Regulatory (Eco)Toxicology

- From the other side of the pond

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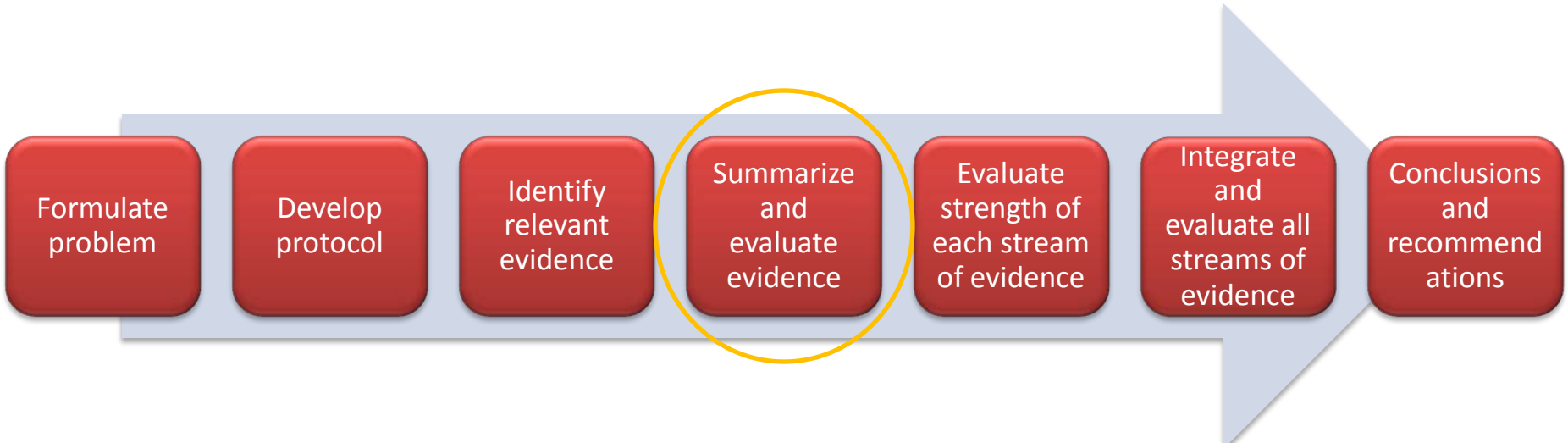


Experts disagree…

Trichloroethene cancer risk assessments 1973 - 1996

Not carcinogenic	Animal but not a human carcinogen	Human carcinogen
NIOSH (-73)	**IARC** (-76)	**NIOSH** (-78)
HSE (-82)	**IARC** (-79)	**Nord. EG** (-79)
VROM (-84)	**AMI/CG** (-81)	**US. EPA** (-85)
ACGIH (-89)	**WHO** (-85)	**IMM/SNV** (-86)
ACGIH (-92)	**IARC** (-87)	**US. EPA** (-88)
ACGIH (-96)	**CEC** (-90)	**ATSDR/EPA** (-89)
	AMI (-91)	**Can. EPA** (-93)
	GDCh (-94)	**OECD/EU** (-96)
	ECETOC (-94)	**ATSDR** (-97)
	HSIA (-96)	**IMM/SNV** (-90)
		IARC (-95)
		DFG (-96)
		MAK (-96)

Rudén 2002

Experts disagree…

Health risk assessments of Bisphenol A

- AIST 2005
- EFSA 2006
- EFSA 2008
- ECB 2008
- US FDA 2008
- EFSA 2010
- SCF 2002
- ECB 2003
- EFSA 2014
- Health Canada 2008
- NTP-CERHR 2008
- US FDA 2010
- WHO 2011
- Chapel Hill 2007
- ANSES 2013

Beronius et al 2009 Reprod Toxicol

Risk Assessments in Europe

Chemicals legislation	Responsible for RA	Evaluation of RA
Industrial Chemicals - REACH	Industry	Minimum 5% by regulators
Biocidal Products Regulation	Industry	100% by regulators
Plant Protection Product Regulation	Industry	100% by regulators
Environmental Risk Assessments of Medicinal Products	Industry	100% by regulators
Cosmetics Directive	Industry	100% by regulators

Risk assessments on substances of concern are also performed by different authorities

