



Food contact materials: Chemical risk assessment and practical challenges

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Food Packaging Forum Foundation

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About Food Packaging Forum (FPF)



- Founded in 2012
 - Charitable foundation, non-profit
 - Based in Zurich, Switzerland
 - Governed by foundation board: independent academic scientists, science communication experts (*pro bono*)
 - Funded by donations and project grants
 - Team of 5 trained scientists
- Science communication on all food contact materials (FCMs): chemicals in FCMs and their impact on health
- Raise awareness w/ professional stakeholders, improve protection of public health



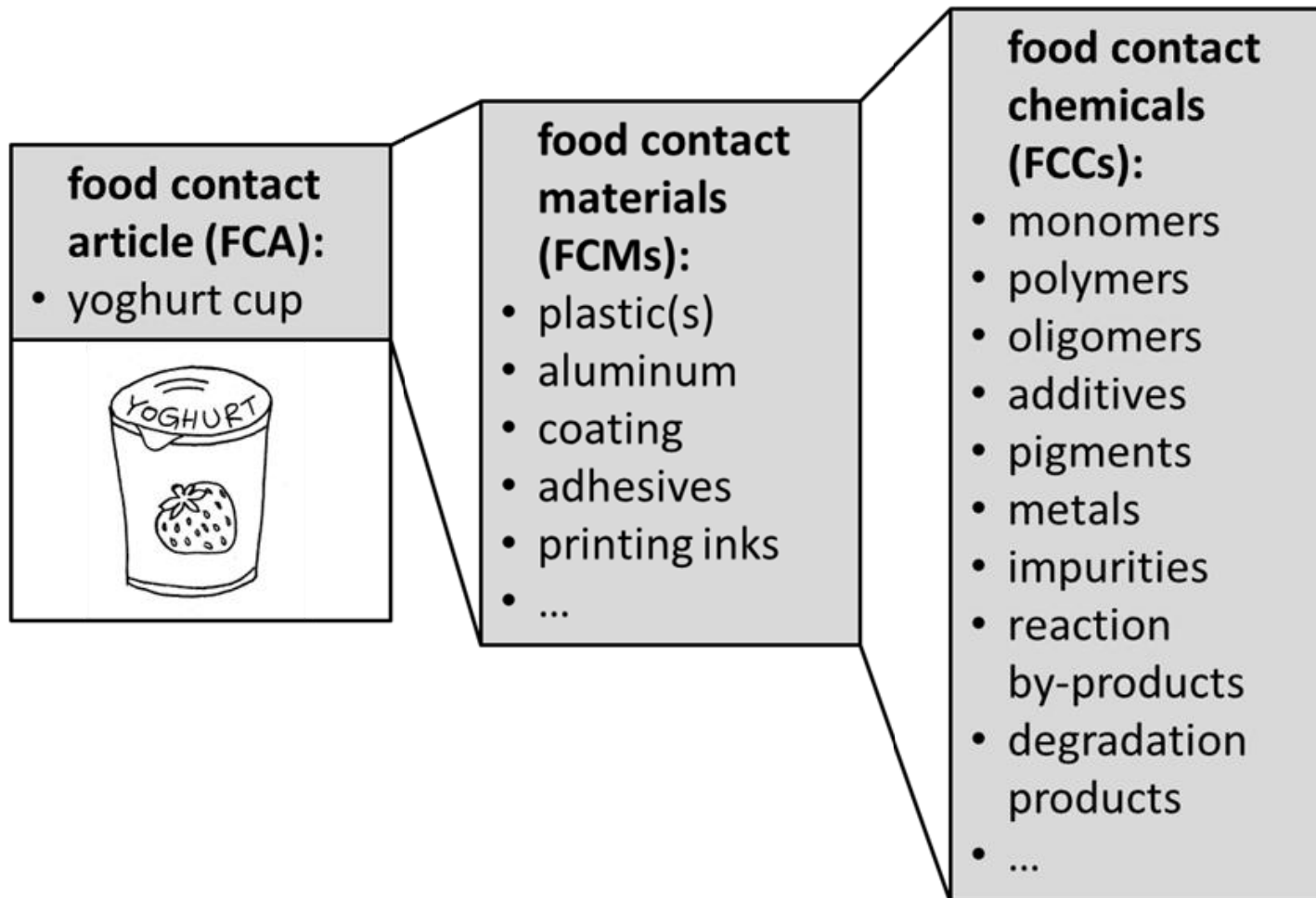
Science communication at FPF

- Daily news updates on website
- Bi-monthly newsletter (free to sign up)
- Background information, researched and compiled by trained scientists (“Dossiers”)
- Annual workshop: stakeholder/experts dialogue
- Issue owner and go-to address for stakeholders: policy makers, experts at NGOs or industry, scientists, journalists
- Peer-reviewed scientific publications

