European Food Safety Authority

Pesticide risk assessment: changes and perspectives for mammalian toxicology in the new EC regulation 1107/2009

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New Pesticide Regulation: Innovative Aspects and Emerging Problems
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Who does what in the peer review

- EFSA - European Food Safety Authority
  - ✓ Pesticide Risk Assessment Peer Review (PRAPeR Unit)
  - ✓ Plant Protection Products & Residues (PPR Unit & Panel)

PRAPeR

- Coordinates Peer Review of active substances at Eu level;
- Involves Member States, EU Commission, Notifiers
- Provides conclusion for single active substances to support the EU decision makers

PPR (Plant protection products and their residues) Unit & Panel

- provides further scientific support and guidance on the risk assessment of pesticides:
  - ➢ Opinions
  - ➢ Guidance documents

Where are we now?

- After 18 yrs of 91/414
- Experience gained with the peer review: 352 a.s. included into Annex I; 821 a.s. not included
- General issues: relevance of impurities, compliance of batches to proposed specification; relevance of isomers
- Issues for mammalian toxicology: “new” effects (neurodevelopmental toxicity, immune effects, endocrine effects), relevance of metabolites, resident exposure, protection of vulnerable people
- To be improved: consistence in the approach of relevance of metabolites in groundwater and in food commodities; transparency in the databases in different assessments
- Lacking tools: guidance documents for Operator, worker, bystander and resident exposure; AOEL; ADI; relevance of metabolites in food commodities

New Regulation 1107/2009/EC General principles

Published 24 Nov 2009
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Applicable as of 14 June 2011

- No use of human data *per se* or to decrease SF
- 'Low risk' a.s.
- Basic substances
- Safeners, synergists: technical rules needed
- Development of non-animal tests
- Vulnerable groups (workers, residents, elderly, pregnant women, infants, children, nursing women)
- *National competent authorities*
- *Efficacy*
- *Mutual recognition (PPP)*

New Regulation 1107/2009/EC General principles

- Shorter timeframes for EFSA
- Hazard based cut-off criteria:
  - endocrine disruptors, POPs, PBTs, vPvBs

- *Comparative RA*
  - *applicable to PPPs containing a candidate for substitution, verify if significantly safer alternative exists*
- *Candidates for substitution*
  - *MS should regularly examine PPPs*
  - *Shall be approved for a period not > 7 years*

EFSA tasks under the new Regulation

- New a.s.: conclusion within 120 days after commenting
- Basic substances: opinion within 3 months
- Review programme safeners and synergists
- Co-formulants?

Contents impacting on Mammalian toxicology

- Art. 8(5): dossier should contain peer-reviewed open literature
- Annex II: CMR criteria

Peer-reviewed open literature

- The summary dossier submitted in view of an approval of an active substance shall include scientific peer-reviewed open literature, as determined by EFSA, on the a.s. and its relevant metabolites dealing with side-effects on health, the environment and non-target species and published within the last 10 years
- EFSA proposed an internal mandate to produce by May 2010 guidance on how to include scientific peer-reviewed open literature; EFSA's Assessment Methodology Unit developed a draft

- **(see EFSA Guidance on Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 - Extended deadline: 15 October 2010 at noon** http://www.efsa.europa.eu/en/consultations/call/amu100723.htm)

CMR criteria: context

- Procedure for active substance approval (1):
- Applicant submits dossier to the rapporteur Member State (RMS)
- RMS performs a completeness check, assesses the dossier, drafts within 1 year a Draft Assessment Report (DAR) and sends it to EFSA
- Within 30 days, EFSA invites for comments on the DAR, to be submitted within 60 days
- Where necessary, EFSA organises an expert consultation
- Procedure for active substance approval (2):
- EFSA drafts a conclusion within 120 days (150 days where an expert consultation is needed)
- The Commission prepares within 6 months a Regulation on approval or non-approval of the active substance

CMR criteria: context

- In its conclusion, EFSA has to indicate whether it can be expected that the approval criteria of art. 4 will be met
- Art. 4 refers to the Annex II: procedure and criteria for the approval of active substances
- Annex II contains criteria in relation to the CMR classification of the active substance

CMR criteria: context

- Annex II CMR criteria: an active substance shall only be approved if on the basis of testing and of scientific literature, reviewed by EFSA, it is not or has not to be classified as:

