2016 Food Packaging Forum workshop, Oct 25, Zurich
"Food contact materials in the circular economy"

Swedish regulatory toxicology perspective

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We work for

- **safe food and drinking water**
- fair practices in the food trade
- healthy eating habits

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Agenda

- ”State of the art” of evaluation FCM substances – more complicated than ever before
- Suggested ways ahead
- Outlook for the future - FCM in the circular economy
- Risk thermometer

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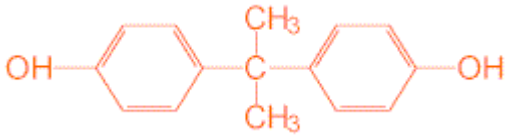
Complexity

Difficulties regarding:

Substance evaluation: oligomers, NIAS, nano, EDC, (GMO), (mixtures), antimicrobials



Materials: multilayers, **biobased, biodegradable**, active and intelligent, nanomaterial, **recycled, reused**

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Challenges for agencies

Substance evaluation

- >10 000; <15 substances in plastics evalutated by Efsa/year (cf CoE-Belgium database)

- Analytical methods: higher sensitivity of analytical methods ->
  - ”We are finding more and more, of less and less” (more NIAS, lower LoDs)

- Toxicology: low dose toxic effects, eg EDC?
- combination effects??

Environment

- environmental requirements
- sustainability in a circular economy

Economy

- less resources in money and toxicologists

Priorities

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List of substances of the European Scientific Cooperation (ESCO) WG (cooperation - EFSA)

Materials	Total	List A/under revision	Country
Paper&board	600	145	DE,FR,IT,NL
Colorants	280	134	FR,CH
Rubber	800	21/400	CZ,DE,FR, IT,NL
Silicones	57	8	DE,FR,ES
Printing Inks	987		CH
Cork&Wood	54	2	NL
Coatings	650	10	NL

List A: substances evaluated after 1991 (according to the first version of Scientific for Foods Guidelines for FCM, EU)

Over 3200 substances are used and not evaluated by MS (see EFSA, 2011; http://www.efsa.europa.eu/en/supporting/pub/139e.htm.)

Thousands more are used and not evaluated by MS

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”Non-evaluated substances”
”Evaluated of concern”

- ”*Printed paper and board FCM as a potential source of contamination”;* Van Bossuyt et al; Reg Tox and Pharm volume 81 (2016), page 10-19- **6000 substances in printed paper and board FCM; 77% non-evaluated**

- Geueke, B.,Wagner, C.C., Muncke, J., 2014. *Food contact substances and chemicals of concern*: a comparison of inventories. Food Add. Contam. Part A. Chem. Anal. Control Expo. Risk Assess. 31 (8), 1438-1450.

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Supportive ways

- Biomonitoring:
  - trends
  - ”real” total exposure
- (Adductomics)

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Biomonitoring - POPUP

- Persistent Organic Pollutants in Primiparous Women from Uppsala
- Basic aim: **Examine changes in chemical exposure over time**
- Financed by: Swedish Environmental Agency (EPA; the Health-Related Environmental Monitoring Program) and National Food Agency
- Randomly recruited first-time mothers covering a full year
- **Sampling of mothers´s milk, hair, urine (from 2009) and blood 3 weeks after delivery**
- Samples were bio-banked

Year	1996-99	2000-2006	2007-2016
No	211 (each year)	30 (every second year)	30 (each year)

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Chemicals monitored

- From 1996 – mother´s milk
  - Dioxins, PCB, chlorinated pesticides, brominated flame retardants (BFR)
- From 1996 - blood
  - **Poly- och perfluorinated alkyl acids (PFAS**), BFR
- From 1996 - hair
  - Mercury
- From 2009 (urine)
  - **Phthalates, phenolic substances (e. g. bisfenols, triclosan**, phenolic metabolites of pesticides, metabolites of phosfor- based flame retardants

