**PESTICIDE PEER REVIEW UNIT**

5th Working Group meeting on Effect Models in Environmental Risk Assessment

6th – 7th March 2024
14:00-18:00

EUROPEAN FOOD SAFETY AUTHORITY

**Location**: Webconference

**Attendees**:

- Chair
  Ivana Teodorović (IT).
- Working Group Members:
  Jon Haselman (JH); Andreas Focks (AF) present during agenda points 1-5; Sandrine Charles (SC).
- Hearing Experts (6th March 2024):
  Brecht Ingels (RMS); Elena Alonso Prados (co-RMS).
- EFSA:
  Alberto Linguadoca (AL); Alessio Ippolito (AI); Franco Ferilli (FF); Kehinde Olajide (KO).

# Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from the RMS.

# Adoption of agenda

The agenda was adopted without changes.

# Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

# Scientific topic(s) for discussion

### a. Avian body burden model for metam

The meeting discussed the aspects of the model evaluation which were not covered in the previous assessment.

The WG discussed the following aspects: i) model description; ii) problem definition; iii) quality of underlying data and their search; iv) conceptual and formal model; v) model implementation; vi) model parameters; vii) environmental scenario; viii) sensitivity and uncertainty analysis.

Several concerns were identified following the model assessment for regulatory ERA purpose including some fundamental issues related to i) the lack of clarity on the model use in risk assessment; ii) uncertainties around the model assumption of a first order decay, given the available data on the ADME in rat. The concerns by the WG were translated into requests and

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

indications for the applicants on how the model(ling) could be improved. These requests will be reflected in a 'data requirement' in the written peer review process. Following the stop of the clock and pending the submission of additional data by the applicant, the assessment by the WG will be reflected in an advice document for consideration by the peer review experts' meeting.

**b. Use of GUTS in terrestrial ecotoxicology**

An application of a GUTS model to bees from a recent open literature peer-reviewed publication was discussed by the WG, to ensure preparedness in future assessments.

It was highlighted that the purpose of this evaluation was not to assess the quality and robustness of this research *per se*. Additionally, the value of this research application was not questioned by the experts.

With the aim of gaining experience on the application of GUTS in terrestrial ecotoxicology, the WG assessed the applicability of the same evaluation criteria normally applied for regulatory assessments of pesticide risks in aquatic ecotoxicology. For this purpose, models are used to prospectively quantify risks of pesticide use (i.e., to inform risk management decisions on the approval of plant protection products or their active substances).

The assessment by the WG covered the following points: i) the problem definition; ii) the supporting experimental data; iii) the conceptual, formal and computer model; iv) the environmental scenarios; v) the parameter estimation; vi) the sensitivity analysis; vii) the model validation and viii) the model documentation. Because the model was not actually presented for a specific risk assessment application (e.g., by quantifying risks for a specific pesticide use), some of the previous criteria could not be fully assessed.

Where possible, the checklists of the EFSA opinions on good modelling practices (EFSA, 2014[3]) and TKTD models (EFSA 2018[4]) were used. The WG recognized that the EFSA opinion did not specifically cover terrestrial organisms. Owing to the inherent differences of the terrestrial compartment relative to the surface water ecosystems it was recognized that several aspects of the application of GUTS to terrestrial organisms require particular attention. These include the conceptualization of exposure; its relationship with the scaled damage and the evaluation of model performances (e.g., use of quantitative criteria originally conceptualized for aquatic organisms).

[3] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2014. Scientific Opinion on good modelling practice in the context of mechanistic effect models for risk assessment of plant protection products. EFSA Journal 2014;12(3):3589, 92 pp. doi:10.2903/j.efsa.2014.3589

[4] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2018. Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD)effect models for regulatory risk assessment of pesticides for aquatic organisms. EFSA Journal 2018;16(8):5377, 188 pp.https://doi.org/10.2903/j.efsa.2018.5377

**PESTICIDE PEER REVIEW UNIT**

4th Working Group meeting on Effect Models in Environmental Risk Assessment

14th February 2024
14:00-18:00
MINUTES - Agreed on 26th February 2024

**Location**: Webconference

**Attendees**:

- Chair
  Ivana Teodorović (IT).
- Working Group Members:
  Jon Haselman (JH); Andreas Focks (AF) present during agenda points 1-5; Sandrine Charles (SC).
- Hearing Experts:
  Elena Alonso Prados (co-RMS).
- EFSA:
  Alberto Linguadoca (AL); Alessio Ippolito (AI); Franco Ferilli (FF); Kehinde Olajide (KO).

# Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from the RMS.

# Adoption of agenda

The agenda was adopted without changes.

# Declarations of Interest of Working Groups members

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

# Scientific topic(s) for discussion

### Avian body burden model for Metam

The pesticide active substance Metam in undergoing EU-level risk assessment in the framework of its renewal under Commission Regulation (EC) 1107/2009 (AIR III). For this process, Belgium and Spain have been appointed as Rapporteur Member State (RMS) and Co-Rapporteur Member State (Co-RMS) respectively. In this framework, a Renewal Assessment Report (RAR) of the supplementary dossier has been submitted by the applicant, forming the basis of the ongoing peer-review process of metam. The supplementary dossier includes Mechanistic Effect Models (MEMs) for use in ERA, which fall under the remit of the EFSA Working Group (WG) on effect models in Environmental Risk Assessment (ERA). Specifically, a body burden was proposed for

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

use in the higher-tier risk assessment of the acute dietary risk for birds of (a subset of) the representative uses.

The Tier-1 hazard and risk assessment of the representative uses was briefly discussed, before carrying out a preliminary assessment following the structure of the EFSA modelling cycle[3]. Specifically, the WG discussed the following:

- the problem formulation (with reference to the species and endpoint selection)
- the model formulation and formalisation, considering the EFSA PPR panel opinion on Pirimicarb[4]
- a subset of the parameter set proposed by the applicant.

A follow-up meeting was deemed necessary before identifying any data requirement for the applicant.

**Next assessments**

As mentioned above, the need of a follow-up discussion on the avian body burden model was identified.

Additionally, the WG discussed the need to ensure preparedness for the evaluation of TKTD and population models in the area of terrestrial ecotoxicology. Therefore, a proposal was made to initially focus on a case-study covering the use of GUTS beyond the remit of the EFSA PPR Panel TKTD opinion[5] (i.e., application to terrestrial organisms). It was considered that this work will likely directly feed into upcoming peer reviews of pesticide active substances.

A general remark was made that future assessments should aim, where possible, to separate the model assessment from the model use assessment. It was acknowledged that such a separation may not always be straightforward, considering that there are aspects of the design of a model which are inherently linked to the model use in risk assessment. However, it was finally suggested that – regardless of the model type – some aspects of the model assessment (e.g., evaluation of the conceptual and formal model; sensitivity analysis etc.) may be easily 'decoupled' from the evaluation of the model use. Overall, there was agreement that future 'advices' by the WG aim, where possible, to ensure a separation between model assessment and model use assessment.

[3] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2014. Scientific Opinion on good modelling practice in the context of mechanistic effect models for risk assessment of plant protection products. EFSA Journal 2014;12(3):3589, 92 pp. doi:10.2903/j.efsa.2014.3589

[4] EFSA Panel on Plant Protection Products and their Residues, 2005. Opinion of the Scientific Panel on Plant protection products and their residues (PPR) on a request from EFSA related to the evaluation of pirimicarb, *EFSA Journal* 2005; 3(8):240, 21 pp. doi:10.2903/j.efsa.2005.240

[5] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues),Ockleford C, Adriaanse P, Berny P, Brock T, Duquesne S, Grilli S, Hernandez-Jerez AF, Bennekou SH,Klein M, Kuhl T, Laskowski R, Machera K, Pelkonen O, Pieper S, Smith RH, Stemmer M, Sundh I, Tiktak A,Topping CJ, Wolterink G, Cedergreen N, Charles S, Focks A, Reed M, Arena M, Ippolito A, Byers H andTeodorovic I, 2018. Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD)effect models for regulatory risk assessment of pesticides for aquatic organisms. EFSA Journal 2018;16(8):5377, 188 pp.https://doi.org/10.2903/j.efsa.2018.5377

**PESTICIDE PEER REVIEW UNIT**

# 3rd Working Group meeting on Effect Models in Environmental Risk Assessment

09 November 2023
14:00-18:00
MINUTES - Agreed on 28 November 2023

**Location**: Teleconference

**Attendees**:

**Chair:** Ivana Teodorović (IT)
**Members:** Jon Haselman (JH); Andreas Focks (AF); Sandrine Charles (SC)
**EFSA:** Alberto Linguadoca (AL); Alessio Ippolito (AI), Kehinde Olajide (KO), Elena Zioga (EZ)
**Hearing experts:** Not applicable

## I. Welcome and apologies for absence

The Chair welcomed the participants. All WG members attended the meeting.