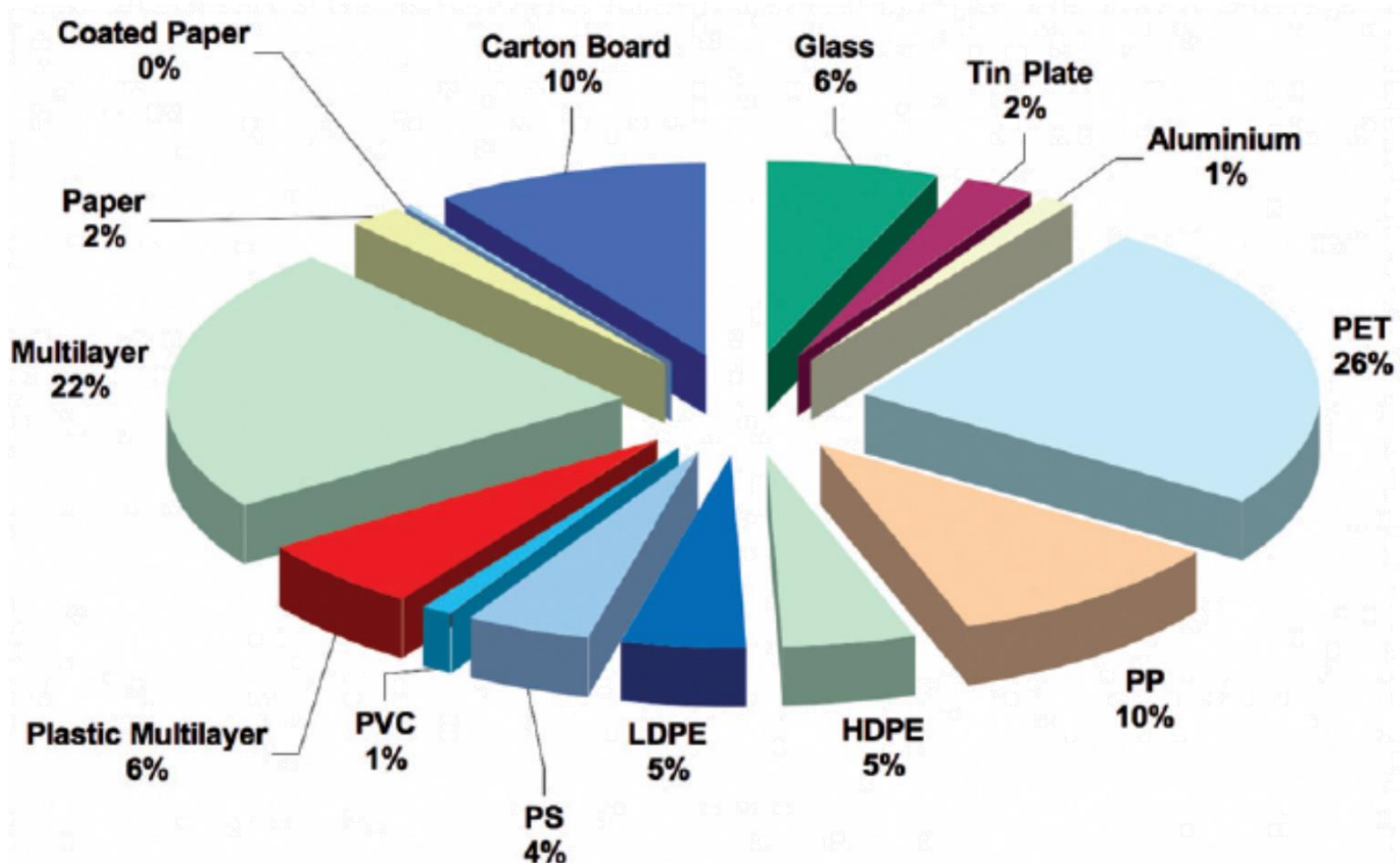




Food contact materials (FCMs), articles (FCAs) and chemicals (FCCs)



Food packaging materials: Portuguese market study (2009)



→ mostly plastic is in direct contact with food (and beverages)

17 FCMs in EU (1935/2004), Annex I

1. Active and intelligent materials and articles*
2. Adhesives
3. Ceramics*
4. Cork
5. Rubbers
6. Glass
7. Ion-exchange resins
8. Metals and alloys
9. Paper and board
10. Plastics* (recycled*)
11. Printing inks
12. Regenerated cellulose*
13. Silicones
14. Textiles
15. Varnishes and coatings
16. Waxes
17. Wood

* FCM with harmonized EU-wide measure in place

Food contact chemicals (FCCs)

1. used in the manufacture of FCMs

intentional use/presence intended*

food contact substances

> 8030 substances [JRC 2016](#)

2. present in the finished FCAs but non-intentional

non-intentionally added substances **NIAS**

number unknown (estimates range: 10'000 – 100'000;
[McCombie 2016](#) talk at [EU Parliament workshop](#) on FCMs)

chemical identity often unknown [FPF 2014](#); [ILSI Europe 2015](#)

