










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

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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

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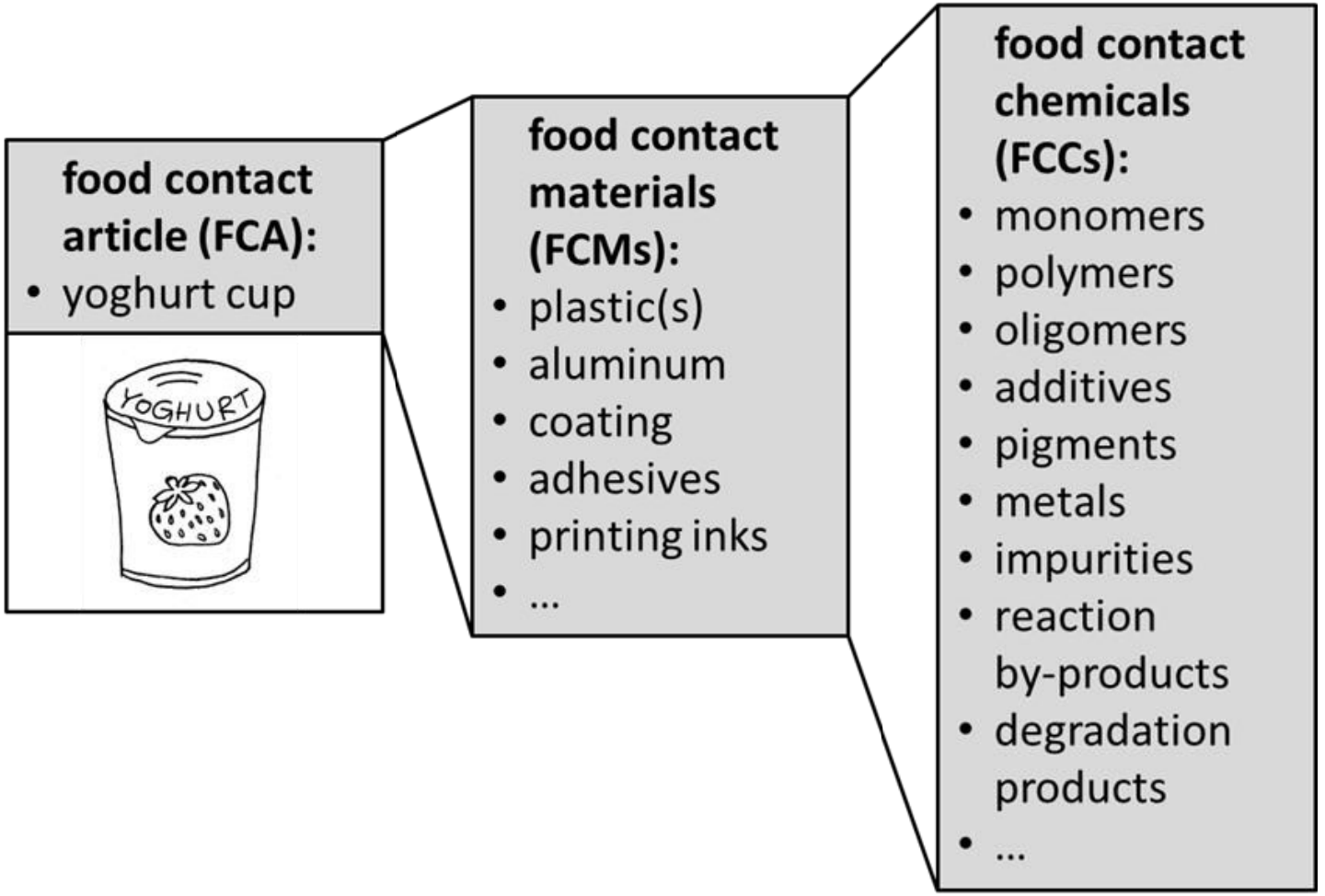
Food contact materials (FCMs), articles (FCAs) and chemicals (FCCs)



Muncke J, Backhaus T, Geueke B, et al., Env Health Persp (in press)