## II. Adoption of the agenda

The agenda was adopted without changes.

## III. Declaration of Interest

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

## IV. Scientific topic for discussion

The WG discussed possible strategies for working towards the definition of a framework for the assessment of MEMs.

An initial discussion aimed to reflect on the "lesson learned" from the previous evaluation of General Unified Threshold models of Survival (GUTS) by the WG. A key outcome of this exchange was a proposal to draft a document summarising the practical aspects of the implementation of quantitative assessment criteria in GUTS modelling. The WG discussed the criteria in the Toxicokinetic/Toxicodynamic (TKTD) opinion[3] in addition to others encountered during the assessments of chlorotoluron and deltamethrin. While an initial reflection on their

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf
[3] EFSA PPR, 2018. Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms. EFSA Journal 2018;16(8):5377

implementation was possible, further discussion and additional experience in a second general meeting was considered necessary before producing a written output.

Another discussion point aimed to reflect on the possibility to take inspiration from the Findability, Accessibility, Interoperability, and Reusability (FAIR)[4] guiding principles to promote best practices on the (re)use of data, models and model assessment in a regulatory context. Specifically, a short-term goal was identified to work towards the application of FAIR principles *sensu lato* to: i) the reporting and use of data; ii) model implementation, including coding practices and iii) the model assessment. A first step in this direction would be a reflection how and which of the FAIR principles could be readapted for application to the abovementioned steps.

Another short-term goal identified was to work towards the drafting of a checklist specific to TKTD models to be used in the regulatory assessment. This could serve as basis to ensure harmonised definition of data requirements in the peer review process of pesticide active ingredients in the framework of the reg. (EC) 1107/2009. It was acknowledged that guidance is already available in the TKTD[3] and Good Modelling Practice (GMP)[5] EFSA opinions, which could be used as basis for the drafting of such a checklist. Additional sources which may be considered preliminarily to the drafting of such checklists are the TRAnsparent and Comprehensive Ecological modelling documentation (TRACE)[6] and Overview, Design concepts, Details (ODD)[7] protocols.

Finally, the WG was given a presentation of the software implementation of a one compartment avian toxicokinetic model in a 'shiny'[8] application.

[4] Wilkinson et al. 2016. The FAIR Guiding Principles for scientific data management and stewardship. Scientific data, 3(1), 1-9.

[5] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2014. Scientific Opinion on good modelling practice in the context of mechanistic effect models for risk assessment of plant protection products. EFSA Journal 2014;12(3):3589, 92 pp. doi:10.2903/j.efsa.2014.3589

[6] Grimm et al., 2014. Towards better modelling and decision support: Documenting model development, testing, and analysis using TRACE. Ecological modelling, 280, 129-139.

[7] Grimm et al., 2020. The ODD protocol for describing agent-based and other simulation models: A second update to improve clarity, replication, and structural realism. Journal of Artificial Societies and Social Simulation, 23(2).

[8] Chang et al., 2023. shiny: web application framework for R. R package version 1.8.0.9000, https://github.com/rstudio/shiny, https://shiny.posit.co/.

**PESTICIDE PEER REVIEW UNIT**

# 2nd Working Group meeting on Effect Models in Environmental Risk Assessment

18-19 July 2023 / 12 September 2023 / 10-11 October 2023
14:00-18:00
MINUTES - Agreed on 31 October 2023

**Location**: Teleconference

**Attendees**:

**Day 1:**

**Date (time)**: 18/July/2023 (14:00 – 18-00 CEST)
**Chair:** Ivana Teodorović (IT)
**Members:** Jon Haselman (JH); Andreas Focks (AF); Sandrine Charles (SC)
**EFSA:** Alberto Linguadoca (AL); Alessio Ippolito (AI)
**Hearing experts:** Desislava Delikirova (RMS, BG) and Harry Byers (co-RMS, FR)