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DiNCH

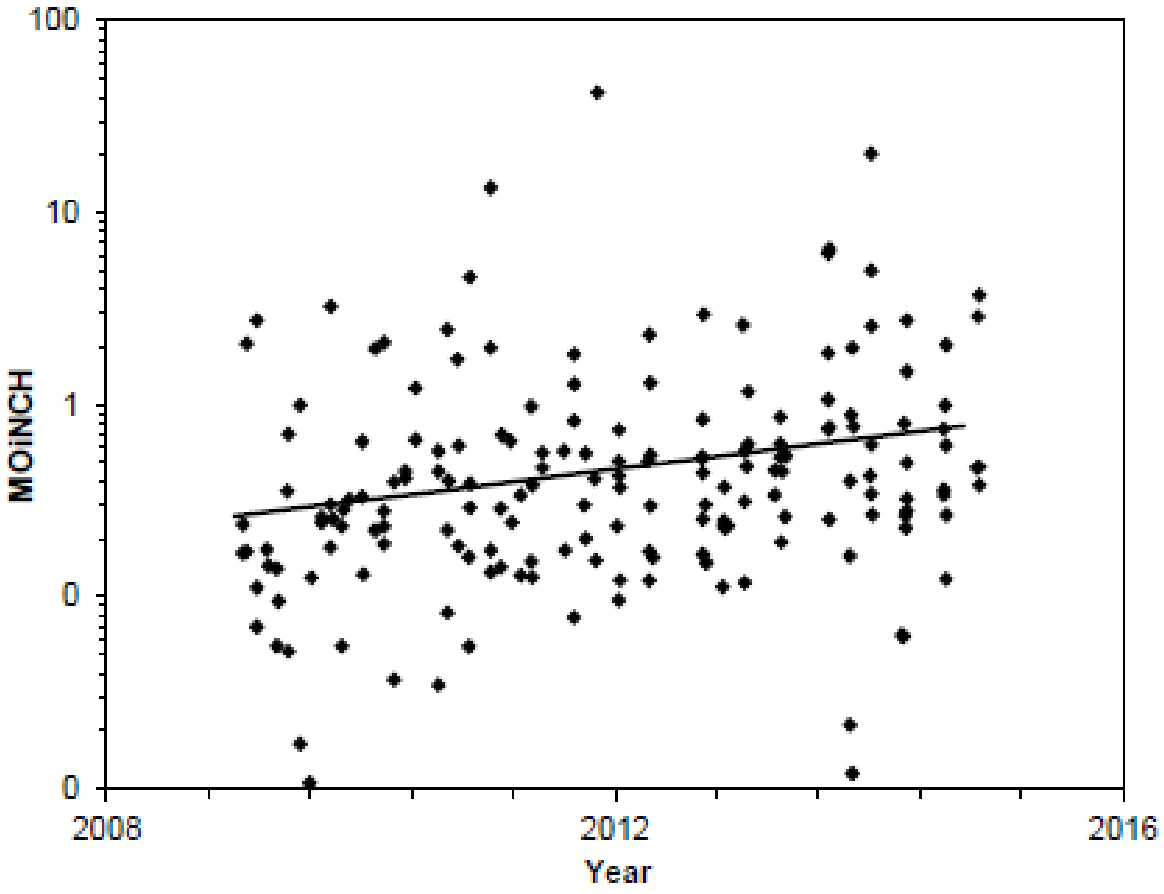

Figure 1. Temporal trend of urine concentrations of MOiNCH (ng/ml), a metabolite to DiNCH, in first-time mothers from Uppsala, Sweden, during the time period 2009-2014.

