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Proposal for critical appraisal tools for the **evaluation of ecotoxicology studies**

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Background

- Regulation (EC) No 1107/2009: "pesticide active substance to be approved shall not pose unacceptable effects on human health, animal health and the environment".
- Applicants must submit an application dossier, containing a complete data package investigating various aspects for a specific active substance in line with the EU data requirements, including ecotoxicology studies.
- The evaluation of these studies by reporting Member States when establishing draft or renewal assessment reports and during the so-called 'peer review' process may be challenging and result in inconsistent outcomes among evaluators when a standard test guideline is not available.
- Critical Appraisal Tools (CATs) provide a structured approach to
  - assess the reliability and relevance of individual studies,
  - make the appraisal more transparent, and
  - increase consistency among dossiers.

Objectives of the project

- Conduct a systematic literature review of existing CATs in ecotoxicology and environmental risk assessment.
- Develop CATs for seven selected non-standard ecotoxicology studies (Table 1) for which harmonised standard protocols are not currently available.
- Develop a methodology to quantify the fulfilment of identified validity criteria.
- Develop a method to assess the overall validity of a study.

Table 1. Non-standard studies selected for the development of CATs

Domain	Studies
Aquatic organisms	• Modified exposure studies (tier 2) • Mesocosms (tier 3)
Bees	• Honeybee brood test (feeding & tent version)
Non-target arthropods other than bees	• Extended laboratory studies • Aged residue studies • Field studies (+comments on the suitability for earthworm studies)
Residue decline studies and related kinetics (currently relevant for birds and mammals risk assessment)	• Field studies

Approach

Based on the literature review, it was decided to base the CATs to be developed on the CRED approach (Criteria for Reporting and Evaluating Ecotoxicity Data) for evaluating reliability and relevance of studies and their endpoints, extended with some elements for overall appraisal based on a recent Risk of Bias approach.

Development of the proposed CATs took place in several steps building on the CRED criteria for aquatic studies (Moermond et al., 2016, ET&C 35: 1297-1309):

- Earlier versions of the CATs and handbooks were tested and internally reviewed by experts from the regulatory partners (ANSES & UBA).
- Harmonisation between CATs and handbooks for the seven study types was necessary and took place at all steps of the development process.
- CATs and handbooks were reviewed in detail several times by members of the EFSA Ecotoxicology team (Pesticides Peer-review Unit).

Results

Systematic literature search:

- Different systems and/or CATs for appraisal of environmental studies exist, varying in their scope and the way the criteria are appraised and scored.
- Only few existing appraisal systems have a regulatory status and/or are applied in regulatory frameworks.
- Definitions and terminology vary considerably between publications.

CATs:

- The CATs developed consist of MS Excel spreadsheets with criteria and scoring tables for reliability and relevance, accompanied by handbooks with detailed instructions for appraising the individual criteria.
- With respect to their importance, key criteria and other (non-key) criteria are distinguished.
- Individual criteria are scored as either fulfilled, partly fulfilled, not fulfilled, or not reported (i.e., insufficient information provided).
- A method for evaluating the overall validity of ecotoxicology studies, based on both a (semi-) quantitative scoring system (Table 2) and expert judgement, is also proposed.

Table 2. Overall appraisal of non-standard studies. Reliability and relevance are evaluated separately

Classification of study	Condition
Class 1 (R1- high reliability or relevance)	All key criteria marked as fulfilled AND At least 67% of the other criteria marked as fulfilled AND none of the remaining other criteria marked as not fulfilled.
Class 2 (R2- moderate reliability or relevance)	At least one key criterion marked as partly fulfilled and the remaining key criteria marked as fulfilled AND Only 10% of the other criteria marked as not fulfilled.
Class 3 (R3- low reliability or relevance)	All remaining cases: At least one key criterion marked as not fulfilled OR More than 10% of the other criteria marked as not fulfilled.

Conclusions

- The project has yielded:
  - An overview and a critical review of existing CATs and study evaluation methods in ecotoxicology and environmental risk assessment.
  - An approach for evaluating the reliability and relevance of studies conducted with non-standard higher tier testing methods.
  - A method for evaluating the overall validity of these studies.
  - CATs (MS-Excel) for seven non-standard test methods, including handbooks.
- It is expected that the CATs and handbooks developed will aid reviewers/ evaluators/risk assessors in their assessments during peer reviews and will significantly improve the structure and the consistency of the evaluations.

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The report, CATs and handbooks can be downloaded with the QR code.

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