**Day 2:**

**Date (time)**: 19/July/2023 (14:00 – 18-00 CEST)
**Chair:** Ivana Teodorović (IT)
**Members:** Jon Haselman (JH); Andreas Focks (AF); Sandrine Charles (SC)
**EFSA:** Alberto Linguadoca (AL); Alessio Ippolito (AI)
**Hearing experts:** Desislava Delikirova (RMS, BG) and Harry Byers (co-RMS, FR)

**Day 3:**

**Date (time)**: 12/September/2023 (14:00 – 18-00 CEST)
**Chair:** Ivana Teodorović (IT)
**Members:** Jon Haselman (JH); Andreas Focks (AF); Sandrine Charles (SC)
**EFSA:** Alberto Linguadoca (AL); Alessio Ippolito (AI); Rachel Sharp (RS)
**Hearing experts:** Desislava Delikirova (RMS, BG) and Harry Byers (co-RMS, FR)

**Day 4:**

**Date (time)**: 10/October/2023 (14:00 – 18-00 CEST)
**Chair:** Ivana Teodorović (IT)
**Members:** Jon Haselman (JH); Andreas Focks (AF); Sandrine Charles (SC)
**EFSA:** Alberto Linguadoca (AL); Alessio Ippolito (AI)
**Hearing experts:** Desislava Delikirova (RMS, BG) and Harry Byers (co-RMS, FR)

**Day 5:**

**Date (time)**: 11/October/2023 (14:00 – 18-00 CEST)
**Chair:** Ivana Teodorović (IT)
**Members:** Jon Haselman (JH); Andreas Focks (AF); Sandrine Charles (SC)
**EFSA:** Alberto Linguadoca (AL); Alessio Ippolito (AI)
**Hearing experts:** Desislava Delikirova (RMS, BG) and Harry Byers (co-RMS, FR)

# I. Welcome and apologies for absence

The Chair welcomed the participants.
A quick round of table was done on day 1, for introducing all the participants, their backgrounds and the scope of the WG.
Apologies were received from the co-RMS (Harry Byers FR) on the 12th of September 2023.

# II. Adoption of the agenda

The agenda was adopted without changes.

# III. Declaration of Interest

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

# IV. Scientific topic for discussion

The pesticide active substance Chlorotoluron in undergoing EU-level risk assessment in the framework of its renewal under Commission Regulation (EC) 1107/2009 (AIR III). For this process, Bulgaria and France have been appointed as Rapporteur Member State (RMS) and Co-Rapporteur Member State (Co-RMS) respectively. In this framework, a Renewal Assessment Report (RAR) of the supplementary dossier has been submitted by the applicant, forming the basis of the ongoing peer-review process of chlorotoluron. The supplementary dossier includes Mechanistic Effect Models (MEMs) for use in ERA, which fall under the remit of the EFSA Working Group (WG) on effect models in Environmental Risk Assessment (ERA).

These include i) a body burden model for use in the acute avian risk assessment; ii) an algae population model and iii) an aquatic macrophyte TKTD model for *Lemna*.

The WG was therefore tasked to assess these MEMs and their use in the ERA of chlorotoluron considering its representative uses. Hence, to produce a written "advice" summarising their assessment, for consideration of the upcoming peer review meeting.

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

**PESTICIDE PEER REVIEW UNIT**

# 1st Working Group meeting on Effect Models in Environmental Risk Assessment

12 May 2023 / 01 June 2023 / 14 June 2023
14:00-18:00
MINUTES - Agreed on 29 June 2023

EUROPEAN FOOD SAFETY AUTHORITY

**Location**: Webconference

**Attendees**:

**Day 1:**

**Date**: 12/05/2023

**Chair**: Ivana Teodorovic (IT)

**Members**: Jon Haselman (JH); Andreas Focks (AF); Sandrine Charles (SC)
**EFSA**: Alberto Linguadoca (AL); Alessio Ippolito (AI); Aude Kienzler (AK); Rachel Sharp (RS); Csaba Szentes (CS); Simone Rizzuto (SR); Maria Arena (MA)

