Updated risk assessment concerning the risk to wild mammals for the active substance gamma-cyhalothrin

European Food Safety Authority (EFSA)

Abstract
The risk assessment for gamma-cyhalothrin in light of confirmatory data requested following approval in accordance with Article 6(1) of Directive 91/414/EEC and Article 6(f) of Regulation (EC) No 1107/2009 concluded that the long-term risk to wild mammals from the proposed representative uses of gamma-cyhalothrin was not fully addressed. Following further considerations during the decision-making process, the European Commission asked EFSA to update the risk assessment for wild mammals and consider a restriction to the proposed good agricultural practice (GAP). The outcome of the updated peer review of the risk assessment for wild mammals is presented.

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Keywords: gamma-cyhalothrin, pesticide, insecticide, ecotoxicology, risk assessment for mammals

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Summary

Gamma-cyhalothrin has been approved on 1 April 2015 under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 1334/2014.

The approval of gamma-cyhalothrin was subject to a requirement for the applicant to provide confirmatory information among other on the long-term risk to wild mammals.

EFSA published on 13 March 2019 a technical report on the outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for gamma-cyhalothrin in light of confirmatory data. At the same time, the assessment carried out by the rapporteur Member State (RMS), the United Kingdom, in the Reporting Table of the Technical Report suggests that in case of a restriction to the proposed GAP (a single application and timing of the application restricted to BBCH < 70), safe use can be demonstrated.

Following discussions, the European Commission asked EFSA on 23 November 2020 for an updated peer review concerning the risk to wild mammals for gamma-cyhalothrin by providing the first-tier risk assessment for the relevant exposure scenarios considering a single application (and considering the impact of application at different growth stages) in order to establish if an acceptable risk to wild mammals can be demonstrated.

EFSA has accepted the request on 11 December 2020.

Based on the available data and risk assessment, a low acute risk to wild mammals was concluded. However, a high long-term risk for the herbivorous mammals is indicated in tier 1 (i.e. BBCH < 30 and ≥ 40 for the large and small herbivorous mammals, respectively), and due to the absence of higher tier data, further refinement was not possible. A low risk to mammals via secondary poisoning and via consumption of contaminated water was concluded for the single application of gamma cyhalothrin.
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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Background information

Gamma-cyhalothrin has been approved on 1 April 2015 under Regulation (EC) No 1107/2009\(^1\), in accordance with Commission Implementing Regulation (EU) No 540/2011\(^2\), as amended by Commission Implementing Regulation (EU) No 1334/2014\(^3\).

It was a specific provision of the approval that the applicant was required to submit to the European Commission further studies on

1) analytical methods for the monitoring of residues in body fluids, tissues and environmental matrices;
2) the toxicity profile of the metabolites CPCA, PBA and PBA(OH);
3) the long-term risk to wild mammals;
4) the potential for biomagnification in terrestrial and aquatic food chains by 31 March 2017.

In accordance with the specific provision, the applicant, Cheminova A/S, submitted an updated dossier in March 2017, which was evaluated by the designated rapporteur Member State (RMS), the United Kingdom, in the form of an addendum to the draft assessment report. In compliance with guidance document SANCO 5634/2009-rev.6.1 (European Commission, 2013), the RMS distributed the addendum to Member States, the applicant and EFSA for comments on 31 July 2018. The RMS collated all comments in the format of a reporting table, which was submitted to EFSA on 14 February 2019. EFSA added its scientific views on the specific points raised during the commenting phase in column 4 of the reporting table.

To this end, a technical report containing the finalised reporting table has been published by the European Food Safety Authority (EFSA) on the outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for gamma-cyhalothrin in light of confirmatory data on 13 March 2019 (EFSA, 2019).

Gamma-cyhalothrin is the ISO common name for \((S)-\alpha\text{-cyano-3-phenoxybenzyl} \,(1R,3R)-3-[(Z)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate\) or \((S)-\alpha\text{-cyano-3-phenoxybenzyl} \,(1R)\text{-cis-3-[(Z)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate}\) (IUPAC).

The representative formulated product for the evaluation was ‘Corello’ (GF-317), a capsule suspension (CS) formulation containing 60 g/L gamma-cyhalothrin (5.92% w/w). The representative uses evaluated were foliar spraying applications to control a range of insects on winter and spring wheat and barley.