	Klimisch et al. 1997	Durda and Preziosi 2000	Hobbs et al. 2005	Schneider et al. 2009 (ToxRTool)
Data type	Tox + Ecotox	Ecotox	Ecotox	Tox
Reliability criteria	12-14	40	20	21
No. of matched OECD criteria	14/37	22/37	15/37	14/37
Relevance criteria	0	0	0	0
Additional guidance	No	Yes	No	Yes
How to summarize the evaluation	Qualitative	Qualitative	Quantitative	Quantitative

Ågerstrand et al. 2011 Env Sciences Europe

	Klimisch et al.	Durda and Preziosi	Hobbs et al.	Schneider et al.
Andreozzi et al. 2004	-	-	-	-
Ferrari et al. 2004	-	-	-	-
Huggett et al. 2002	-	-	+	-
Robinson et al. 2005	+	-	+	-
Schmitt-Jansen et al. 2007	+	-	+	-
Quinn et al. 2008	-	-	+	-
Metcalfe et al. 2001	-	-	+	+
Nentwig, 2007	+	-	+	++
Halm et al. 2002	+	-	+	++

- Unacceptable reliability
+ Acceptable reliability
++ High reliability

Ågerstrand et al. 2011 Env Sciences Europe

We need!

- Guidance documents that emphasize use of all relevant data
- New evaluation method
  - Systematic, transparent, consistent, and sufficiently detailed
  - Works in all type of regulatory frameworks
  - Works for a diverse group of risk assessors
  - Applicable to the current legislation

Reliability and Relevance

- Reporting recommendations for peer-reviewed studies

What did we do?

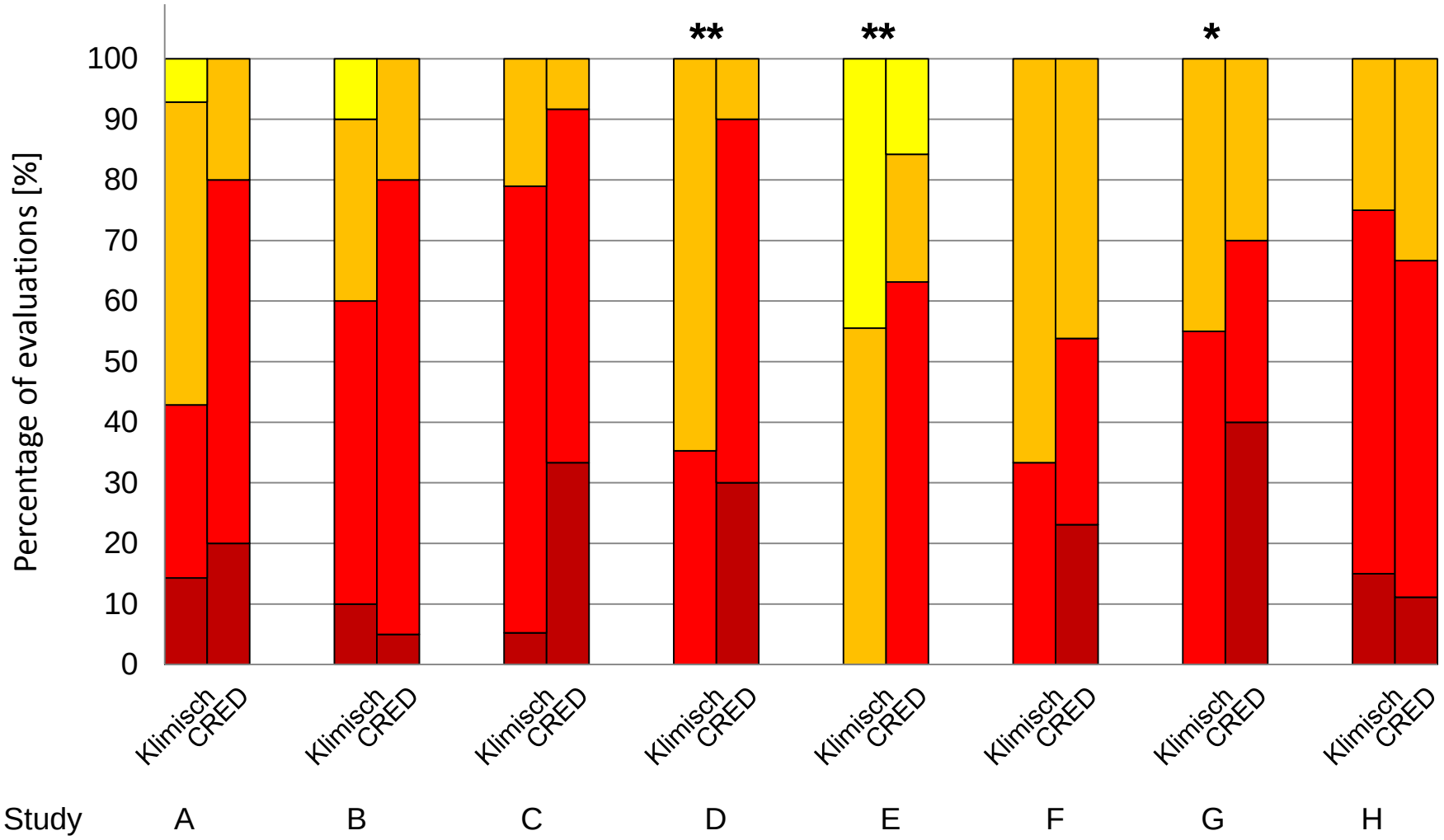
1. Developed the CRED-evaluation method for ecotoxicity studies