- M, 1A or 1B
- C, 1A or 1B, unless exposure is negligible
- R, 1A or 1B, unless exposure is negligible

- Where the RMS is of the opinion the CMR approval criteria are not met, the DAR is limited to that part

CMR criteria: problem

- In its conclusion, EFSA has to give a view on CMR properties of active substances within 7-8 months after receipt of the DAR
- The Commission will have to decide within 6 months on the basis of the EFSA conclusion on approval or non-approval

CMR criteria: role of EFSA and ECHA

- Can ECHA participate in the process under the new Regulation by:
  - Participating in the 60 days period of commenting on the RMS' DAR?
  - Participating in the expert consultation EFSA may organise in view of the drafting of its conclusion?
- Would ECHA wish to participate in the commenting on DARs where the RMS is of the opinion that the CMR approval criteria are met?

Scientific criteria vs interim measures

The Commission shall present to the Standing Committee on the Food Chain and Animal Health a **draft of the measures** concerning specific scientific criteria for the determination of endocrine disrupting properties to be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 79(4).

INTERIM MEASURES

Pending the adoption of these criteria, substances that are or have to be classified

as carcinogenic category 1A or 1B and

toxic for reproduction category 1A or 1B

shall be considered to have endocrine disrupting properties.

In addition, substances such as those that are or have to be classified

as toxic for reproduction category 2 and

which have toxic effects on the endocrine organs

may be considered to have such endocrine disrupting properties.

Indications from candidates for substitution

Candidate for substitution

An active substance shall be approved as a candidate for substitution pursuant to Article 24 where any of the following conditions are met:

– its ADI, ARfD or AOEL is significantly lower than those of the majority of the approved active substances within groups of substances/use categories,

– it meets two of the criteria to be considered as a PBT substance,

– there are reasons for concern linked to the nature of the critical effects (such as developmental neurotoxic or immunotoxic effects) which, in combination with the use/exposure patterns, amount to situations of use that could still cause concern, for example, high potential of risk to groundwater; even with very restrictive risk management measures (such as extensive personal protective equipment or very large buffer zones),

– it contains a significant proportion of non-active isomers,

– it is or is to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogen category 1A or 1B, if the substance has not been excluded in accordance with the criteria laid down in point 3.6.3,

– it is or is to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 1A or 1B if the substance has not been excluded in accordance with the criteria laid down in point 3.6.4,

– if, on the basis of the assessment of Community or internationally agreed test guidelines or other available data and information, reviewed by the Authority, it is considered to have endocrine disrupting properties that may cause adverse effects in humans if the substance has not been excluded in accordance with the criteria laid down in point 3.6.5.

Low risk active substances

Low-risk active substances

An active substance shall **not** be considered **of low risk** where it is or has to be classified in accordance with Regulation (EC) No 1272/2008 as at least one of the following:

– **carcinogenic**,
– **mutagenic**,
– **toxic to reproduction**,
– sensitising chemicals,
– very toxic or toxic,
– explosive,
– corrosive.

It shall also not be considered as of low risk if:

– persistent (half life in soil is more than 60 days),
– bioconcentration factor is higher than 100,
– it is deemed to be an **endocrine disrupter**, or
– it has **neurotoxic** or **immunotoxic** effects.

Open issues

- **ACTIVE SUBSTANCE APPROVAL CRITERIA**
- **What will be the impact of the application of hazard, rather than risk based, criteria?**
- **What is “negligible” exposure?**

- **When will new criteria such as assessment of cumulative and synergistic effects apply?**
- These criteria will apply when scientific methods accepted by the European Food Safety Authority (EFSA) are available to assess such effects. EFSA are currently establishing priorities for the development of new guidance.

Open issues

- **The a.s. classification is critical to the decisions to be made on the substance approval: how will the EFSA procedure be integrated with procedures operated by the European Chemicals Agency (ECHA)?**

  The integration of the peer review of active substances and the substance classification is still under discussion. Regulation 1107/2009 does allow the Commission to take decisions on substance approval without a definitive classification having been agreed.

  Issues being discussed include prioritisation of the pesticides classifications to fit in with the substance renewal timetable, or involvement of ECHA in the EFSA peer review procedures for (PPPs).

Thanks for your attention

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