* i.e. intentionally formed from different intentionally used substances

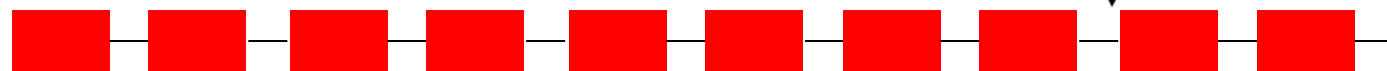



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Plastics

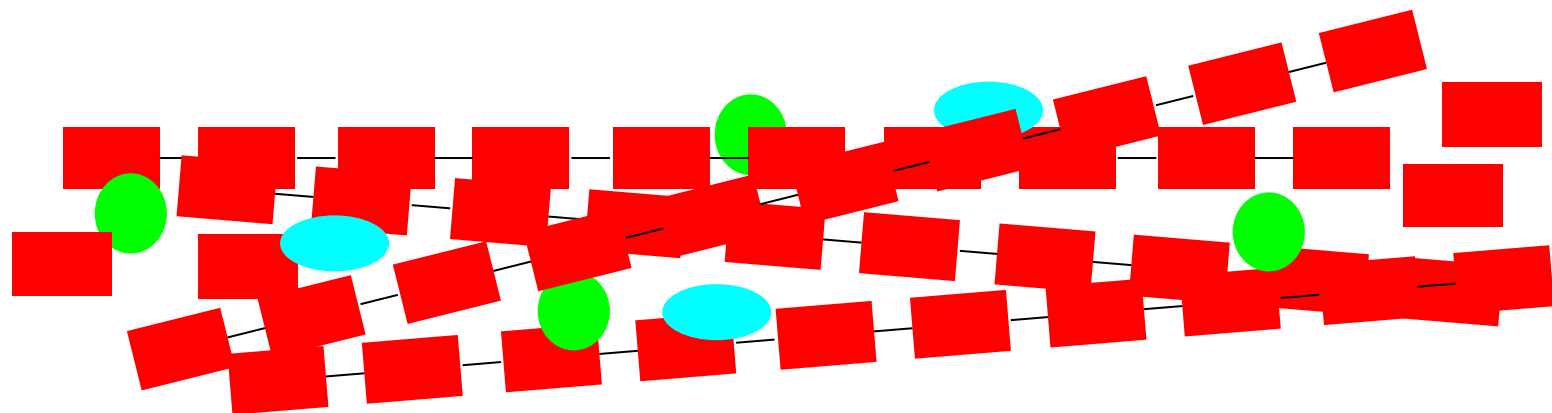


 monomer

 polymer

 additives: optimization of plastic material properties

 NIAS (non-intentionally added substances): side products, impurities, break down products

 plastic: complex chemical mixture

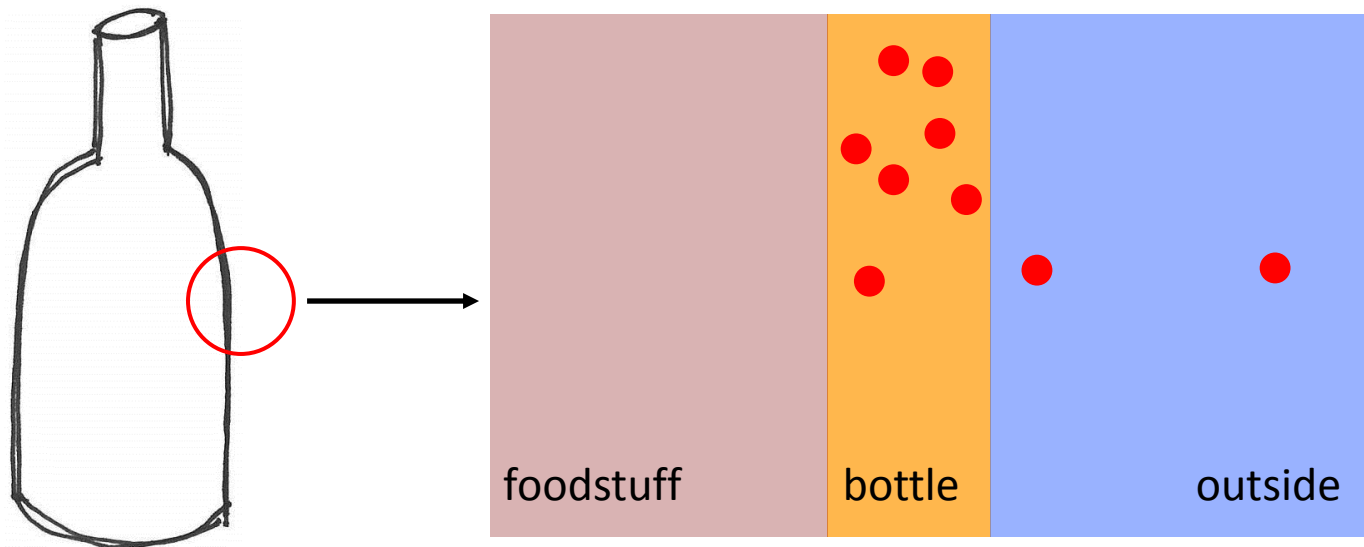
→ Identification of all NIAS is technically highly challenging and not always possible

Bradley and Coulier 2007 UK FSA Report FD 07/01 An investigation into the reaction and breakdown products from starting substances used to produce food contact plastics.

[Hoppe et al. 2016 Trends in Food Science & Technology 50: 118-130.](#); [Pieke et al. 2017](#)

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Migration of FCCs



heat higher temperature increases leaching

time long storage time increases leaching

food chemistry fatty foods, acidic foods, aqueous foods: **it depends on food stuff what chemicals migrate from the packaging**