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BPA

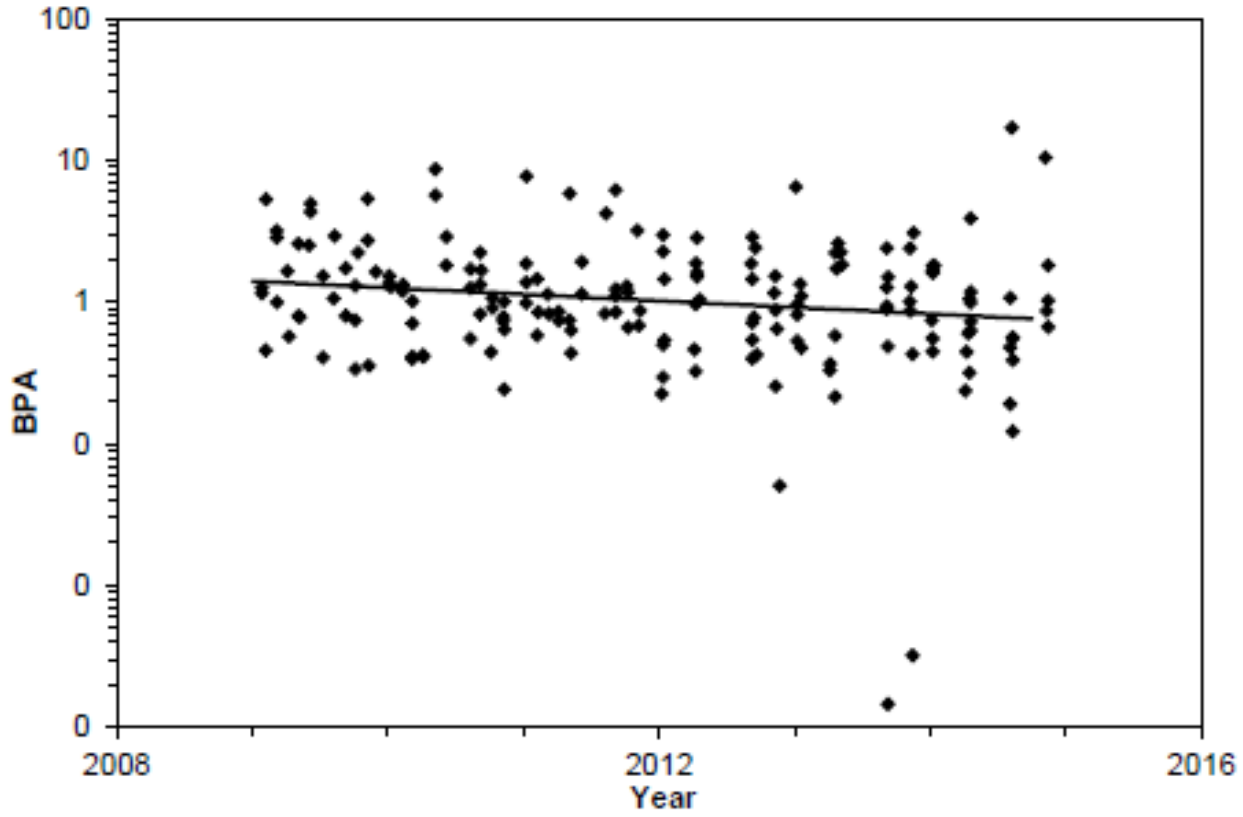

Figure 2. Temporal trend of urine concentrations of BPA (ng/ml) in first-time mothers from Uppsala, Sweden, during the time period 2009-2014.

