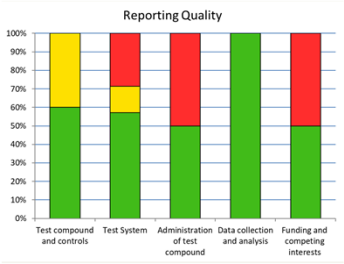
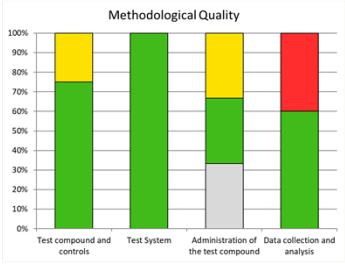
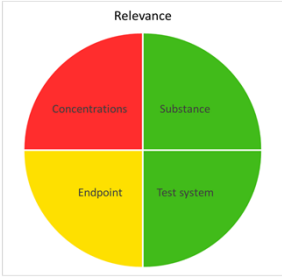
The SciRAP tool for evaluating the quality of *in vitro* studies







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Science in Risk Assessment and Policy (SciRAP)

- Promote structure and transparency in the evaluation of toxicity and ecotoxicity data for hazard and risk assessment.
- Bridge the gap between academic research and regulatory assessment of chemicals.
- User-friendly, facilitate structured qualitative evaluation

Web-based platform: www.scirap.org

A collaboration with Stockholm University

Science in Risk Assessment and Policy (SciRAP)

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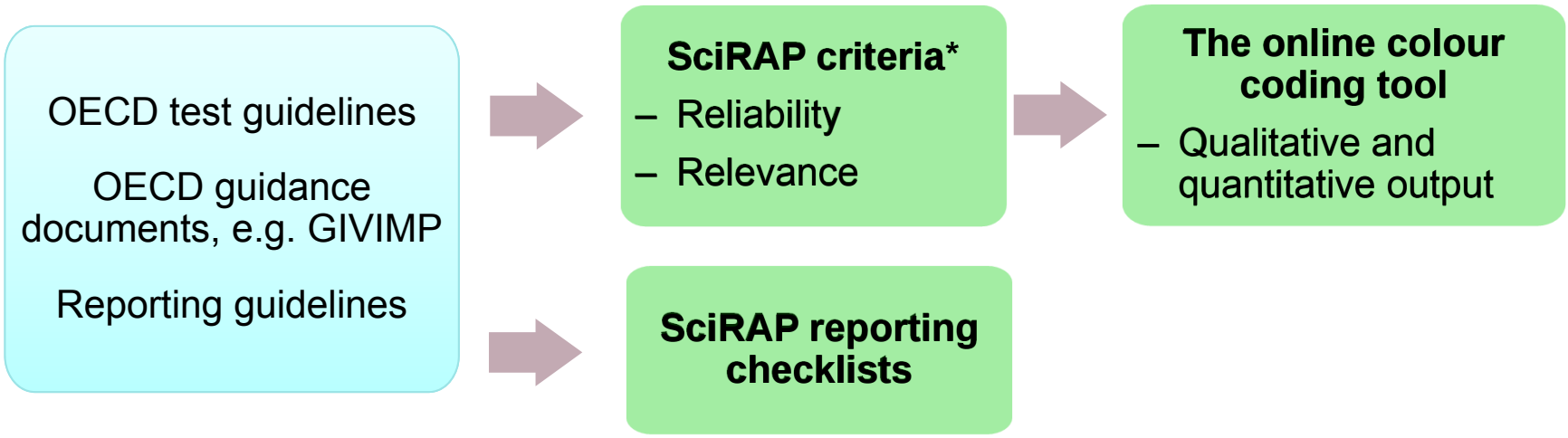
Research within regulatory toxicology and risk assessment methodology

The SciRAP web-based platform (www.scirap.org)

- First online 2014
- Criteria for evaluating **reliability** and **relevance** of studies
  - *In vivo* toxicity studies – first published 2014, up-date published 2018
  - *In vitro* toxicity studies – first version online spring 2018, ongoing testing and assessment by experts
  - Ecotoxicity studies (+ nano) – the CRED criteria
- Online tool for application of the criteria
- Reporting checklists for researchers
- Video tutorials and recorded webinars

Development of SciRAP *in vivo* and *in vitro*



*Requirements should not be stricter than those in standardized test guidelines.
Compliance with standardized test guidelines or GLP not a requirement.