2. 75 risk assessors evaluated ecotoxicity studies using
   - Klimisch et al. (1997)
   - CRED-evaluation method

3. Comparison of results and refinement of the CRED-evaluation method

4. Developed the CRED-reporting recommendations for authors of peer-reviewed studies

	Klimisch et al. 1997	CRED-method
Data type	Tox + Ecotox	Aquatic ecotox
Number of reliability criteria	12-14 (Ecotox)	Reporting 59 Evaluating 20
Number of matched OECD reporting criteria	14/37	All
Number of relevance criteria	0	13
Additional guidance	No	YES!
How to summarize the evaluation	Qualitative	Qualitative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Percentage of evaluations [%]
Klimisch
CRED
Study
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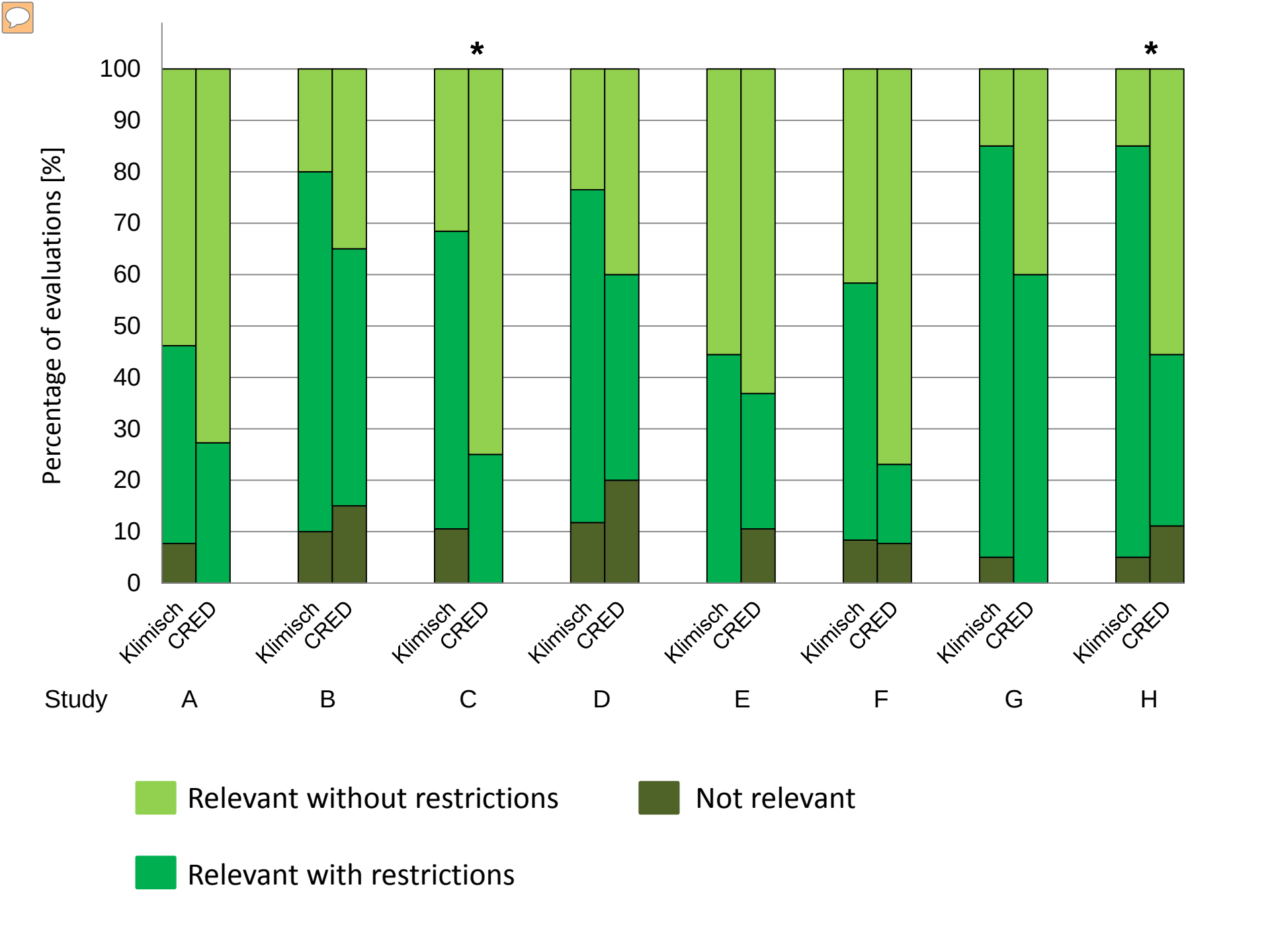
B
C
D
E
F
G
H
Reliable without restrictions
Not reliable
Reliable with restrictions
Not Assignable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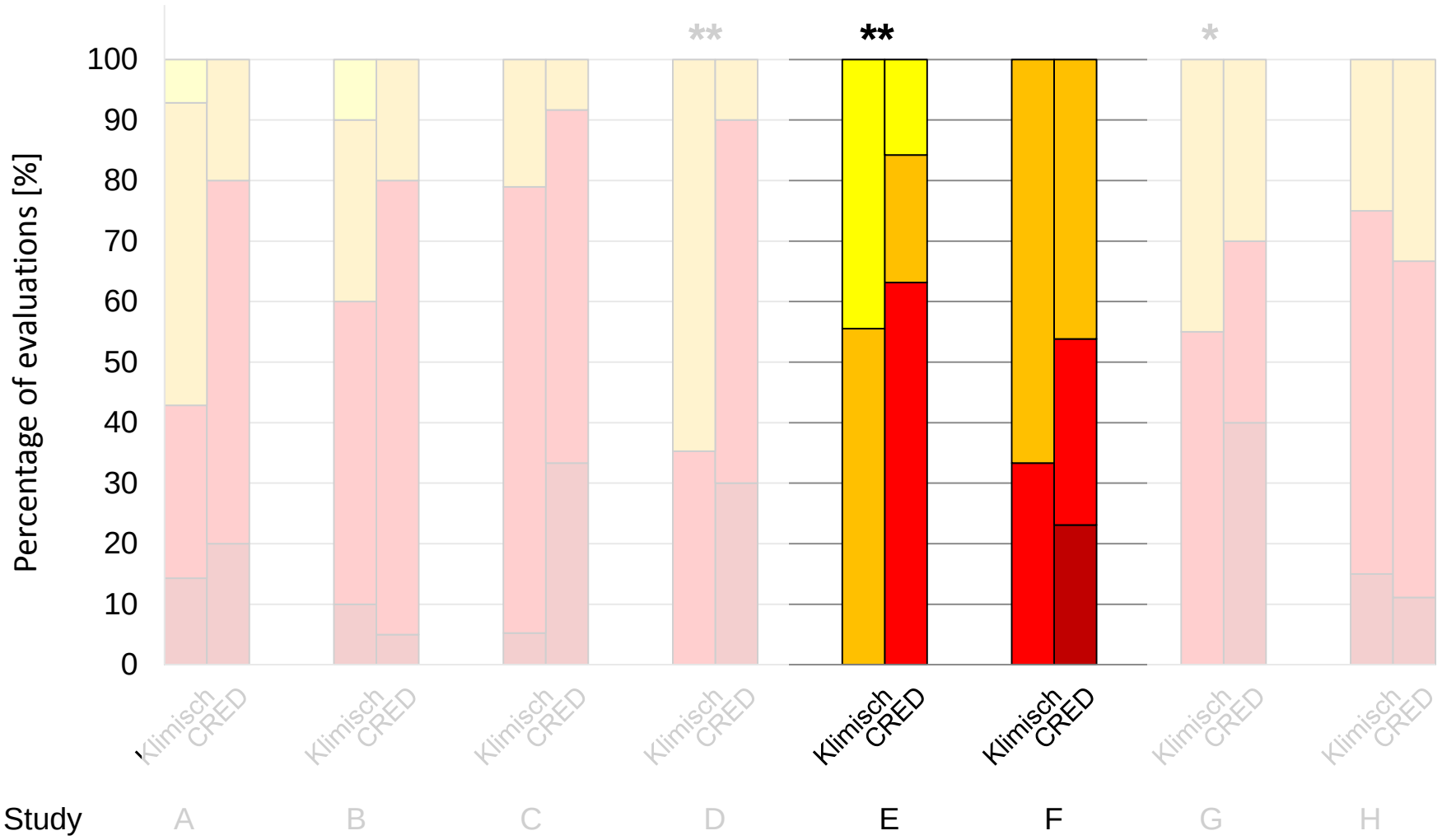
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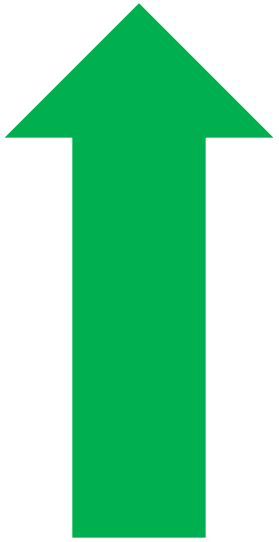
Other effects when CRED is used?