Two foliar residue decline studies on cereals and oil seed rape were submitted and the estimated DT50 of 4.9 days was used by the applicant in the higher tier mammalian risk assessment. However, due to several shortcomings in the study design and in the kinetic evaluation, it was concluded that the default 10 days DT50 should be used in the higher tier assessment. Based on the information provided to fulfill the confirmatory data requirement, the long-term risk to herbivorous and omnivorous mammals from the proposed representative uses of gamma-cyhalothrin was not addressed. The risk from potential for biomagnification in terrestrial and aquatic food chains was concluded as low.

At the same time, the assessment carried out by the RMS, the United Kingdom, in the Reporting Table of the Technical Report suggests that in case of a restriction to the proposed good agricultural practice (GAP) (a single application and timing of the application restricted to BBCH < 70), safe use can be demonstrated.

The European Commission before proceeding with the decision-making process as regards gamma-cyhalothrin asked EFSA with a means of a mandate to update the risk assessment for wild mammals by providing the first tier risk assessment for the relevant exposure scenarios considering a single

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1 Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.
2 Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.
3 Commission Implementing Regulation (EU) No 1334/2014 of 16 December 2014 approving the active substance gamma-cyhalothrin, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011 and allowing Member States to extend provisional authorisations granted for that active substance. OJ L 360, 17.12.2014, p. 1–5.
application (and considering the impact of application at different growth stages) in order to establish if an acceptable risk to wild mammals can be demonstrated.

The present statement contains the outcome of the updated peer review concerning the risk to wild mammals for gamma-cyhalothrin.

All other aspects and conclusions from the peer review of the risk assessment of the active substance and the assessment of confirmatory data (EFSA 2014, 2019) remain unchanged.

A key supporting document to this Statement is the peer review report (EFSA, 2021), which is a compilation of all the documents developed during the evaluation and the assessment requested in the mandate. The peer review report comprises the following documents, in which all views expressed during the process, including minority views, where applicable, can be found:

- the comments received on the draft statement;

Given the importance of the peer review report, this document is considered as a background document to this statement and thus is made publicly available.

Terms of Reference

On 23 November 2020 the European Commission requested EFSA for an updated peer review concerning the risk to wild mammals for gamma-cyhalothrin by providing the first tier risk assessment for the relevant exposure scenarios considering a single application (and considering the impact of application at different growth stages) in order to establish if an acceptable risk to wild mammals can be demonstrated.

It should be noted that the representative use of gamma-cyhalothrin considered during the peer review of the risk assessment of the active substance was three applications per season (EFSA 2014, 2019). It is acknowledged that further refinements and risk assessment based on GAP restriction (e.g. single application as mentioned) were not part of the peer review. EFSA has accepted on 11 December 2020 the request to update the risk assessment to wild mammals and consider a restriction to the proposed GAP (a single application restricted to BBCH < 70) as proposed by the European Commission.

This document is not a stand-alone document and should be read together with other background documents including the EFSA conclusion (EFSA, 2014), EFSA technical report (EFSA, 2019) and the addendum to the assessment report (United Kingdom, 2019).

2. Assessment

2.1. Risk assessment for wild mammals

Mammalian Risk assessment for gamma-cyhalothrin single application, BBCH < 70:

The agreed acute and long-term no observed adverse effect level (NOAEL) end points were obtained from the list of endpoints (EFSA, 2014). The long-term study was performed with the cyhalothrin where the end point was then converted into gamma-cyhalothrin (i.e. divided by four).

A screening assessment was performed according to the mandate using these endpoints for cereals for a single application by foliar spray (0.0045 Kg a.s./ha). The risk assessment was performed for the growth stage range from BBCH 12 to < 70 as requested.