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BPF

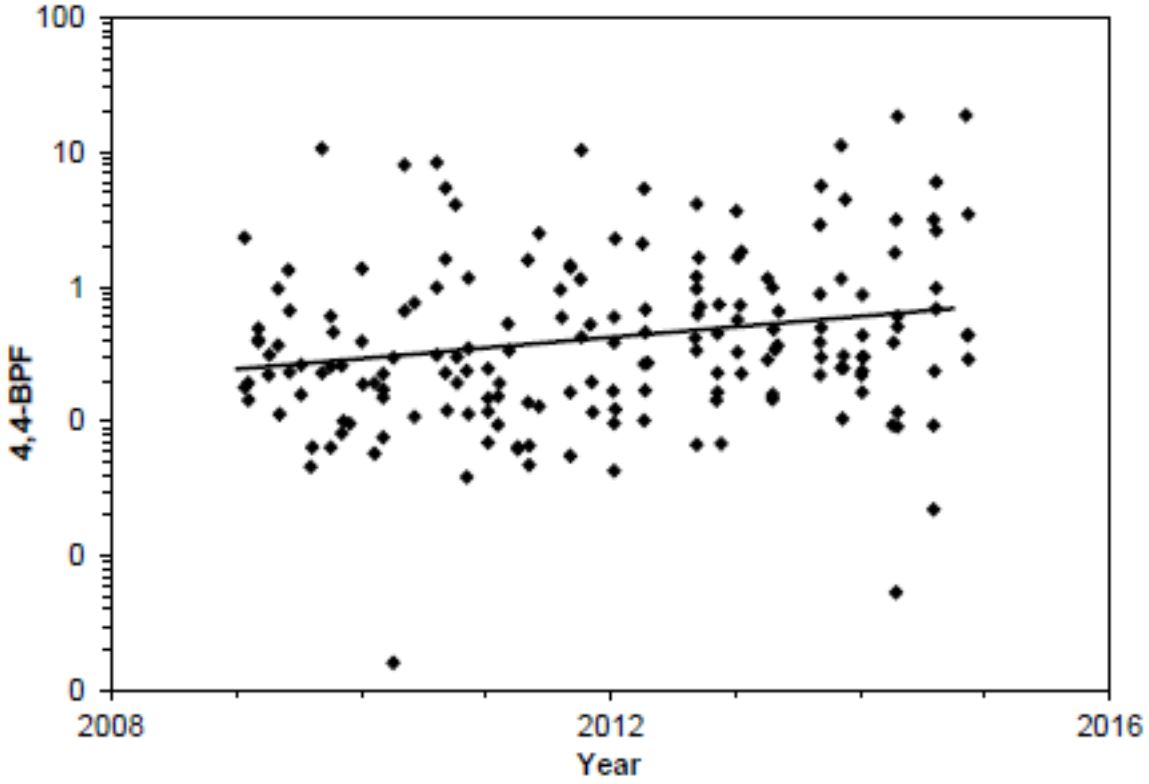

Figure 3. Temporal trend of urine concentrations of the bisphenol 4,4-BPF (ng/ml) in first-time mothers from Uppsala, Sweden, during the time period 2009-2014.

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Adductomics

Hb-adduct
DNA-adduct
(from reaction
of electrophile)

Screening of unknowns using adductomics

- In blood, variuos tissues - DNA, Hb (hemoglobin) etc
- Identify reactive (electrophiles) using Hb and LC/MS/MS
- Papers by e.g. H. Carlsson:
- Carlsson, H et. al; (2015) Characterization of a Hemoglobin Adduct from Ethyl Vinyl Ketone Detected in Human Blood Samples. Chem. Res.Toxicol 28, 2120-2129
- Carlsson H. and Törnqvist M. (2016) Strategy for identifying unknown hemoglobin adducts using adductome LC-MS/MS data: Indentification of adducts corresponding to acrylic acid, glyoxal, methylglyoxal and 1-octen-3-one Food and Chemical Toxicology 92, 94-103

- **Combined with in vitro gen tox test (micronucleus test)**

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However?? Food safety <–> Environmental concern - sustainability?

- **What is sustainability?**
- *Is made from a material that is grown (biobased)* - ***moisture sensitivity, natural toxic compounds?***
- *Is recyclable (paper and board)* – ***unknowns?***
- *Has been recycled (paper and board)* – ***unknowns?***
- Results in no air pollution
- *Has the potential to be reused* - ***unknowns***
- *Is bio-degradable* - ***moisture sensitivity, natural toxic compounds?***
- Is made using renewable energy
- Generates zero landfill waste
- Minimizes water usage
- Lasts a long, long time
- Creates no greenhouse gases
- Protects human health
- Helps to minimise food loss

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Suggested ways ahead for evaluation of un(knowns) and mixtures

- **Evaluation**
- **Transparency**
- **Collaboration**
- **Legislation**

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Suggestions

Evaluation – need for multiple ways:

What is in the packaging/materials? Risks?