- More consistent results
- More transparent evaluations

Risk assessors opinions Klimisch → CRED

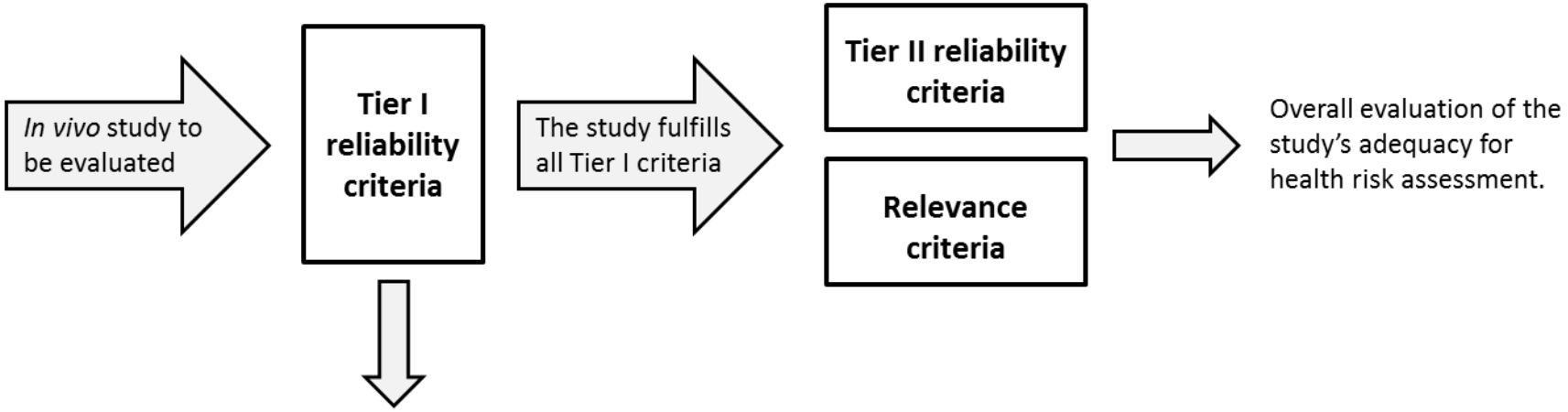
- Accuracy of reliability evaluation
- Accuracy of relevance evaluation
- Easy and applicable for routine use
- Consistency
- Dependence on expert judgment
- Transparency
- Useful additional guidance for CRED



Take home message

- The CRED method: Useful and appreciated tool
- Should be used in combination with expert judgment
- Quality never goes out of style
- Looks can be deceiving

