National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Mixture risk assessment from science to policy

BfR Symposium One Substance one Approach, the next 20 years

Jacob van Klaveren

Content

- European cooperation is essential for implementing mixture risk assessment in to policy (EU funded projects, EFSA-RIVM Partnership)
- Chemical Strategy for Sustainability and EFSA Roadmap RACEMiC (Risk Assessment Combined Exposure to Multiple Chemicals)
- Partnership PARC and the use of Human Biomonitoring Data covering all routes of exposure

European Regulation (EC) 396/2005

Article 14 (Decision on applications concerning MRLs):

"…account shall be taken of:

a) the scientific knowledge available

b) the possible presence of pesticide residues arising from other sources than current plant protection uses of active substances, **and their known cumulative and synergistic effects, <u>when the methods to assess such effects are available</u>…"**

Why mixture risk assessment in 2001?

- Consumer concern
- European Parliament
- Regulation 396/2005, art 14
- EFSA in charge to propose the methodology
- EU funded project funded by the European Commission in 2010 (tools, methods and training)

Dutch Government RIVM and EFSA Framework Partnership I, II and III

- First partnership 2015-2019 (as follow-up of the ACROPOLIS project) aiming to help EFSA with the pilot projects on cumulative risk assessment
- Second partnership 2019-2021 aiming to implement pilot projects in regulatory process
- Third partnership 2022-2025 open MCRA, make models available for European regulatory process and FAIR models

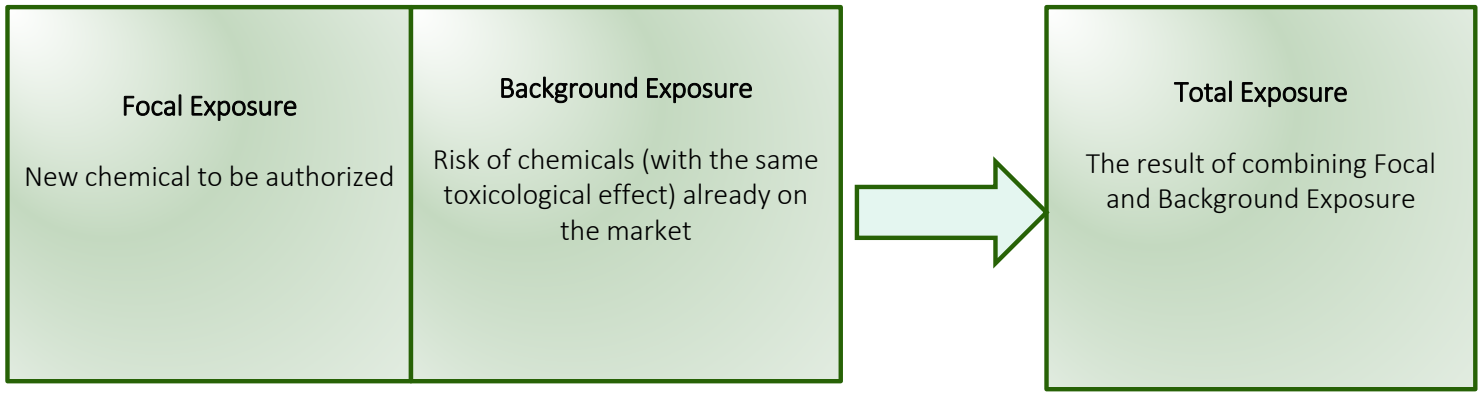
Protection goals set by the European Commission

- Threshold of regulatory consideration

- Margin of Exposure Total (MOET) at P99.9 > 100

- DG SANTE Sco PAFF agreed on settings to perform exposure assessment here

EFSA – RIVM FPA II how to assess the cumulative risk of a new pesticides to be authorised (prospective CRA)



RIVM report Proposed prospective scenarios for cumulative risk assessment pesticides Click **here**

EFSA-RIVM Partnership III tools (models)

EFSA-RIVM Partnership III (2022-2025)

