

Halle, 4. März 2013

## AK Reg Tox: Advanced Course 2013

# „Read-Across und Grouping zur Füllung von Datenlücken unter REACH“

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**Klaus Schneider**

**FoBiG, Forschungs- und Beratungsinstitut Gefahrstoffe GmbH**

**Freiburg, [www.fobig.de](http://www.fobig.de)**

## Einführung

- Definitionen und ECHA Guidance 2008: Read-across: was ist das und wie geht das?
- Aktuelle Entwicklungen

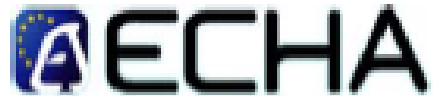
## Strategien zur Füllung von Datenlücken

- **In vitro Tests:** akzeptierte Tests für Hautreizung/-ätzung und (teilweise) Augenreizung (<http://tsar.jrc.ec.europa.eu/>)
  - bescheidener Erfolg angesichts jahrzehntelanger Bemühungen
- **(Q)SAR:** OECD Validierungskriterien erfüllt? Hohe Anforderungen an Formate / Berichterstattung unter REACH
- **Read-across (analogy approach oder category):** am häufigsten angewendet, Berichtsformate gegeben, Validitätskriterien unklar

## Wie geht „read-across“?

- Ähnliche Struktur → ähnliche Wirkung
  - Enge Verwandtschaft: z.B. Hydrochlorid einer Base, Säure/Salz
  - Weitere Verwandtschaft: gemeinsame Strukturmerkmale bedingen Eigenschaftsprofil, z.B. Nicht-Verfügbarkeit für den Organismus
  - Vorhersehbare Änderung von Struktur und Wirkung: z.B. aliphatische Kettenlänge
- Unterschiedliche Struktur → ähnlicher Mechanismus
  - Metabolit(e) ist toxisches Prinzip: Daten zum Metaboliten verwenden
  - Metabolomics: Gruppierung nach gemeinsamen „Aktivitätspfaden“ (van Ravenzwaay et al., 2012, Mut Res, 746, 144-150)

## ECHA Guidance



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# Guidance on information requirements and chemical safety assessment

## Chapter R.6: QSARs and grouping of chemicals

## ECHA Guidance

- Read-across (Analogie-Ansatz: wenige Substanzen; Kategorie: große Gruppe): Wert von einer Substanz wird auf andere oder auf Gruppe übertragen
- Trendanalyse: kontinuierliche Merkmalsänderung (Kettenlänge): „Extrapolation/Interpolation“
- (QSAR)

**Aber:** keine Kriterien für eine hinreichende Begründung der Kategorie

## Aktuelle Entwicklungen



EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

About ECETOC

Science Strategy

Activities

Publications

News

Links

Members' Website

Technical Reports

Monographs

JACC Reports

Special Reports

Workshop Reports

Documents

ECETOC Articles

TR 116 : **Category approaches, read-across, (Q)SAR** | 21 November 2012

### Background

An accepted practice for the assessment of human health and environmental safety of chemicals is the use of models and analogues to fill data gaps for specific endpoints either for single or multiple chemicals that share structural similarities, and/or comparable reactivity or similarities in metabolism in mammals, fish and other organisms. For example, this approach is acceptable, with limitations, in preparing dossiers for REACH, and it supports efforts for reducing animal testing. The OECD has published guidance on the formation and use of chemical categories for data gap filling. In December 2010, an ECETOC Task Force produced TR 109: *High information content technologies in support of read-across in chemical risk assessment*, a project that has highlighted methods for read-across.

With the plethora of models and guidance growing for both human health and the

## Aktuelle Entwicklungen



### Experts Workshop on Read-Across Assessment with active support from Cefic-LRI

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The workshop was divided into two parts: the objective of the first day (2 October, closed session) was to exchange views between ECHA, the Commission and the Member States on the assessment of the read-across approach in a dossier. During the second day (3 October), the discussion expanded to what constitutes a robust scientific justification for read-across. The second day was organised with the active support of Cefic Long-range Research Initiative (LRI) and was open to various stakeholders.

- [Agenda for 3 October 2012](#)

### Background materials

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- [Background paper: an introduction to the assessment of read-across in ECHA](#) [PDF] [EN]
- [Background document on read-across highlights from a forthcoming ECETOC report](#) [PDF] [EN] - ECETOC

### Presentations

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- [Introduction to the Experts Workshop on Read-Across Assessment, with the active support of Cefic LRI, 3 October 2012](#) [PDF] [EN] – **Mike Rasenberg** (ECHA)
- [Assessment of read-across in ECHA](#) [PDF] [EN] – **Karel de Raat** (ECHA)

[http://www.echa.europa.eu/en/web/guest/view-article/-/journal\\_content/c6dd5b17-7079-433a-b57f-75da9bcb1de2](http://www.echa.europa.eu/en/web/guest/view-article/-/journal_content/c6dd5b17-7079-433a-b57f-75da9bcb1de2)



## Aktuelle Entwicklungen



**Experts Workshop on Read-Across Assessment**  
**Organised by ECHA with the active support from Cefic-LRI (October 3, 2012)**  
Use of "read-across" for Chemical Safety Assessment under REACH

### Workshop Report

#### Abstract Summary

An Experts Workshop on Read-Across Assessment organised by ECHA with the active support from Cefic-LRI was held on the 3<sup>rd</sup> October 2012. The aims of the Workshop were threefold; to explore Industry experiences with "read-across approaches" to date, to try to reach common understanding to characterise scientifically valid "read-across" are and to provide insight in ECHA's rationale for assessing read-across proposals, the so-called RAAF.

Overall the workshop was successful in its aims. The forum provided an opportunity for direct interaction between different interested stakeholders and thus enabled a useful exchange to clarify many misconceptions and highlight existing opportunities. The RAAF was viewed as a useful construct not only for the evaluation of read-across proposals but also for their development. Experience from ECHA so far has been that many of the submitted REACH dossiers with read-across leave substantial room for improvement. The workshop helped to identify what improvements could be made. The discussions helped to clarify and address some of the difficulties raised in the use and acceptance of read-across.

Both ECHA and Cefic LRI expressed a willingness to continue cooperation on read-across. ECHA considered LRI as providing a good platform to address research and information needs for read-across. In the near future, illustrative examples for broad public access could be prepared.

## Aktuelle Entwicklungen

### ECHAs Read-across Assessment Framework (RAAF):

- Tiered approach:
  1. Klare Fälle
  2. Abwägungsfälle: Bewertungsmethodik in der Entwicklung
- „The **uncertainty in the read-across result** ...should subsequently be accounted for. It may be appropriate to use **assessment factors** for this”
- Höhere Anforderungen bei Übertragung negativer Studienergebnisse
- ECETOC/ECHA: Toxikokinetische Daten sind hilfreich

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Thank you for your attention!