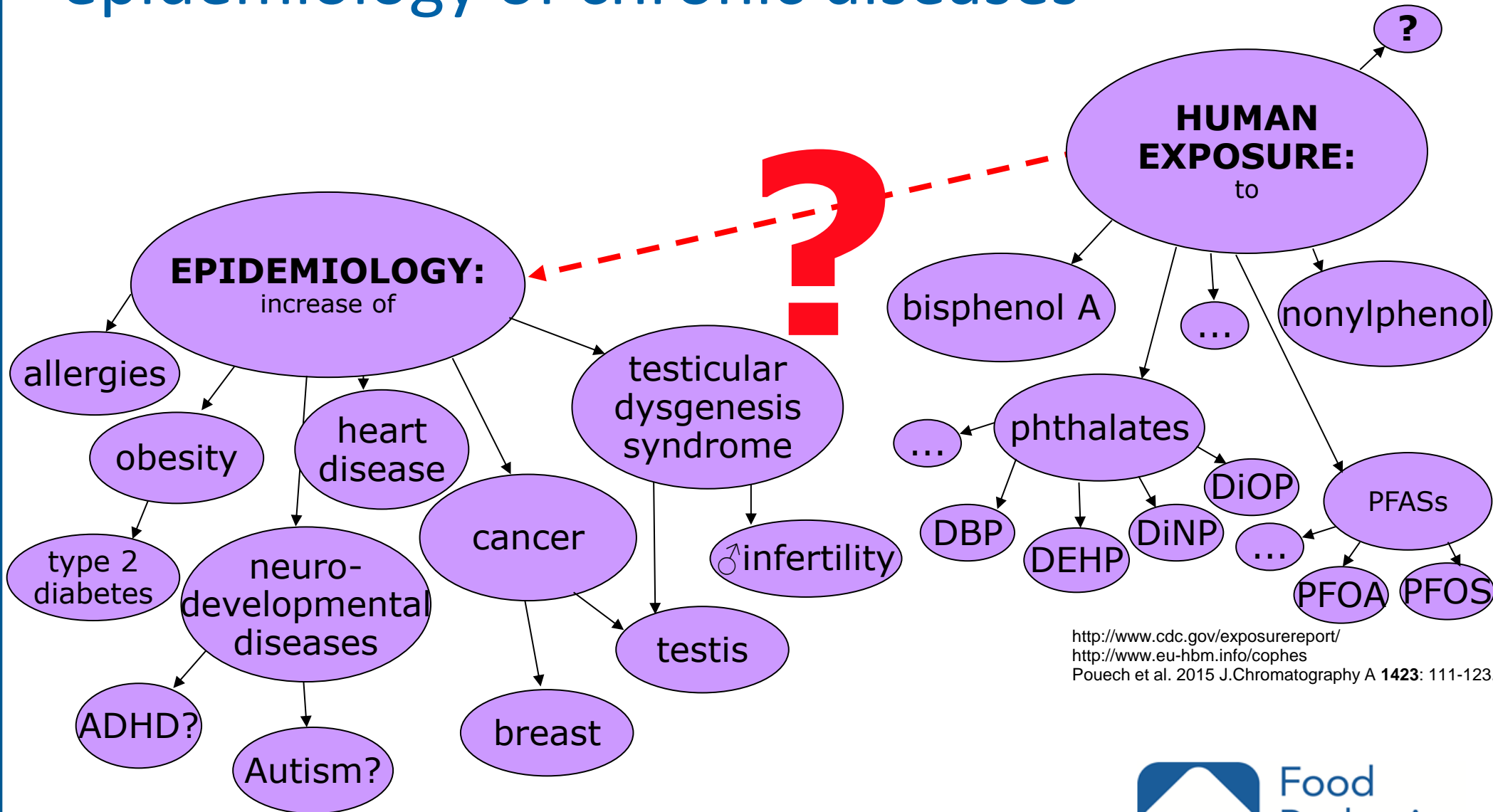
packaging size smaller packaging has proportionally larger surface area, more migration per volume of food



safe

100% Natural & Ozonated Packaged Drinking Water

Evidence from biomonitoring of FCCs and epidemiology of chronic diseases



<http://www.cdc.gov/exposurereport/>
<http://www.eu-hbm.info/cophes>
 Pouech et al. 2015 J.Chromatography A 1423: 111-123

<http://www.who.int/mediacentre/factsheets/fs310/en/index2.html>
<http://www.who.int/mediacentre/news/releases/2015/noncommunicable-diseases/en/>

Are food contact materials a relevant source of exposure to chemicals?



- Few studies available, incl. TV documentaries ([NDR 2014](#))
 - Dietary intervention study in 5 US families, up to 66% decrease in BPA, 56% DEHP ([Rudel et al. 2011](#))
 - Others have found increase in phthalates → contamination upstream in the supply chain ([Sathyanarayana et al. 2013](#))
 - Pre-packaging FCMs contribute significantly to chemical migration ([van Holderbeke et al. 2014](#))
- for some chemicals food packaging, other FCMs seem to be most relevant source.
- More studies needed to verify this assumption.

EU Regulation



foto: Michael Coghlan @flickr

1. ALL 17 FCMs:

Framework Regulation 1935/2004, Article 3:

FCMs and FCAs must not transfer their components into food **in quantities that could endanger human health**

2. SPECIFIC MEASURES *harmonized* FOR FCMs:

e.g. Plastics Regulation 10/2011:

Annex I “Union List”:

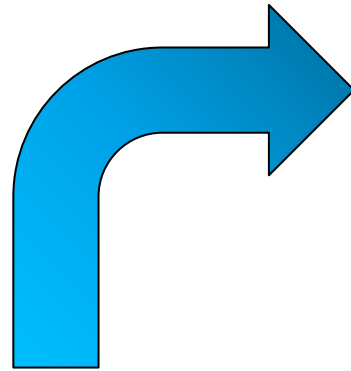
positive list for authorized starting substances, additives

Art. 19 on NIAS, not specifically authorized FCCs:

“Compliance with Article 3 ... shall be assessed in accordance with **internationally recognised scientific principles on risk assessment.**”



Chemical risk assessment for FCCs



Toxicity data: based on exposure; extrapolation



Hazard estimate

$$\text{risk} \propto \text{exposure} \cdot \text{hazard}$$

Exposure estimate



Migration assessment/estimate



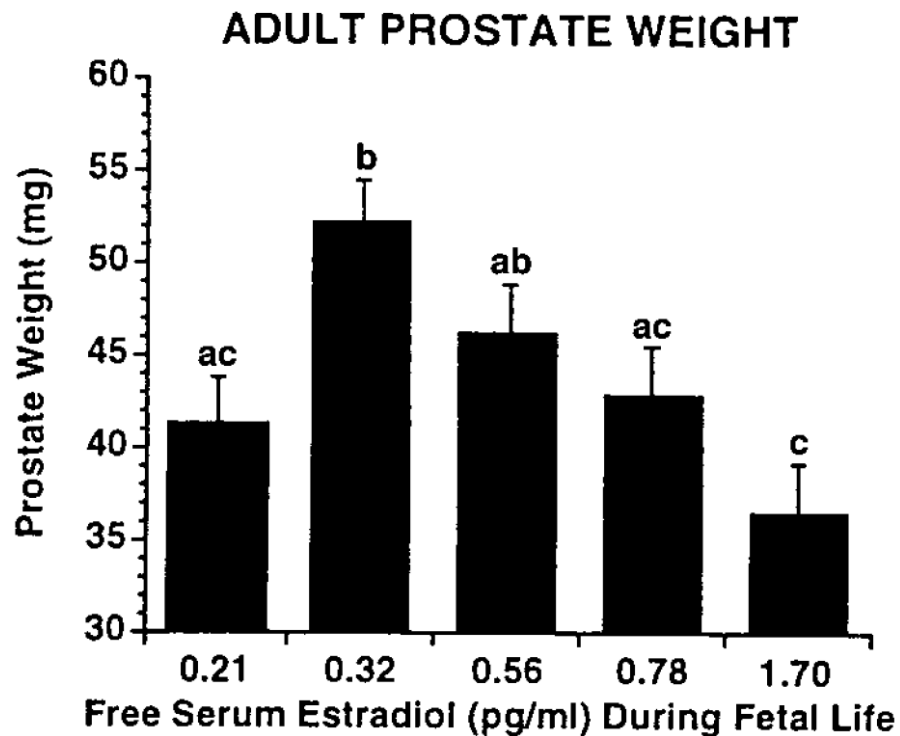
Migration models used for plastics ([JRC 2015](#))

[EFSA scientific opinion RA for FCMs 2016](#)

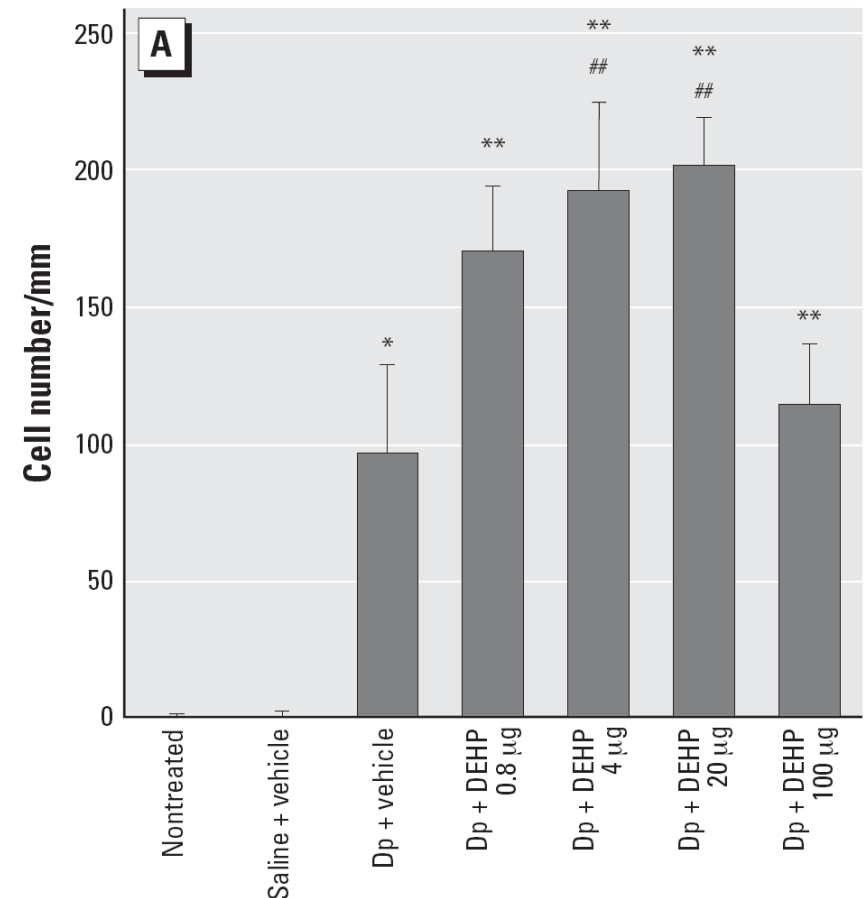
„Only the dose makes the poison“ ?



