Literature review in toxicological research and chemical risk assessment: the state of the science

Paul Whaley & Crispin Halsall Lancaster Environment Centre, Lancaster University, LA1 4YQ, UK p.whaley@lancaster.ac.uk

Objective: Building on techniques developed in evidence-based medicine, develop a novel literature review appraisal toolkit to evaluate the methodological quality of reviews of evidence conducted in chemical risk assessments

The Problem

Valid synthesis of large volumes of toxicological research is crucial to identifying risks to health posed by chemicals such as bisphenol-A (BPA).

However, many such syntheses disagree about BPA's health risks. How do we know which ones to believe?

Conclusion

There are major obstacles to accepting that current review practices at the European Food Safety Authority (EFSA) yield valid syntheses of toxicological data relating to the toxicity of BPA.

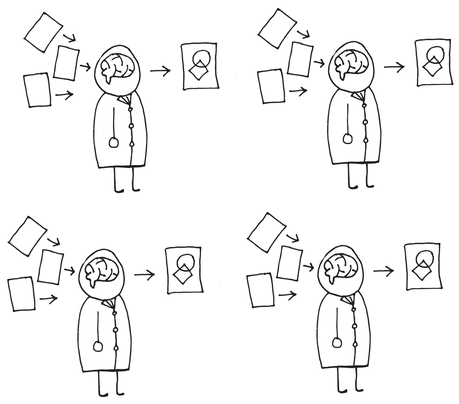
Next steps

1. Broaden the analysis to encompass more agencies and general scientific practice.
2. Engage regulators in discussion of how to implement systematic review techniques to advance conduct of chemical risk assessments.

The Policy from Science Project Literature Review Appraisal Toolkit (LRAT): We took the key themes we identified in literature review appraisal tools used in medicine and adapted them into a questionnaire to aid evaluation of the credibility of toxicological reviews

Target of assessment

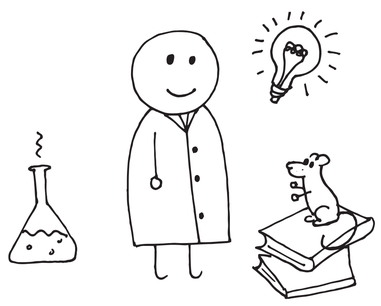
The utility, validity and reproducibility of the review process, i.e. does it ask the right question; are the methods sufficiently likely to yield a correct answer; is documentation sufficient to allow reproduction of results?



Traffic-light user responses to LRAT questions

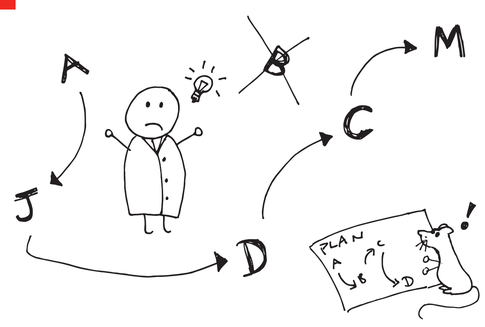
- **Satisfactory //** Clear, valid & consistent procedure
- **Unclear //** Insufficient documentation to evaluate
- **Unsatisfactory //** Positive evidence of inconsistent or invalid procedure

1 Is there a clear objective?



A review should answer a clear question, the relevance of which is justified

2 Was there a pre-published protocol?

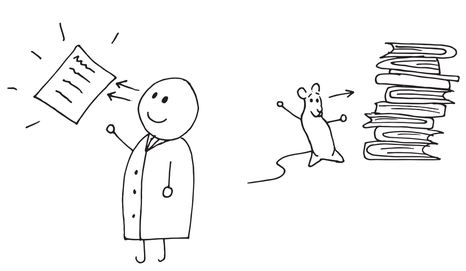


Protocols help prevent ad-hoc changes to method from biasing review results

3 Is there a comprehensive declaration of interests and contributions?

So users can put review findings in full context

4 Did the search strategy find all literature of possible relevance to the review?

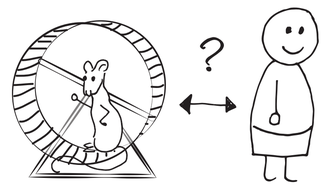


Prevents sampling bias in evidence base of review

5 Were inclusion criteria used which selected for analysis all studies of actual relevance to the review?

Prevents selection bias in evidence base of review

6 Is there a fair test of *external validity* of evidence?

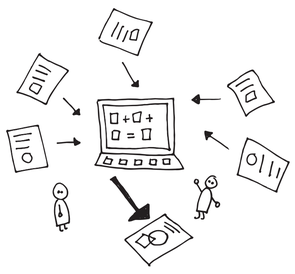


A review should subject every included study to a consistent, valid test of directness of evidence in relation to review objective

7 Is there a fair test of *internal validity* of evidence?

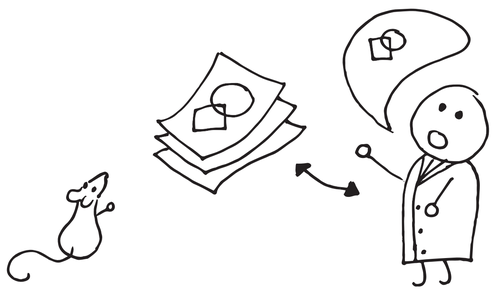
A review should subject every included study to a consistent, valid test of methodological quality

8 Is the data synthesis valid?



The review should combine, according to a clear and valid method, the results, directness and methodological quality of evidence into a statement of how existing research supports its objective

9 Does the answer to the review accurately reflect its principal findings?



Applying LRAT: European Food Safety Authority regulatory risk assessments of BPA

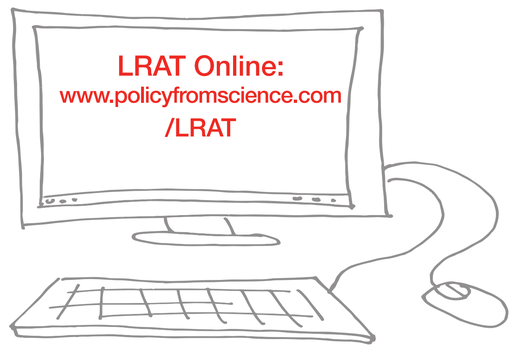
	2010 Opinion	2013 Draft Exposure Assessment	2014 Draft Opinion
Objective	●	●	●
Protocol	●	●	●
Interests	●	●	●
Search Method	●	●	●
Study Selection	●	●	●
External Validity	●	●	●
Internal Validity	●	●	●
Synthesis	■	●	●
Answer	●	●	●

Key: ● Satisfactory ● Unclear ● Unsatisfactory ■ Not Appraised

A literature search quickly finds papers of relevance to BPA toxicity from 2010-2012 which are relevant but not referenced in the Opinion; EFSA openly acknowledges that the search for 2013 data was partial.

Many of the criteria for measuring methodological quality of studies are concerned with e.g. reporting quality or conformity with OECD guidelines instead of features which actually determine the validity of a given study.

The approach to synthesising data into a weight-of-evidence analysis appears inconsistent between health end-points and study quality is a poor indicator of final attributed weight in analysis; however, EFSA's documentation is ultimately too sparse to come to a conclusion about validity of their analysis.



- Detailed explanation of the key issues relating to methodological quality of literature reviews
- Step-by step guidance to applying the toolkit to reviews of your choice

Policy from Science Project

LANCASTER UNIVERSITY

Research supported by grants from the *European Environment and Health Initiative*, *Fondation pour une terre humaine* and *Radical Futures for Social Sciences*

Design: miriam@linemaker.co.uk