New evaluation method for Toxicity studies



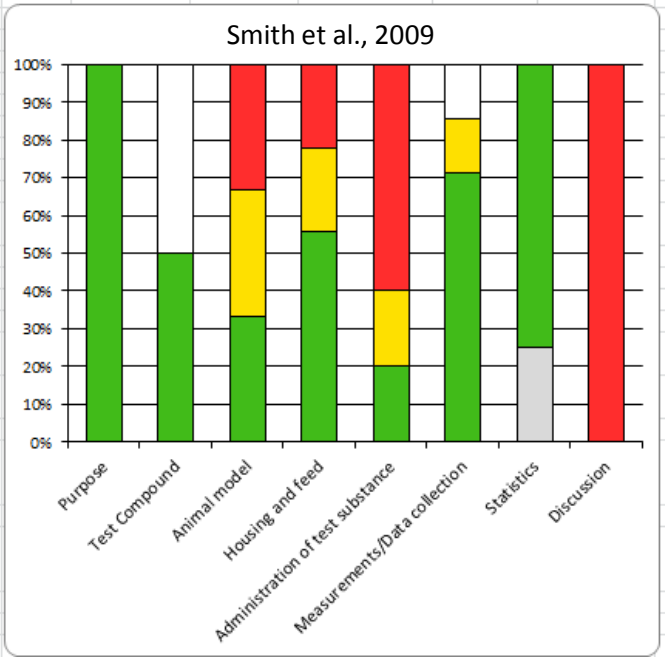
Wanted! Ringtest participants

Beronius et al. 2014. J Appl Toxicol.

SciRAP: Web-based color-coding tool

Not determined	1
Fulfilled	18
Partially fulfilled	5
Not fulfilled	7
Not applicable	2

Purpose	
The purpose of the study has been stated.	Fulfilled
The endpoints to be investigated have been stated.	Fulfilled
Test Compound	
The vehicle is described.	Fulfilled
Any fluorescent- or radiolabelling, etc. is described.	Not applicable
Animal model	
The motivation behind the choice of animal model (species and strain) is given, i.e. why one species or strain is preferred above	Not fulfilled
Animals have been individually identified.	Fulfilled
The method for individual identification of animals is stated.	Partially fulfilled
Housing and feed	
Housing conditions are described, i.e. temperature, relative humidity, light-dark cycle and number of animals per sex in each cage.	Fulfilled
Cage materials, including any physical enrichment, and water bottle materials are described.	Fulfilled
The bedding material used is described.	Not fulfilled
Considerations have been made to minimize the content of substances in the selected bedding material that may affect the toxicity of the compound being investigated, such as	Partially fulfilled
The type and source of feed are reported.	Fulfilled
The feed has been analyzed for contaminants that could impact study objectives, such as pesticide residues, persistent organic pollutants, heavy metals and mycotoxins.	Partially fulfilled
The feed has been analyzed for phytoestrogen content.	Fulfilled
The source of drinking water is reported.	Fulfilled
The drinking water has been analyzed for contaminants that could	



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Molander et al. 2014. Hum Eco Risk Assess

Future work

- Evaluation method for nanoecotoxicity studies

- ”Weight of evidence” method for EDCs

“From daily life everybody is familiar with the essence of Weight of Evidence reasoning and its basic mechanism may be regarded as a matter of common sense.“

REACH guidance (2011)

Future work

- Evaluation of dossiers for industrial chemicals within the REACH legislation
  - Best chemicals legislation in the world?
  - “No data, No market”: 70% are non-compliant
  - 70% of companies claimed to be smaller to get reduced fee
  - 73-95 % of REACH risk limits were numerically higher than Dutch environmental quality standards
  - “going beyond the legal requirement of checking 5% of the dossiers is not in the interest of the registrants”

SETAC Pellston workshop Sep 2015

Chair: Marlene Ågerstrand and Jane Staveley. Wanted! Participants

1. *Ecotoxicity science quality: Improve quality and reporting of science*

2. *Reliability criteria for evaluation of ecotoxicity studies: Improve evaluation*

3. *Relevance of research to inform regulatory decisions: Increase acceptance of non-GLP studies*

4. *Weight of evidence: Identify available methods and problems in this process*

5. *Regulatory impact: Identify successful examples and strategies*

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Thank you!
Questions?

Please contact me for copy of publications and presentation

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MISTRA
The Swedish Foundation for Strategic Environmental Research