Typical hormone dose-response is *non-monotonic*



Vom Saal et al. 1997 PNAS

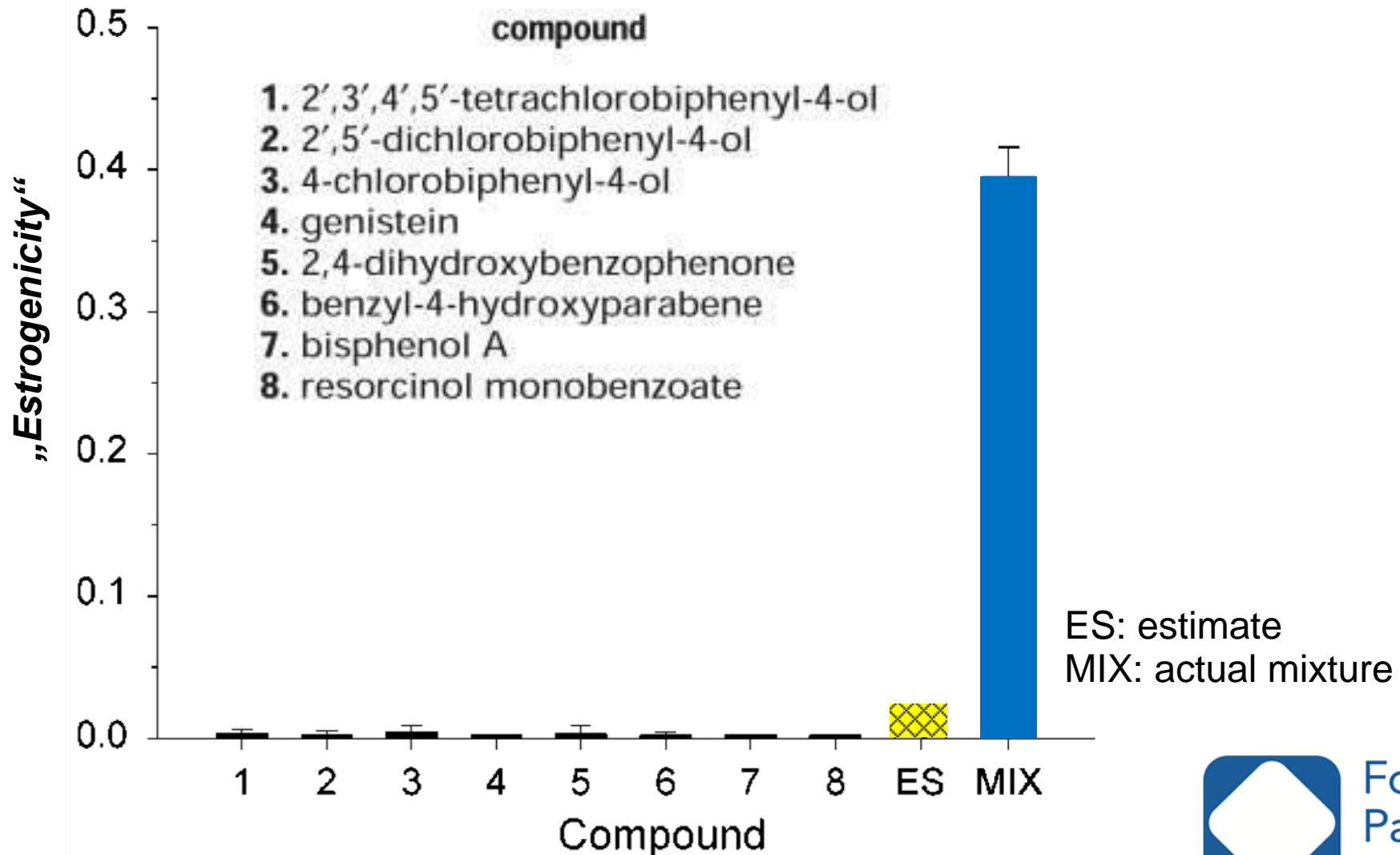


Takano et al. 2006 EHP

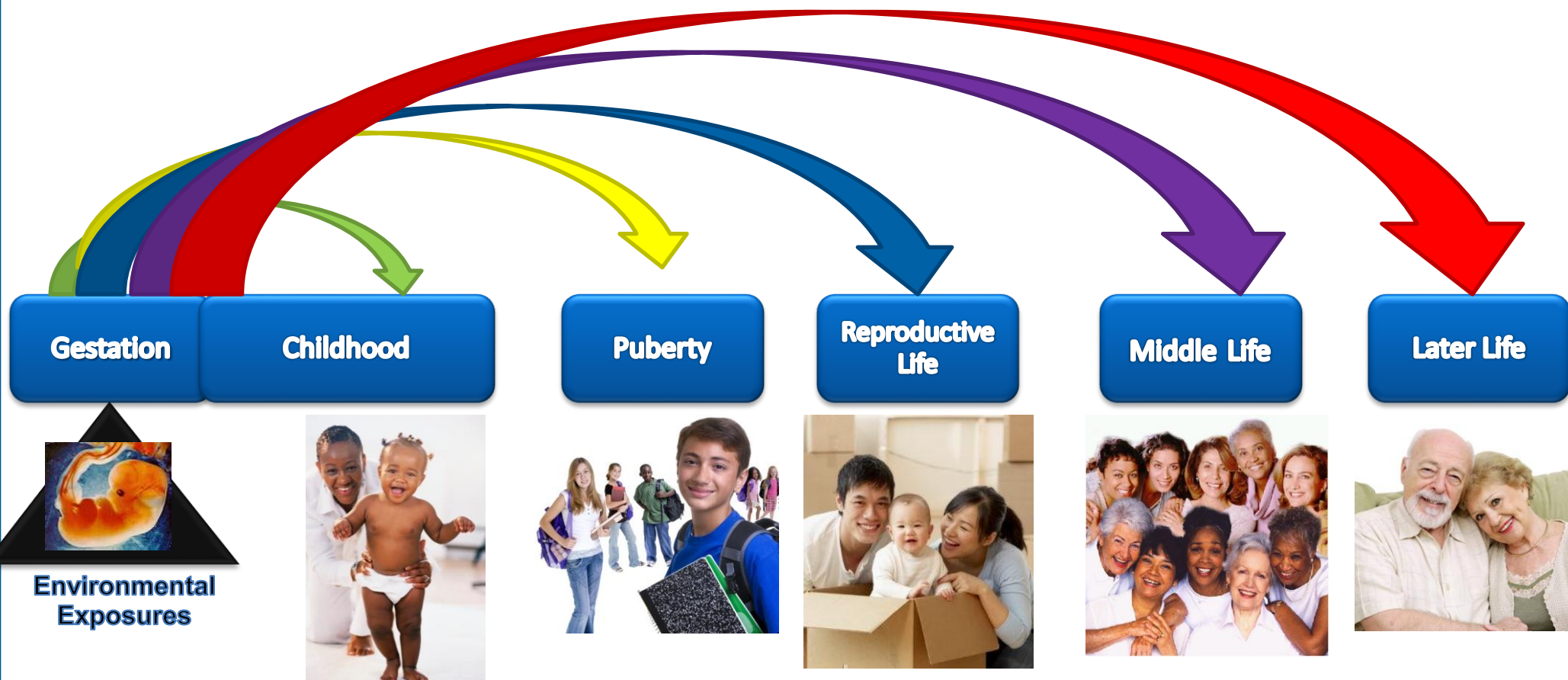
Vandenberg et al. 2012 "Hormones and Endocrine-Disrupting Chemicals: Low-Dose Effects and Nonmonotonic Dose Responses" *Endocrine Reviews* 33(3):378-455



Mixture Toxicity: „Something from Nothing“



Developmental Exposure Can Lead to Disease Throughout Life