The screening risk assessment was performed in accordance with the recommendations of EFSA (2009) and the results summarised in the following table.

| Scenario                      | Time-scale                          | Endpoint (mg/kg bw per day) | Maximum application rate (g as/ha) | DDD single (mg a.s./Kg bw per day) | TER  | Trigger |
|-------------------------------|-------------------------------------|-----------------------------|-----------------------------------|-----------------------------------|------|---------|
| Screening assessment          |                                     |                             |                                   |                                   |      |         |
| Small herbivorous mammal      | Acute                               | LD_{50}: > 50               | 4.5                               | 0.5328                            | > 93.8 | 10      |
|                              | Chronic/reproduction                 | NOAEL: 0.125               | 4.5                               | 0.115                             | **1.1** | 5       |

TERs in **bold** are below than the assessment factor.
The screening assessment was indicated a low acute risk to mammals. However, the screening assessment triggered the need for a tier 1 long-term risk assessment. The Tier 1 risk assessment required for the generic focal species following the EFSA (2009) is summarised in Table 2.

The representative use of gamma-cyhalothrin results in a high long-term risk to small herbivorous mammals (BBCH ≥ 40) and large herbivorous mammals (for early shoots, considered to be equivalent to BBCH < 30). No suitable higher tier refinement was available to resolve the identified risk.

According to EFSA (2014), a low risk to mammals via secondary poisoning and via consumption of contaminated water was concluded for multiple applications (3 applications of 4.5 g a.s./ha). Therefore, on the basis of the previous assessment, a low risk can be concluded for the single application.

To summarise, a low risk to small insectivorous and omnivorous mammals is indicated in the tier 1. However, there is long-term high risk to herbivorous mammals for the representative use of gamma-cyhalothrin, assuming a single application to cereals (i.e. BBCH < 30 and ≥ 40 for the large and small herbivorous mammals, respectively).

**Table 2:** Tier 1 risk assessment for mammals following a single application of gamma-cyhalothrin to cereals

| Scenario | Generic focal species | Shortcut value for mean RUDs | DDD repro (mg a.s./Kg bw per day) | TERrepro | Annex VI Trigger |
|----------|-----------------------|------------------------------|-----------------------------------|----------|-----------------|
| BBCH 10–19 | Small insectivorous mammal ‘shrew’ | 4.2 | 0.0100 | 12.6 | 5 |
| BBCH > 20 | Small insectivorous mammal ‘shrew’ | 1.9 | 0.0045 | 27.8 | 5 |
| BBCH ≥ 40 | Small herbivorous mammal ‘vole’ | 21.7 | 0.0514 | **2.4** | 5 |
| Early (shoots) | Large herbivorous mammal ‘lagomorph’ | 22.3 | 0.0529 | **2.4** | 5 |
| BBCH 10–29 | Small omnivorous mammal ‘mouse’ | 7.8 | 0.0185 | 6.8 | 5 |
| BBCH 30–39 | Small omnivorous mammal ‘mouse’ | 3.9 | 0.0092 | 13.5 | 5 |
| BBCH ≥ 40 | Small omnivorous mammal ‘mouse’ | 2.3 | 0.0055 | 22.9 | 5 |

TERs in bold are below than the assessment factor.

The representative use of gamma-cyhalothrin results in a high long-term risk to small herbivorous mammals (BBCH ≥ 40) and large herbivorous mammals (for early shoots, considered to be equivalent to BBCH < 30). No suitable higher tier refinement was available to resolve the identified risk.

According to EFSA (2014), a low risk to mammals via secondary poisoning and via consumption of contaminated water was concluded for multiple applications (3 applications of 4.5 g a.s./ha). Therefore, on the basis of the previous assessment, a low risk can be concluded for the single application.

To summarise, a low risk to small insectivorous and omnivorous mammals is indicated in the tier 1. However, there is long-term high risk to herbivorous mammals for the representative use of gamma-cyhalothrin, assuming a single application to cereals (i.e. BBCH < 30 and ≥ 40 for the large and small herbivorous mammals, respectively).

**3. Conclusions**

A screening assessment was performed according to the mandate using the endpoints for cereals for a single application by foliar spray (0.0045 kg a.s./ha). The risk assessment was performed for the growth stage range from BBCH 12 to < 70 as requested. The screening assessment triggered the need for a tier 1 long-term risk assessment for mammals.

Based on the available data and risk assessment, a low acute risk to wild mammals was concluded. However, a high long-term risk for the herbivorous mammals is indicated in tier 1 (i.e. BBCH < 30 and ≥ 40 for the large and small herbivorous mammals, respectively) and due to the absence of higher tier data, further refinement was not possible. A low risk to mammals via secondary poisoning and via consumption of contaminated water was concluded for the single application of gamma cyhalothrin.