- More data sharing (e. g. EFSA-ECHA)

- Screening of packaging/materials X bioassays (tox)
  - *e. g. "Emerging Chemicals in food packaging – toxicological profiling of knowns and unknowns"* (DK)
  - In vitro bioassays (e.g. Tox Cast)
- Computional toxicology (in silico methods) →

- Priority setting for further tox studies

What gets into my body?

- **Biomonitoring (including e.g. adductomics)**
- Exposure driven - > based on exposure, not migration (cf Efsa)-> more realistic exposure!

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Suggestions

Transparency:

- *What chemicals are used?* Industry!

- *Better risk communication* – Agencies etc ->gain in consumer confidence

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Suggestions

Collaboration:

- Nordic cooperation
- Council of Europé work
- **Efsa network**
- **EURL**
- **Joint projects etc**

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Suggestions

Legislation:

- Mutual recognition (national legislations)?
- Iniate further harmonisation – paper and board – save time for tox studies
- Tracebility – better source control
- Develop RASFF

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Nordic collaboration projects

- Plastförpackningar till livsmedel (1989, in Swedish)
- Papper och kartong i kontakt med livsmedel (1992, in Swedish)
- Packaging materials and cookware for food contact at high temperatures (1993)
- Paper and board based on recycled fibres in food contact (1994)
- Laquers in cans (1998)
- Active and intelligent food packaging (2000)
- FCM control
- Adhesives in food contact materials and articles (2001)
- Food reduction/consumption factors (2003)
- Food contact materials - Check lists (2008)
- Surface coatings
- Paper and board food contact materials (2008)
- Food contact materials and articles: Printing Inks (2012)
- Food contact materials - metals and alloys (2015)
- Food control – DoC (2015)

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CoE cooperation projects

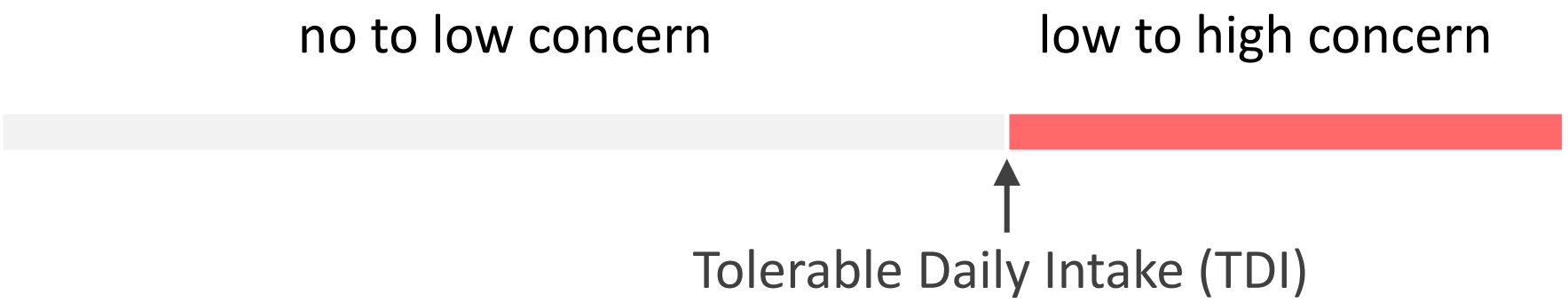
- Resolution AP (89) 1 on the use of colourants in plastic materials coming into contact with food
- Resolution AP (92) 2 on control of aids to polymerisation for plastic materials and articles
- Resolution AP (96) 5 on surface coatings intended to come into contact with foodstuffs
- Resolution AP (99) 3 on silicones used for food contact applications
- Resolution AP(2002) 1 on paper and board materials and articles intended to come into contact with foodstuffs
- Framework Resolution AP (2004) 1 on coatings intended to come into contact with foodstuffs
- Resolution AP (2004) 2 on cork stoppers and other cork materials and articles intended to come into contact with foodstuffs
- Resolution AP (2004) 3 on ion exchange and adsorbant resins used in the processing of foodstuffs (superseding Resolution AP (97) 1)
- Resolution AP (2004) 4 on rubber products intended to come into contact with foodstuffs
- Resolution AP (2004) 5 on silicones used for food contact applications
- Resolution AP (2005) 2 on packaging inks applied to the non-food contact surface of food packaging materials and articles intended to come into contact with foodstuffs
- - Guidelines on metals and alloys ;
- - Guidelines on lead leaching from glass tableware into foodstuffs;
- - Guidelines on tissue paper kitchen towels;
- Metals and alloys used in food contact materials and articles (2013)

