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Scientific publications in the regulatory practice: An NGO perspective

WORKSHOP:
What does the Future Hold for Harmonized Human Health Risk Assessment of Plant Protection Products?

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Guidance of EFSA: Submission of scientific peer-reviewed open literature for the approvals of pesticide active substances under Regulation (EC) No 1107/2009:

"Scientific peer-reviewed open literature… shall be added by the applicant to the dossier."

Q: Is the "addition" used? And How?

Regulatory vs. academic studies

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Regulatory studies

- Methodological „shackles“ (OECD Guidelines)
  (facilitates comparability with other chemicals)
- Formal quality ensured (GLP)
- Scientific quality variable (not hypothesis-driven)

Academic studies

- Innovative approaches possible
- Formal quality variable
- Scientific quality higher (if hypothesis-driven)

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Guidance of EFSA: Submission of scientific peer-reviewed open literature for the approvals of pesticide active substances under Regulation (EC) No 1107/2009:

<u>"Other toxicological studies"):</u>

IS

"Their use is **generally limited to help** addressing species sensitivity and safety factors."

SHOULD

Their use is **important to address … and mechanisms of action**

Current practice concerning „other“ toxicological studies

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- Listing of publications with abstract.
- Sometimes: “quality” and “relevance” evaluated using questionable assessment systems (e.g. Klimisch et al. 1997)

Klimisch et al. (1997): A Systematic Approach for Evaluating the Quality of Experimental Toxico-Logical and Ecotoxicological Data

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Problems:

- use for epidemiological studies
- unjustified dismissal („not relevant, because not reliable“)

2009: Schneider et al.: “ToxRTool”, a new tool to assess the reliability of toxicological data

2013: Instruments for Assessing Risk of Bias and Other Methodological Criteria of Published Animal Studies: A Systematic Review

2017: Kaltenhäuser et al.: Relevance and reliability of experimental data in human health risk assessment of pesticides

What is missing?

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<u>According to 1107/2009, Article 11 (2):</u>

"The rapporteur Member State **shall make an** independent, objective and transparent **assessment** in the light of current scientific and technical knowledge."

Assessment should be ➔ Synopsis of knowledge

i.e.

⬇

Joint assessment of academic and regulatory studies

(Negative) Example

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Addendum to RAR (glyphosate), p. iii

For an overall conclusion, the large volume of animal data for glyphosate has been evaluated using a weight of evidence approach. It should be avoided to base any conclusion only on the statistical significance of an increased tumour incidence identified in a single study without consideration of the biological significance of the finding. In summary, based on the data from five carcinogenicity studies in mice and seven chronic toxicity and carcinogenicity studies in rats, **the weight of evidence suggests**

Addendum to RAR (glyphosate), p. 78

considerations for classification of Guidance on the Application of the CLP criteria, ECHA-13-G-10-EN, ECHA 2013, ASB2015-8592). However, from the sole observation of oxidative stress and the existence of a plausible mechanism for induction of oxidative stress through uncoupling of mitochondrial oxidative phosphorylation alone, genotoxic or carcinogenic activity in humans cannot be deduced for glyphosate and glyphosate based formulations.

What else is missing?

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- More specific legal requirement for making a “synopsis” (overarching weight of evidence).
- True independent assessment of literature by regulatory authorities.
- Better legal opportunities for requiring follow-up investigations and political will to sanction, if not delivered.
- Opportunity to publish negative outcomes is reasonable, but such studies need to be clearly disconnected from industry, and precautionary principle is to be kept in mind.