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United Kingdom, 2019. Addendum to the assessment report on gamma-cyhalothrin, confirmatory data, July 2018, updated in January 2019. Available online: www.efsa.europa.eu.

**Abbreviations**

\[ \lambda \] wavelength  
\[ \varepsilon \] decadic molar extinction coefficient  
\[ \mu g \] microgram  
\[ \mu m \] micrometer (micron)  
\[ \text{a.s.} \] active substance  
\[ \text{ADE} \] actual dermal exposure  
\[ \text{AF} \] assessment factor  
\[ \text{AP} \] alkaline phosphatase  
\[ \text{AST} \] aspartate aminotransferase (SGOT)  
\[ \text{AV} \] avoidance factor  
\[ \text{BLAST} \] Basic Local Alignment Search Tool  
\[ \text{BUN} \] blood urea nitrogen  
\[ \text{bw} \] body weight  
\[ \text{CAS} \] Chemical Abstracts Service  
\[ \text{CHO} \] Chinese hamster ovary cells  
\[ \text{CI} \] confidence interval  
\[ \text{CL} \] confidence limits  
\[ \text{cm} \] centimetre  
\[ d \] day  
\[ \text{DAR} \] draft assessment report  
\[ \text{DAS-ELISA} \] double-antibody sandwich enzyme linked immunosorbent assay  
\[ \text{DAT} \] days after treatment  
\[ \text{DDD} \] daily dietary dose  
\[ \text{DM} \] dry matter  
\[ \text{DNA} \] deoxyribonucleic acid  
\[ \text{DT}_{50} \] period required for 50% dissipation (define method of estimation)  
\[ \text{EEC} \] European Economic Community  
\[ \text{FID} \] flame ionisation detector  
\[ \text{FIR} \] food intake rate  
\[ \text{FOB} \] functional observation battery  
\[ \text{FOCUS} \] Forum for the Co-ordination of Pesticide Fate Models and their Use  
\[ g \] gram  
\[ \text{GAP} \] Good Agricultural Practice  
\[ \text{GS} \] growth stage  
\[ h \] hour(s)  
\[ \text{ha} \] hectare  
\[ \text{HR} \] hazard rate  
\[ \text{ISO} \] International Organization for Standardization  
\[ \text{IUPAC} \] International Union of Pure and Applied Chemistry  
\[ \text{iv} \] intravenous  
\[ \text{kg} \] kilogram  
\[ \text{L} \] litre  
\[ \text{LD}_{50} \] lethal dose, median; dosis letalis media  
\[ m \] metre  
\[ M \] mol  
\[ mg \] milligram  
\[ M/L \] mixing and loading  
\[ \text{mm} \] millimetre (also used for mean measured concentrations)  
\[ \text{NOAEL} \] no observed adverse effect level  
\[ \text{OECD} \] Organisation for Economic Co-operation and Development  
\[ \text{PHI} \] preharvest interval  
\[ S \] svedberg, S (10^{-13} s)  
\[ \text{SMILES} \] simplified molecular-input line-entry system
| Abbreviation | Full Form |
|--------------|-----------|
| TER          | Toxicity exposure ratio |
| TK           | Technical concentrate |
| TWA          | Time-weighted average |
| UV           | Ultraviolet |
| W/S          | Water/sediment |
| w/v          | Weight per unit volume |
| w/w          | Weight per unit weight |
| WBC          | White blood cell |
| WHO          | World Health Organization |
## Appendix A – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup>                                                                                                                                                                                                 | Structural formula<sup>(c)</sup>                                                                                     |
|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| gamma-cyhalothrin               | *(S)*-α-cyano-3-phenoxybenzyl *(1R,3R)*-3-[(Z)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate or *(S)*-α-cyano-3-phenoxybenzyl *(1R)*-cis-3-[(Z)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropane-carboxylate | ![Structural formula](image)                                                                                                                                               |

<sup>(a)</sup> The metabolite name in bold is the name used in the conclusion.

<sup>(b)</sup> ACD/Name 2017.2.1 ACD/Labs 2017 Release (File version N40E41, Build 96719, 6 September 2017).

<sup>(c)</sup> ACD/ChemSketch 2017.2.1 ACD/Labs 2017 Release (File version C40H41, Build 99535, 14 February 2018).