The Risk Thermometer

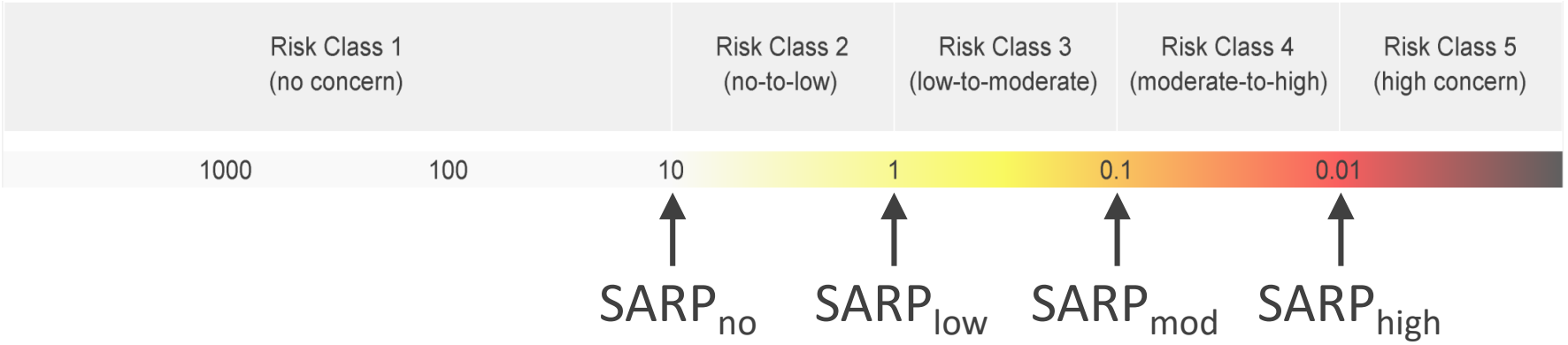
- **Risk communication**
- **Priority setting**

http://www.livsmedelsverket.se/globalassets/rapporter/2015/the-risk-thermometer.pdf