- We- based MCRA software: mcra.rivm.nl
- Standard regulatory user interfaces for regulators
- Co-creation new models (e.g. aggregated exposure)
- Data connectivity (e.g. data from all EU Member States)
- Capacity building & training

Cooperation in EuroMix and beyond

ELSEVIER

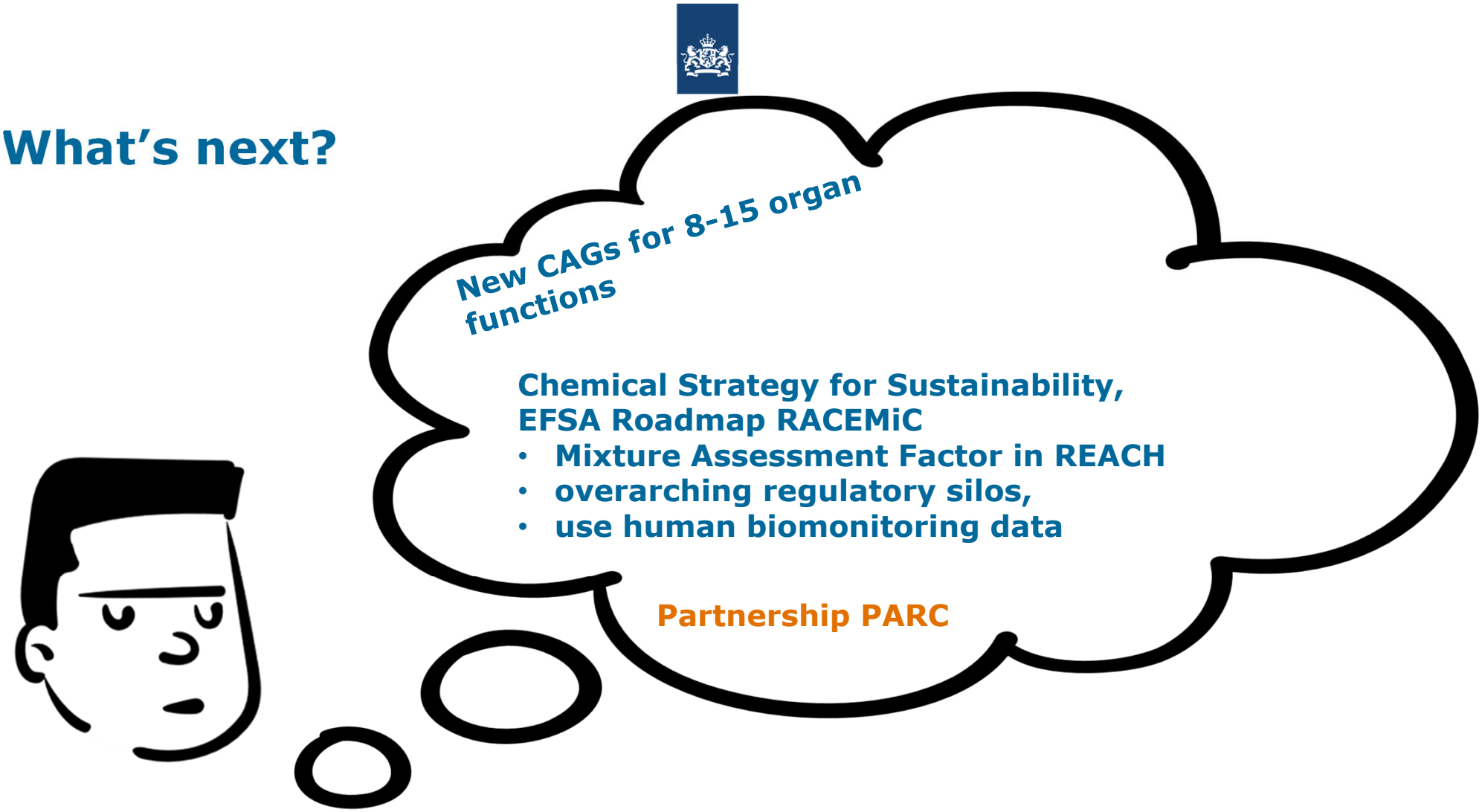
Food and Chemical Toxicology

Volume 141, July 2020, 111388

Recommendations for international harmonisation, implementation and further development of suitable scientific approaches regarding the assessment of mixture effects

Benjamin C. Fischer [1], Stefanie Rotter [1] ✉, Jens Schubert, Philip Marx-Stoelting, Roland Solecki

What's next?