SciRAP *in vitro*

Reliability: Criteria for reporting and methodological quality

- Test compound and controls,
- test system,
- administration of the test compound,
- data collection and analysis, and
- funding and competing interests (only reporting).

Each criterion judged as ”fulfilled”, ”partially fulfilled”, or ”not fulfilled”

Relevance: Four items to consider

- The identity of the tested substance,
- the test system used,
- the endpoint studied,
- the concentrations used.

Each item judged as ”directly relevant”, ”indirectly relevant”, or ”not relevant”

Structure of the SciRAP approach:

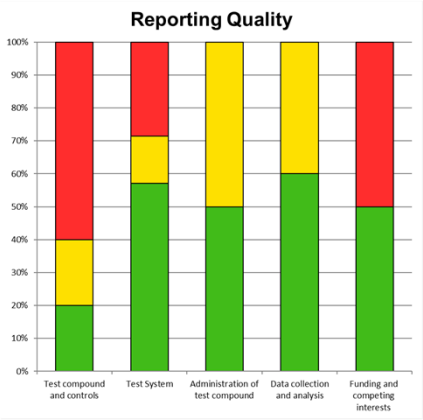
Evaluate reliability

Evaluate relevance

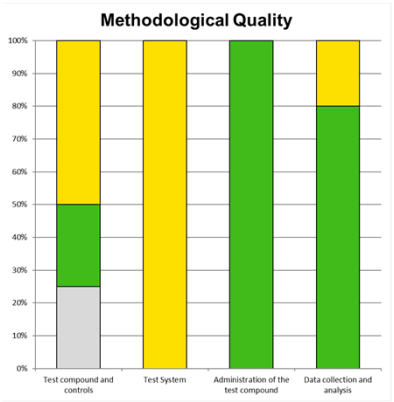
Reporting quality

Methodological quality

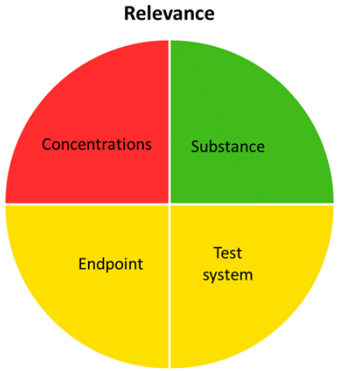
Colour-coding tool

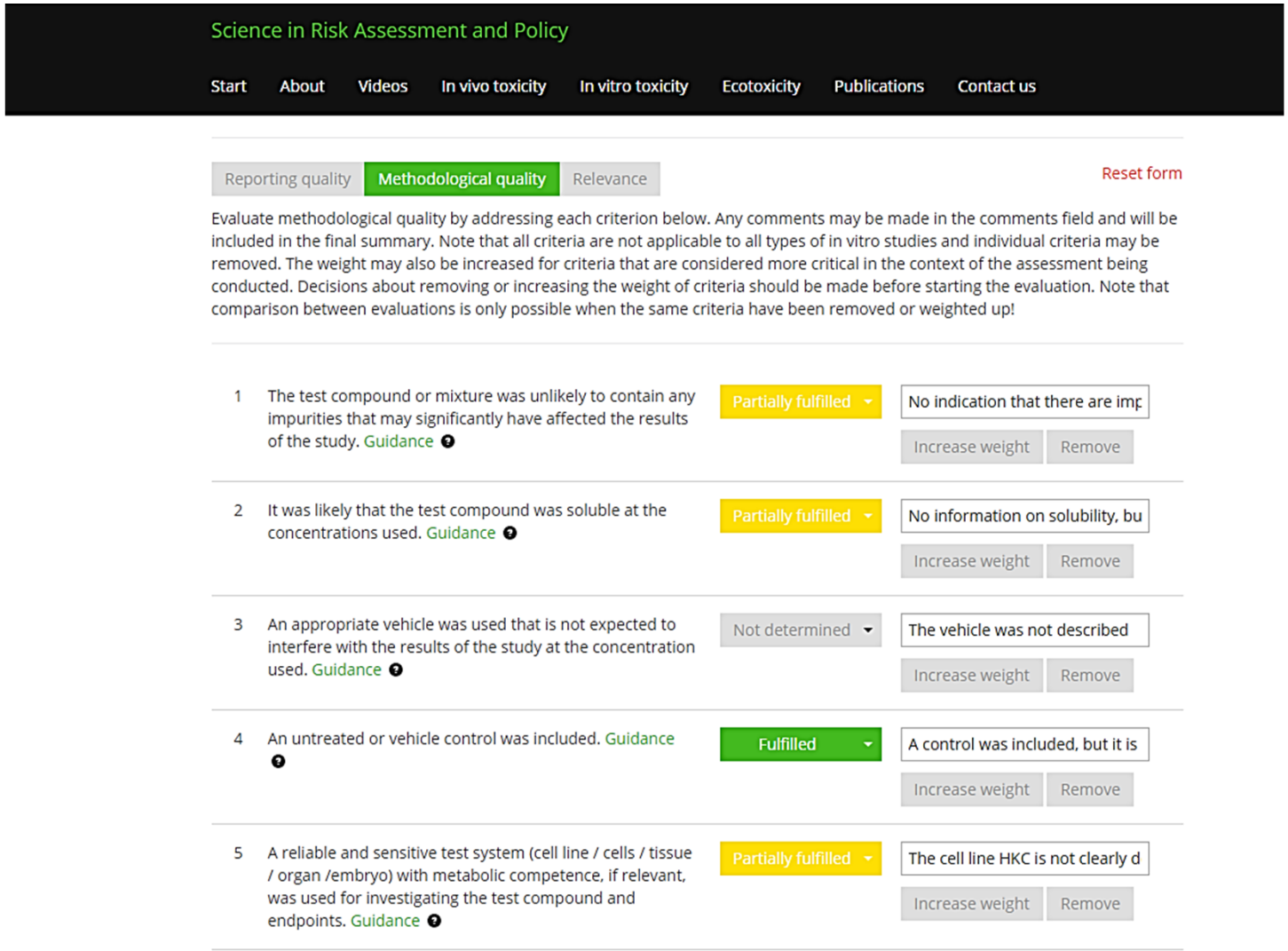


Score: 60.87 (reporting)



Score: 75.00 (method)