**Hearing experts**: None

**Day 2:**

**Date**: 01/06/2023

**Chair**: Ivana Teodorovic (IT)

**Members**: Jon Haselman (JH); Andreas Focks (AF); Sandrine Charles (SC)
**EFSA**: Alberto Linguadoca (AL); Alessio Ippolito (AI);
**Hearing experts**: Matthias Fürst, representing the Rapporteur Member State (RMS)

**Day 3:**

**Date**: 14/06/2023

**Chair**: Ivana Teodorovic (IT)

**Members**: Jon Haselman (JH); Andreas Focks (AF); Sandrine Charles (SC)
**EFSA**: Alberto Linguadoca (AL); Alessio Ippolito (AI)

**Hearing experts**: None

## I. Welcome and apologies for absence

The Chair welcomed the participants. A quick round of table was done on day 1, for introducing all the partecipants and their backgrounds. Apologies were received from the RMS on day 3.

## II. Adoption of the agenda

The agenda was adopted without changes on 12/05/2023; 1/06/2023 and 14/06/2023.

## III. Declaration of Interest

In accordance with EFSA's Policy on Independence[1] and the Decision of the Executive Director on Competing Interest Management[2], EFSA screened the Annual Declarations of Interest filled out by the Working Group members invited to the present meeting. No Conflicts of Interest related to the

[1] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf
[2] http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf

issues discussed in this meeting have been identified during the screening process, and no interests were declared orally by the members at the beginning of this meeting.

# IV. Approval of the last meeting minutes

Not relevant.

# V. Scientific topic for discussion

The WG discussed the need to harmonise of the evaluation of models in the context of the peer-review process of pesticides.

The terms of reference of the working group were introduced. It was clarified that the main goal is to establish a framework for the assessment of mechanistic effect models (MEMs) in the context of the peer-review of pesticide active substance (i.e., in the framework of regulation (EC) 1107/2009).

The WG discussed the possibility to expand the current set of expertise in view of future model assessment.

It was agreed that the WG could initially work towards assessing specific cases related to the EU peer-review activities. Consequently, sufficient experience may be gathered in order to generalize the principles of individual evaluations into rules and guidance that could later be followed at the MS level.

A set of targeted discussions covered the following topics:

- The history, scope and key written outputs of the working group on Model Acceptability criteria and scenario Development of the Society of Environmental Toxicology and Chemistry (SETAC MAD WG), in relation to the possible use for the EFSA working group
- The use of MEMs in the US-EPA, in relation to the similarities and differences with EFSA
- The application of MEMs in the context of the EU regulatory environmental risk assessment of plant protection products[3]; their use i) across non target organism groups (i.e., links between model types and biological groups) ii) over time and iii) across chemical groups. Finally, key limitations of the application of complex models in risk assessment were highlighted.
- The EFSA scientific opinions on "good modelling practice in the context of MEMS for the risk assessment of plant protection products"[4] and on "the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms"[5]

The MEMs submitted in the framework of the peer review of deltamethrin were discussed by the WG.

The RAR for deltamethrin included TKTD (GUTS) modelling on the following non-standard species:

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[3] Larras et al. (2022). A meta-analysis of ecotoxicological models used for plant protection product risk assessment before their placing on the market. *Science of the Total Environment*, 157003.
[4] EFSA PPR (2014). Scientific Opinion on good modelling practice in the context of mechanistic effect models for risk assessment of plant protection products. EFSA Journal, 12(3), 3589.
[5] EFSA PPR (2018). Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms. EFSA journal, 16(8), e05377.

- *Asellus aquaticus*
- *Cloeon dipterum*
- *Gammarus pulex*

The WG discussed these models, based on a preliminary assessment of the data conducted by EFSA. The assessment of the abovementioned models covered the following topics:

1. Consideration of the most appropriate assessment endpoint (i.e., if mortality/immobility as modelled by GUTS would cover for the likelihood of sublethal effects) to address the RA for aquatic invertebrates at tier 2c.
2. Problem formulation, including the:
    - Selection of the most appropriate species for addressing the risk assessment for deltamethrin
    - Consideration of the quality of the experimental data
3. Parameter estimation
4. Model validation

The assessment by the WG was summarised in a written advice for consideration by the pesticide peer review meeting Pesticide Peer Review TC 113 Ecotoxicology (27-30 June 2023).