New CAGs for 8-15 organ functions
Chemical Strategy for Sustainability,
EFSA Roadmap RACEMiC
• Mixture Assessment Factor in REACH
• overarching regulatory silos,
• use human biomonitoring data
Partnership PARC

EFSA's 20 years anniversary (One Conference)

2022 EU CONFERENCE one
HEALTH • ENVIRONMENT • SOCIETY

Published on the conference website.

- Regulatory needs from scientific perspective
- Regulatory needs to implement MAF
- Experiences from US-EPA
- How to use Human Biomonitoring Data
- Scientific and data driven methods
- Need to act now to protect humans and the environment

Legal provisions to take account of unintentional mixtures are needed in the relevant legislation, such as REACH, cosmetics, toys, food contact materials, food additives

- *Introducing mixture assessment factor(s) for the chemical safety assessment of substances under REACH*
- *Further development of more specific and targeted methodologies for specific policy areas*

European Commission

Targeted and science based methods

Development of a roadmap for action on: Risk assessment of combined exposure to multiple chemicals

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WAGENINGEN UNIVERSITY & RESEARCH

DTU

BfR
Bundesinstitut für Risikobewertung

Overview of the RACEMiC project

E. de Jong, H. van der Voet, P. Marx-Stoelting, S. Hougaard Bennekou, C. Sprong, D. Block, A. Burchardt, A. Lasch, T. Opialla, S. Rotter, E. Bay Wedebye, A. Zwartsen, A. Leys, M. Zare Jeddi, G. Wolterink, J. Kruisselbrink, W. de Boer, J. van Klaveren

Why the need for a roadmap on mixture risk assessment?

Current risk assessment practices mainly rely on the assessment of chemicals within separate legislative frameworks.