Traditional risk assessment

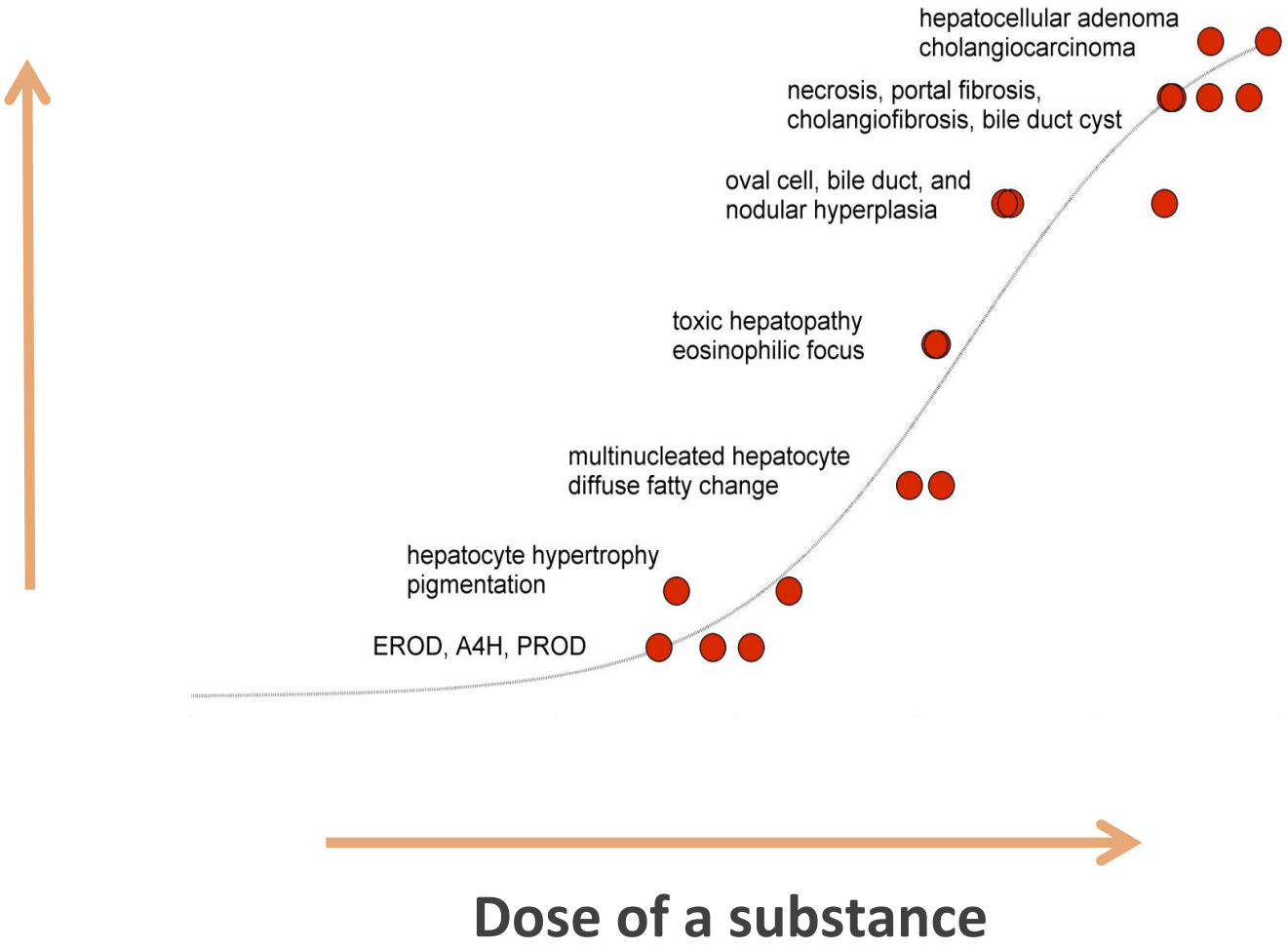


Risk thermometer - *5 "risk classes"*



"SAMOE approach = severity adjusted margin of exposure approach"

SARP = Severity adjusted reference point


Severity
hepatocellular adenoma
cholangiocarcinoma
necrosis, portal fibrosis,
cholangiofibrosis, bile duct cyst
oval cell, bile duct, and
nodular hyperplasia
toxic hepatopathy
eosinophilic focus
multinucleated hepatocyte
diffuse fatty change
hepatocyte hypertrophy
pigmentation
EROD, A4H, PROD
Dose of a substance

