are expected from the uses assessed for this Art. 21 Review of indoxacarb in GB.

Short-term dietary intakes for several of the proposed uses have been calculated to exceed the ARfD. The following uses were found to exceed intakes calculated by either the PRIMo v 3.1 or the UK acute model (v 1.2):

IESTI (% ARfD) according to EFSA PRIMo	Pears: 665 % (based on NL toddler) Apples: 517 % (based on NL toddler) Sweet peppers: 250% (based on DE child) Cauliflowers: 151% (based on UK infants) Cucumbers: 131% (based on CZ 4-6)
NESTI (% ARfD) according to UK acute model v 1.2	Apples: 470% (infants) Pears: 407% (toddlers) Cauliflower: 151% (infants)

For the following uses short-term dietary intakes for all consumer groups are below the ARfD of 0.005 mg/kg bw/day, therefore no dietary health effects are expected:

Head cabbage

Gherkin

Courgette

Melon

Pumpkin

Tomato

Oilseed rape