EU legislation on pesticides

EC No. 396/2005 and 1107/2009

EU legislation on contaminants

EEC No. 315/93

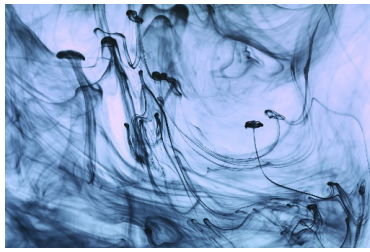
EU legislation on food additives

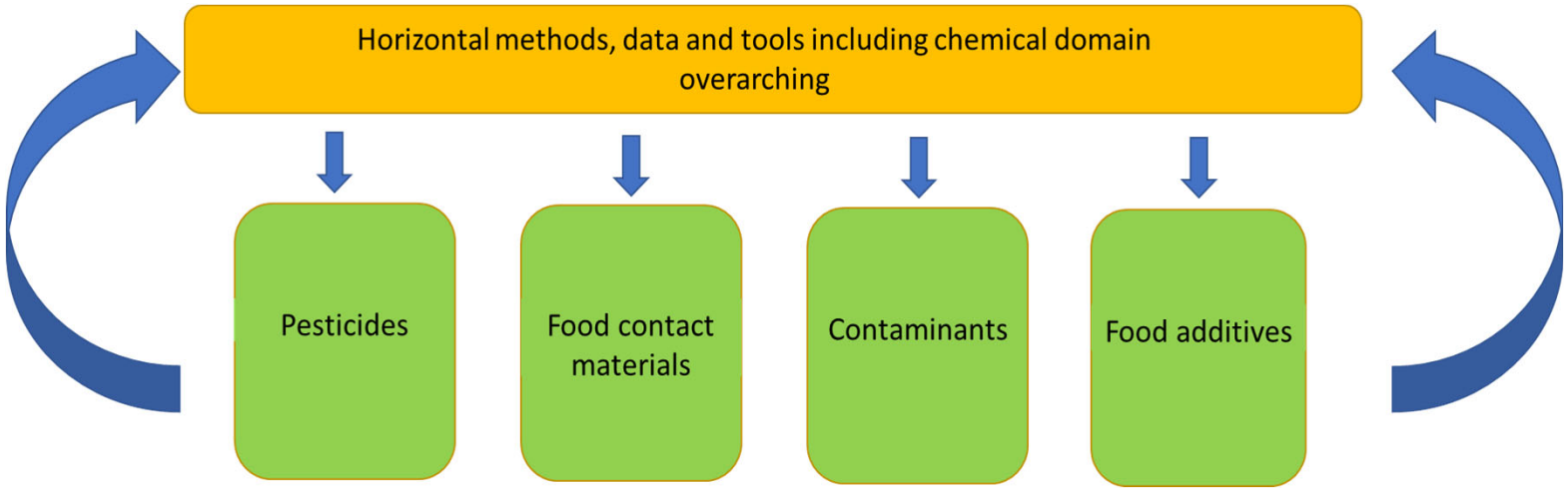
EC No. 1331/2008

EU legislation on food contact materials

EC No. 1935/2004

Methodology to develop the roadmap





Overview of working areas

PARC WP6 innovation in regulatory risk assessment (RIVM-KEMI leadership)

Task 6.1: To establish **quantitative AOP networks** and assess their **human relevance** using a **pragmatic workflow**. This output is then used for the development of **IATAs for selected health effects**

Joint annual WP6 workshop with stakeholders to collect feedback & input

WP5-WP6 interaction

Task 6.2: To perform integrative exposure assessments
PARC Project Aggregated Exposure
PARC Project Kinetics through life
PARC Project Real-life mixtures

BfR German Federal Institute for Risk Assessment
Philip Marx-Stoelting - BfR

anses
Gilles Rivière - ANSES

WP5

PARC project real-life mixture using HBM data from Member States

1

Selection HBM dataset, populations and chemical groups from HBM data inventory (done)

2

Integration in MCRA of statistical analysis and format HBM data for uploading (training 7-11 November)