Developmental Origins of Disease Hypothesis (DOHAD)

from Jerry Heindel, NIEHS

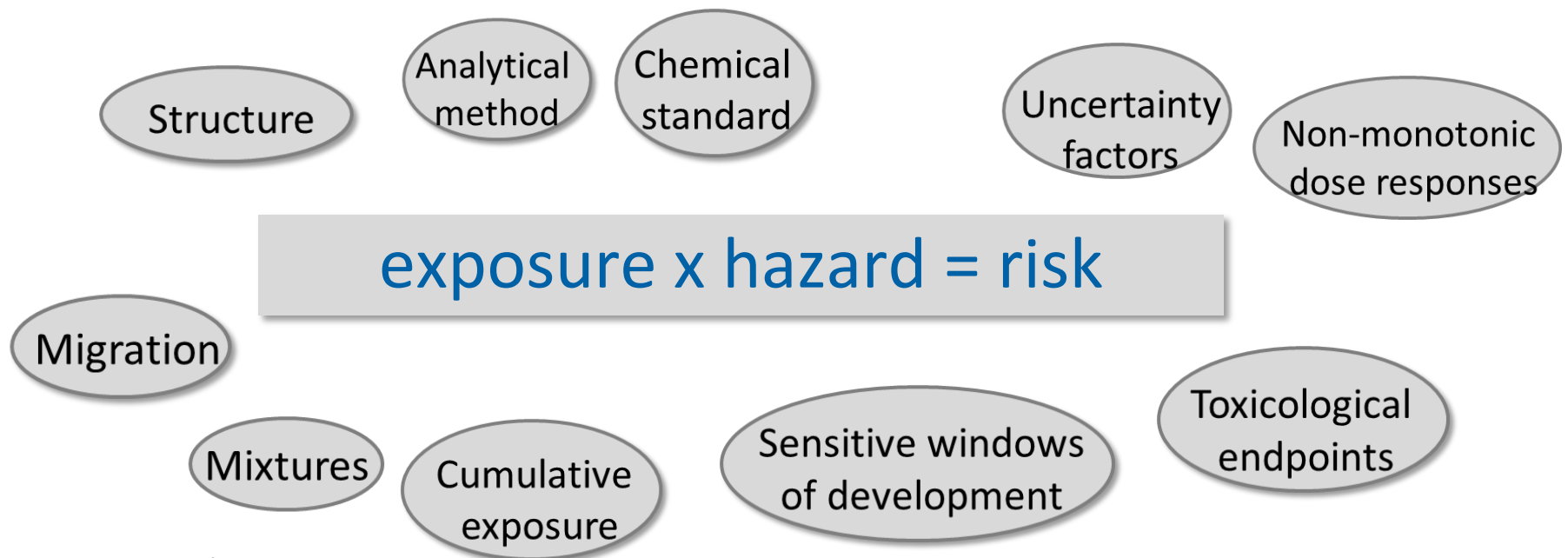
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Challenges for risk assessment of food contact chemicals (FCCs)

- Focus is on **starting substances and additives**, not finished food contact article's chemical composition (and actual exposure)
- Unknown substances (**NIAS**) ([Pieke et al. 2017](#); [Hoppe et al. 2016](#))