Science in Risk Assessment and Policy
Start
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In vivo toxicity
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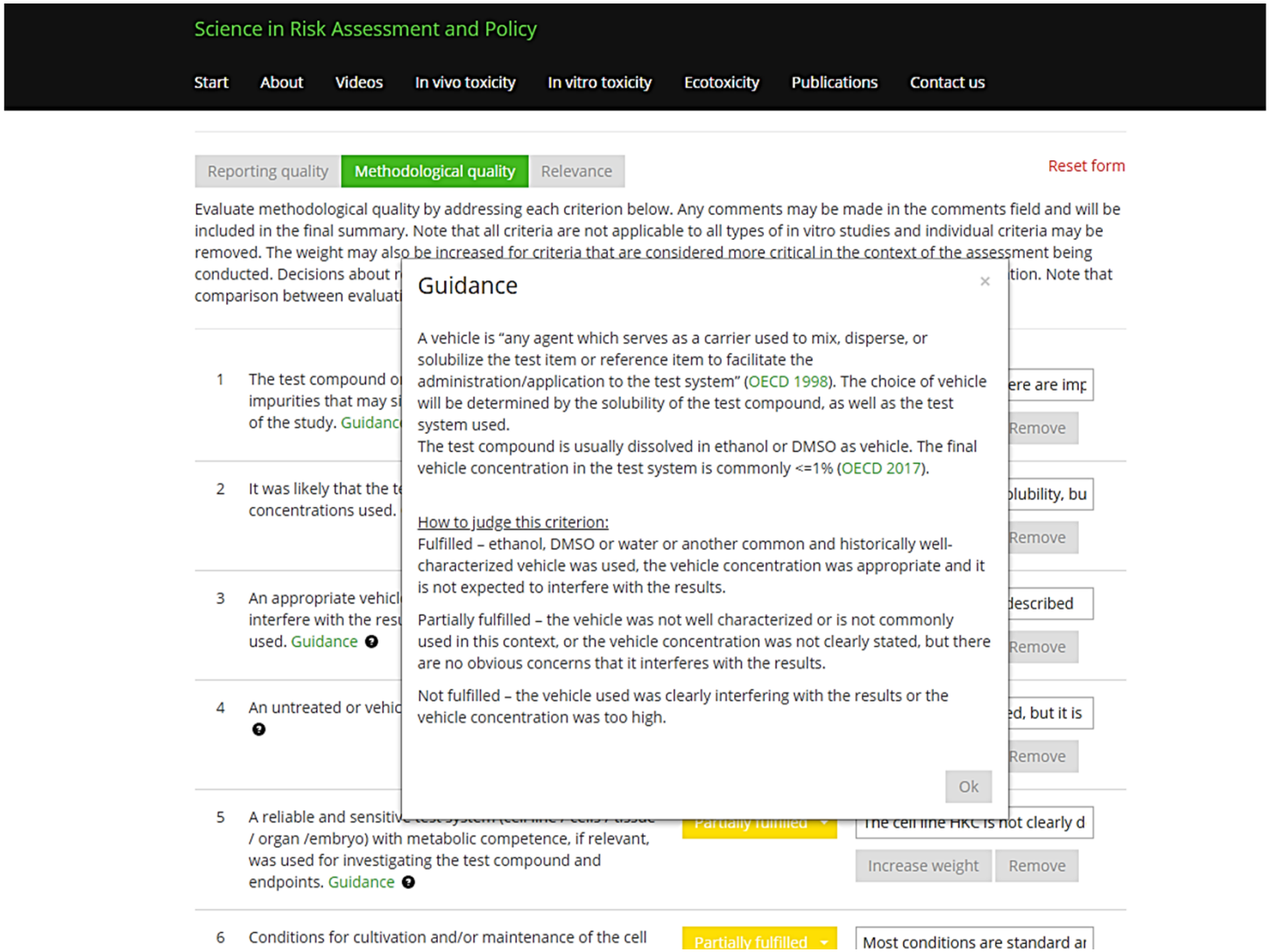
Reporting quality
Methodological quality
Relevance
Reset form
Evaluate methodological quality by addressing each criterion below. Any comments may be made in the comments field and will be included in the final summary. Note that all criteria are not applicable to all types of in vitro studies and individual criteria may be removed. The weight may also be increased for criteria that are considered more critical in the context of the assessment being conducted. Decisions about removing or increasing the weight of criteria should be made before starting the evaluation. Note that comparison between evaluations is only possible when the same criteria have been removed or weighted up!
1
The test compound or mixture was unlikely to contain any impurities that may significantly have affected the results of the study. Guidance
Partially fulfilled
No indication that there are imp
Increase weight
Remove
2
It was likely that the test compound was soluble at the concentrations used. Guidance
Partially fulfilled
No information on solubility, bu
Increase weight
Remove
3
An appropriate vehicle was used that is not expected to interfere with the results of the study at the concentration used. Guidance
Not determined
The vehicle was not described
Increase weight
Remove
4
An untreated or vehicle control was included. Guidance
Fulfilled
A control was included, but it is
Increase weight
Remove
5
A reliable and sensitive test system (cell line / cells / tissue / organ /embryo) with metabolic competence, if relevant, was used for investigating the test compound and endpoints. Guidance
Partially fulfilled
The cell line HKC is not clearly d
Increase weight
Remove



December 10, 2018

Comparing and summarizing studies in the same line of evidence

	Test compound and controls				Test System		Adm. of the test compound			Data collection and analysis				
SciRAP criterion:	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Study 1														
Study 2														
Study 3														
Study 4														
Study 5														
Study 6														
Study 7														
Study 8														
Study 9														

SciRAP does not provide a qualitative descriptor for overall reliability of the study

= fulfilled

= partially fulfilled

= not fulfilled

= not determined

Reliability and internal validity/risk of bias

- **Reliability**: the inherent quality of the study; is tightly linked to the reliability of the methods used and how the results have been interpreted, as well as clarity and plausibility and how methods and results have been reported (ECHA 2011).

- **Internal validity/risk of bias**: “Measure of the credibility of study findings that reflects the ability of a study's design and conduct to protect against systematic errors that may bias (over- or under estimate) the results or estimate of effect” (Rooney et al. 2016).