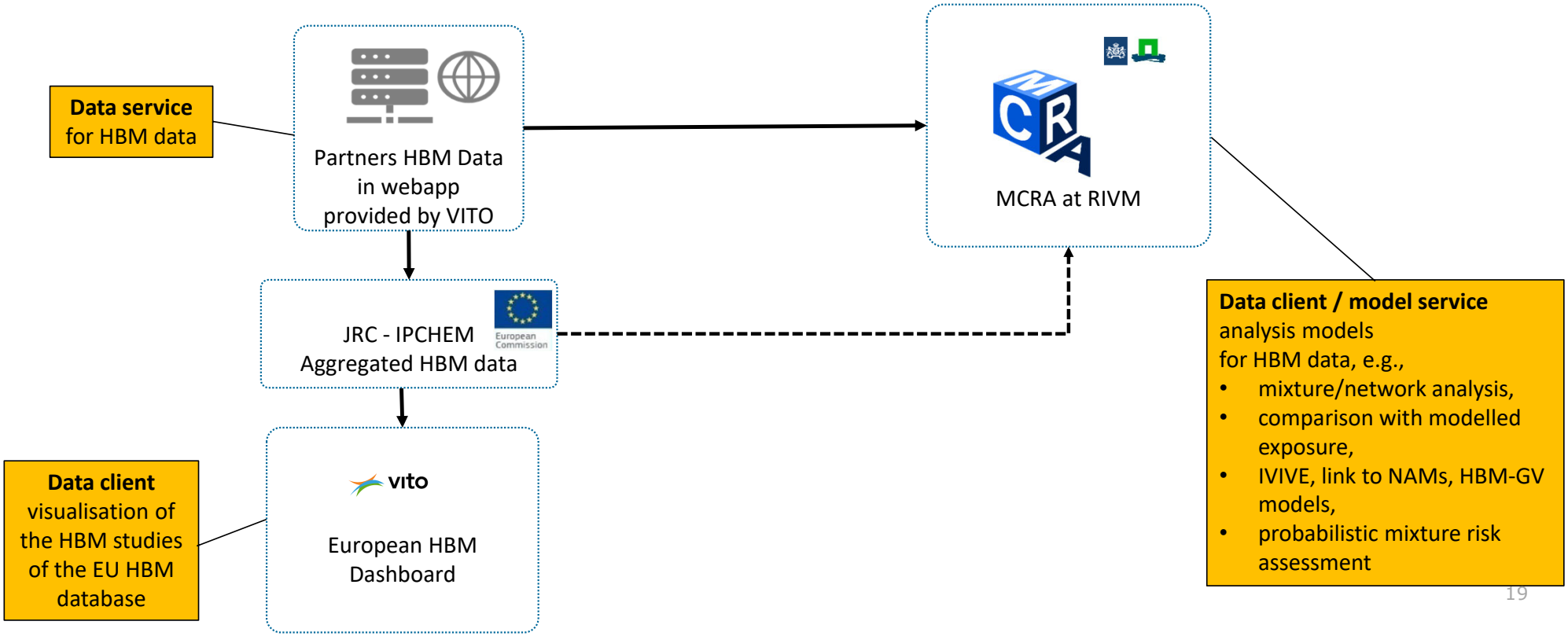
3

Application of statistical analysis by each partner using MCRA software

4

Send results to ANSES and RIVM for combination and integration in a joint scientific paper

PARC cooperation on mixture risk assessment using HBM data and MCRA



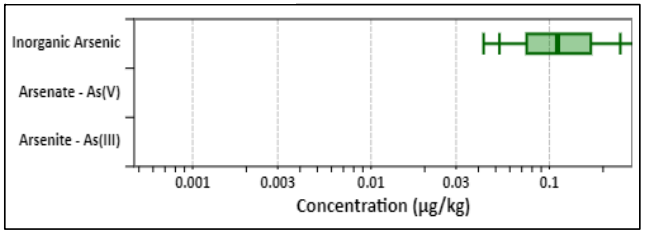
PARC cooperation on kinetic models for MRA

Short term (for application in PARC project real-life mixtures):

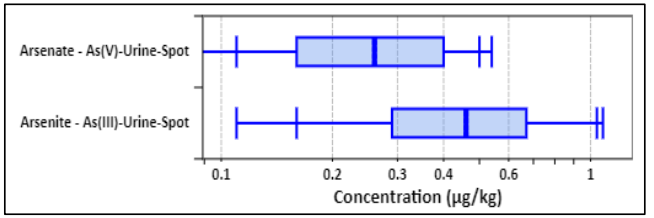
- MCRA contains kinetic models from EuroMix project and Dutch projects
- 10 cooperation partners on kinetic modelling of the PARC prioritised chemicals

Potential link to kinetic models in WP5

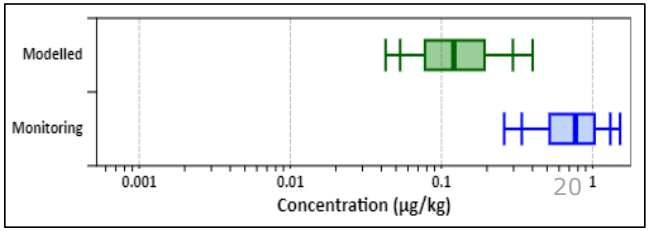
Modelled



Monitoring



Modelled vs monitoring



What if your twenty years older

- International cooperation on mixture risk assessment is a critical success factor for implementing MRA

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Thank you for your attention!

Acknowledgement: RIVM colleagues, EuroMix partners, PARC project real-life mixture partners and Wageningen Research Biometris