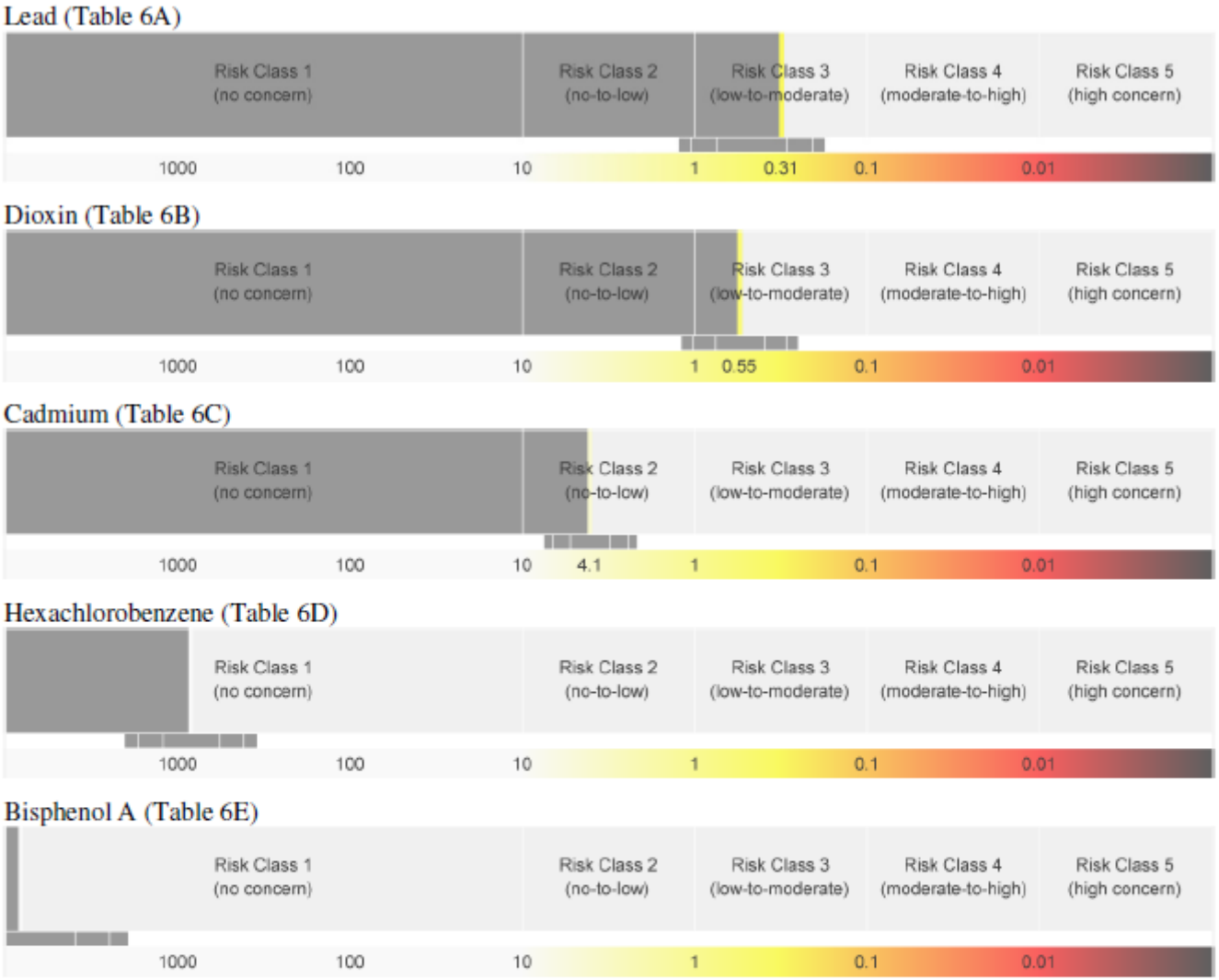


Figure 4: Illustrations of the results in Tables 6A-6E.
The wide gray bars describe the SAMOE estimate that classifies in a particular Risk Class that corresponds to a level of health concern (see Table 4). The thin gray bars describe the uncertainty in the SAMOE. The full uncertainty interval describes the lower 5th and upper 95th confidence limits. The 10th/90th confidence limits, as well as the 25th/75th confidence limits are also shown. For lead and dioxin, the 90 % confidence limit spans another Risk Class (Risk Class 2). Therefore the uncertainty in the risk classification is "moderate" (in the downward direction) for these two compounds (see also Table 5 and Table 6A-E).

Conclusion – ways ahead

- **Evaluation**: data sharing, screening of mtrls, human biological samples, prioritize
- **Transparency** (chemical identification, risk communication)
- **Collaboration** (networks, projects)
- **Legislation** (mutual recognition, tracebility, harmonisation)

- ***Acknowledgement*:**
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