Assessment of the SciRAP tool for evaluation of *in vivo* animal toxicity studies in the context of systematic review

Jennifer Waspe[1], Thuy Bui[2], Laura Dishaw[3], Andrew Kraft[3], April Luke[3], Anna Beronius[1]

Aim: investigate to what extent the SciRAP tool covers elements important for evaluating domains of bias and sensitivity included in tools developed specifically for systematic review

- Matching the SciRAP criteria to the reporting quality, RoB, and study sensitivity domains in the IRIS tool for study evaluation.
- Comparisons to the OHAT RoB-domains and ToxRTool.
- Case study evaluating nine studies for triphenyl phosphate.

[1]Institute of Environmental Medicine, KI; [2]Department of Environmental Science and Analytical Chemistry, Stockholm University; [3]US Environmental Protection Agency

Assessment of the SciRAP tool for evaluation of *in vivo* animal toxicity studies in the context of systematic review

Preliminary conclusions:

- The SciRAP tool covers many of the elements included for study evaluation the IRIS and OHAT tools.
- Although different (domain-based vs criteria-based), both IRIS and SciRAP aim to facilitate expert judgment in a structured and transparent manner.
- Aspects that can be improved in the SciRAP tool (for *in vivo* studies) include evaluation of:
  - Blinding
  - Attrition
  - Results presentation

Can currently be considered under “other” in SciRAP

What can the SciRAP tool be used for?

As an evidence appraisal tool, e.g:

- → For categorizing studies into categories for reliability, e.g. within REACH
- → In weight of evidence evaluation and evidence integration
- → In systematic review
- → In the development and evaluation of adverse outcome pathways (AOPs)

As guidance for researchers (also the “reporting checklists”).

Regulatory applications

- the Swedish Chemicals Agency
  - SciRAP *in vivo* criteria used in the assessment of Dicyclohexyl phthalate (DCHP) as a substance of very high concern (SVHC) under REACH
- the Swedish Environmental Protection Agency and Swedish Agency for Marine and Water Management
  - Derivation of European environmental quality standards (EQS)
- the European Food Safety Authority (EFSA)
  - SciRAP *in vivo* criteria integrated in the hazard assessment protocol for bisphenol A

SciRAP is mentioned in the European Chemical Agency's (ECHA) guidance for weight of evidence evaluation and in EU's Water Framework Directive.

Ongoing activities

- Using SciRAP (*in vivo*) for risk assessment of substances within REACH (Ingre-Khans et al. *accepted manuscript*).
- Using SciRAP (*in vivo* and *in vitro*) for the evaluation of EDs according to new EU criteria and guidance (several case studies).
- Applying SciRAP *in vivo* and *in vitro* criteria (HAWC platform) within the SYRINA framework - triphenyl phosphate case study (Bui *et al*.).
- Expert assessment of SciRAP *in vitro* – please join us!

Thank you for your attention!

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Thuy Bui
Jennifer Waspe

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Selected publications

Beronius A, Molander L, Zilliacus J Rudén C, Hanberg A: **Testing and refining the Science in Risk Assessment and Policy (SciRAP) web-based platform for evaluating the reliability and relevance of in vivo toxicity studies.** *J Appl Toxicol.* 2018; **38**:1460-1470.

Beronius A, Ågerstrand M, Rudén C, Hanberg A: **SciRAP workshop report: Bridging the gap between academic research and chemicals regulation - the SciRAP tool for evaluating toxicity and ecotoxicity data for risk assessment of chemicals**. Nordic Working Papers. Nordic Council of Ministers. Copenhagen, 2017, 33 pp.

Molander L, Ågerstrand M, Beronius A, Hanberg A, Rudén C. **Science in Risk Assessment and Policy (SciRAP): An Online Resource for Evaluating and Reporting In Vivo (Eco) Toxicity Studies**. *Human and Ecological Risk Assessment*. 2015; **21**:753-762

Beronius A, Molander L, Ruden C, Hanberg A: **Facilitating the use of non-standard in vivo studies in health risk assessment of chemicals: a proposal to improve evaluation criteria and reporting**. *J Appl Toxicol.* 2014: **34**:607-617.

(See the SciRAP web page for a complete list of publications.)