([Geueke 2015](#))

→ the current approach is ineffective for preventing population-wide exposures to hazardous FCCs

EU Parliament report on implementation of FCM regulation (October 2016)



- Framework regulation EC 1935/2004 does not sufficiently protect public health
- The framework regulation on FCMs is a trade barrier

[Implementation of the Food Contact Materials Regulation](#)

European Parliament resolution of 6 October 2016 on the implementation of the Food Contact Materials Regulation (EC) No 1935/2004 (2015/2259(INI))




In silico “hazard” assessments of FCCs

- TTC is controversial ([Bschir 2016](#)) and can't be used for EDCs → TiPED: [Schug et al. 2012](#), www.tiped.org
- Substances of very high concern are authorized and used for FCM manufacture ([Geueke et al. 2014](#)), and some migrate into food ([Geueke and Muncke 2017](#)) → Comparison of inventories for FCCs, hazardous substances
- [Danish \(Q\)SAR database](#) (DTU collaboration)
- Genotoxicants are present on FCC inventories for varnishes and coatings (Mertens et al. 2017), in printing inks ([van Bossuyt et al. 2016](#)) or as NIAS in baby bottles ([Mertens et al. 2016](#)) → evaluation using Tox Tree, Derek Nexus, ECHA database and published literature
→ use for **prioritization of toxicity testing** ([van Bossuyt et al. 2017](#))



Safeguarding human health using *in silico* tools?

Melissa Van Bossuyt^{1,2}  · Els Van Hoeck¹ · Tamara Vanhaecke² · Vera Rogiers² · Birgit Mertens¹

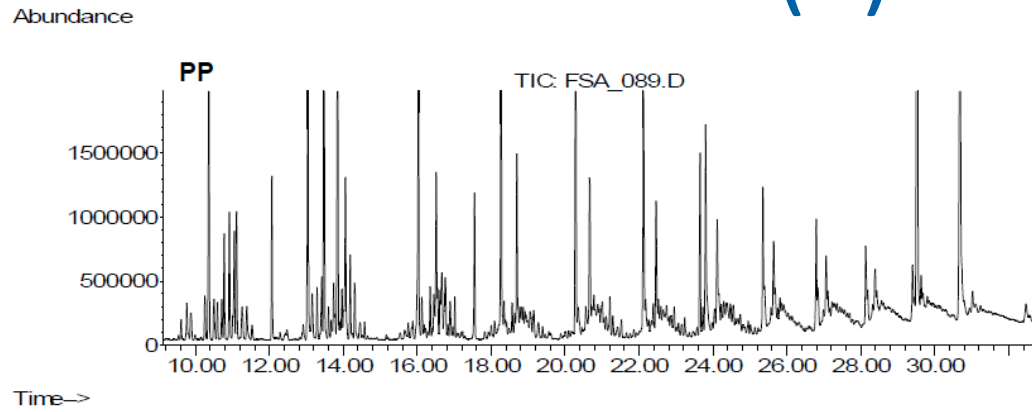
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During the last years, the 3Rs (Replacement, Reduction, Refinement) principle is increasingly taken into consideration in setting up integrated testing strategies. As such, *in silico* methods received substantial attention, which stimulated their development and made them become more

Therefore, the most promising application of *in silico* tools today remains its use in priority setting upon screening of a large number of compounds. The general public is exposed, intentionally or not, to a large variety of different substances, sometimes not or not recently evaluated for

The way forward: some research needs (1)

Chemical risk assessment:
address actual exposures from finished food contact articles



1. Tools for filling tox. data gaps (e.g. of NIAS) for prioritization:

- Threshold of Toxicological Concern (TTC) (or: ToxTree): update using more current toxicity data, include most recent scientific understanding, uncertainty

2. Develop tools for quantification of unidentified substances with **significant exposure levels** (prioritization)

- Semi-quantitative non-targeted screening in LC-MS ([Pieke et al. 2017](#))

3. Develop tools for identification of substances with biological activity of interest (**significant hazards**)

- Effect-directed analysis (planar-YES, etc.)

The way forward: some research needs (2)



3. Bioassays for food contact material (FCMs) – mixture toxicity, unknown substances (Groh and Muncke 2017 Critical Reviews in Food Science and Food Safety *in press*; [Severin et al. 2017](#))

- Standardized extraction procedures for ALL FCM types
- Selection of *in vitro* assays based on sensitivity/specificity and validation
- development of *in vitro* assays for cardiovascular disease, metabolic disease, neurological, etc.

4. Improve understanding of FCAs as exposure sources for FCCs (dietary intervention studies, biomonitoring)

Conclusions

- Over 8'000 substances used in the manufacture of FCMs
- Many non-intentionally added substances (NIAS) are present in FCAs → often unidentified or w/out tox. data
- Regulation requires “safety” but data are not available
- *In silico* tools for genotoxicity are considered useful for prioritization of toxicity testing, TTC needs more work
- Migration modelling established for intentionally added substances in plastics
- But: challenge are the unknown FCCs in FCMs—need to develop *in vitro* testing, including for non-genotoxic hazards

SAVE THE DATE!

FPF workshop 5 October 2017, Zurich
“Scientific challenges in the risk assessment
of food contact materials”

<http://www.foodpackagingforum.org/events/2017-workshop>

THANK YOU!



www.foodpackagingforum.org