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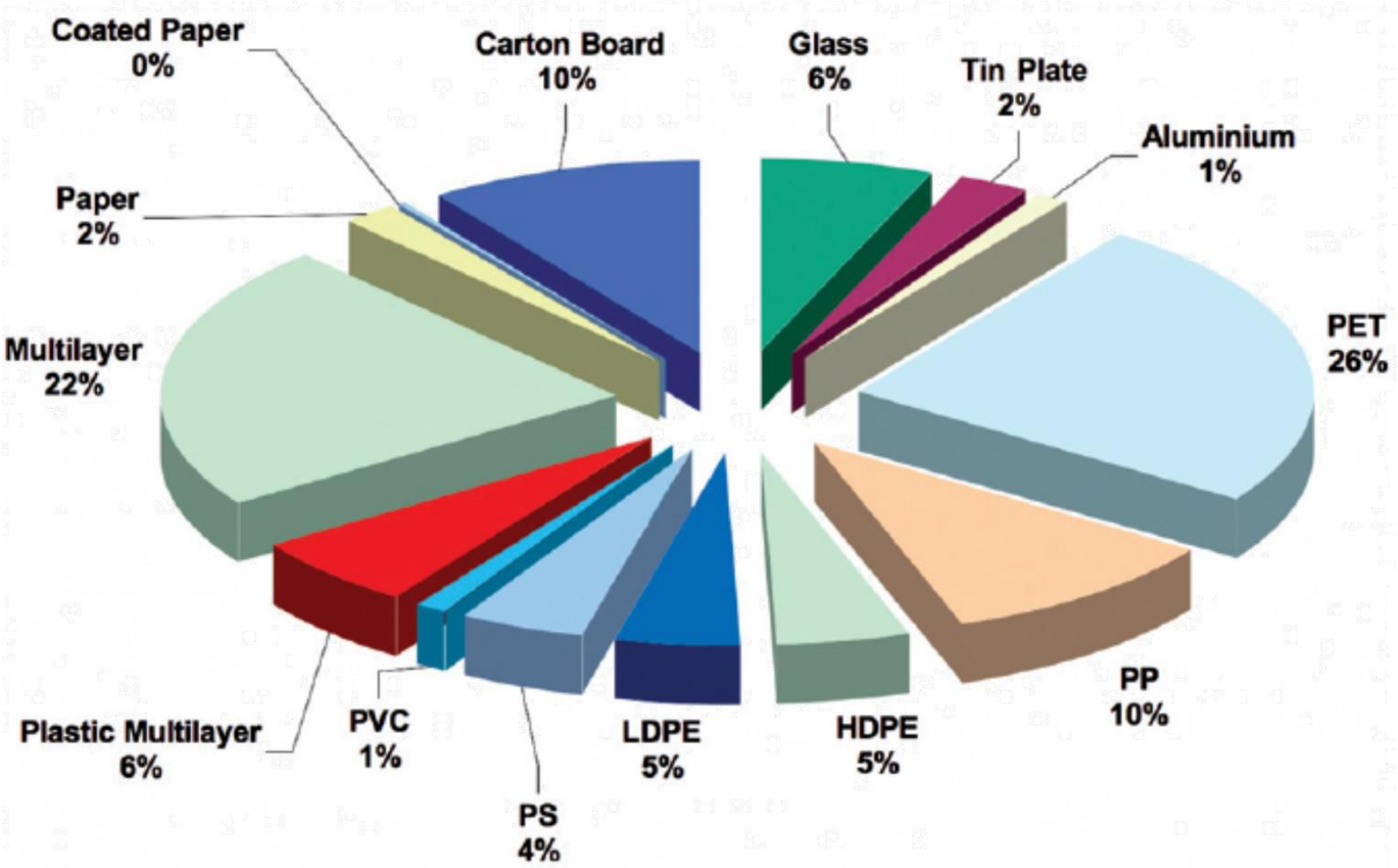
Food packaging materials: Portuguese market study (2009)



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

Pocas et al. (2009) Food Addit. Contam., Part A, 29(6):1314-1324

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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

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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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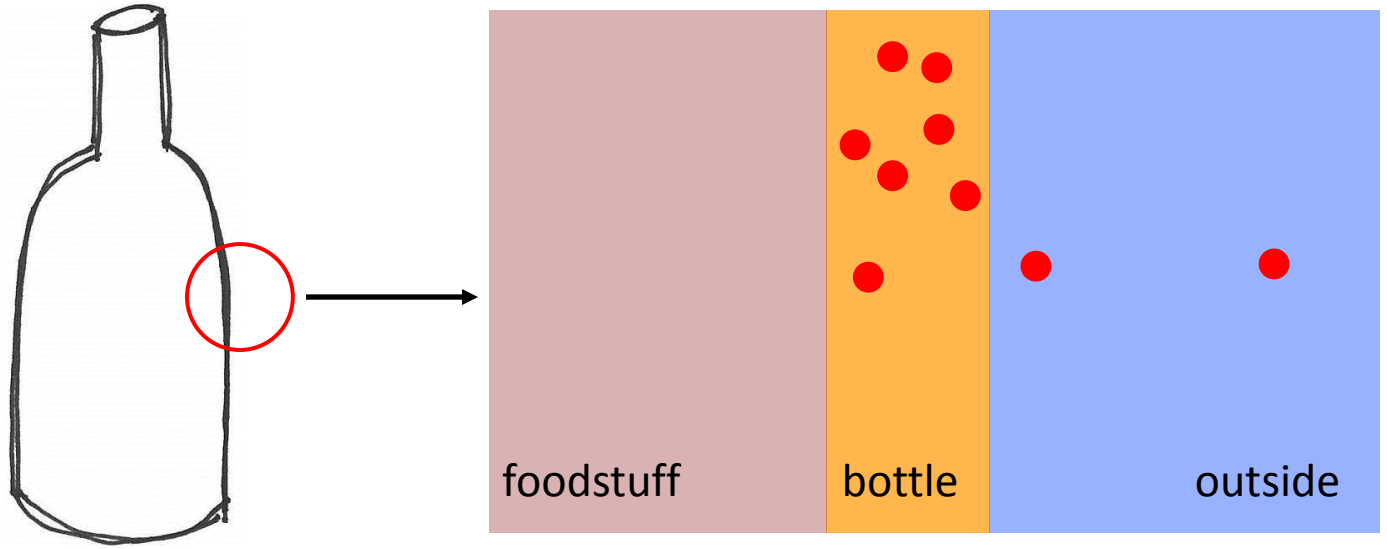
Migration of FCCs



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

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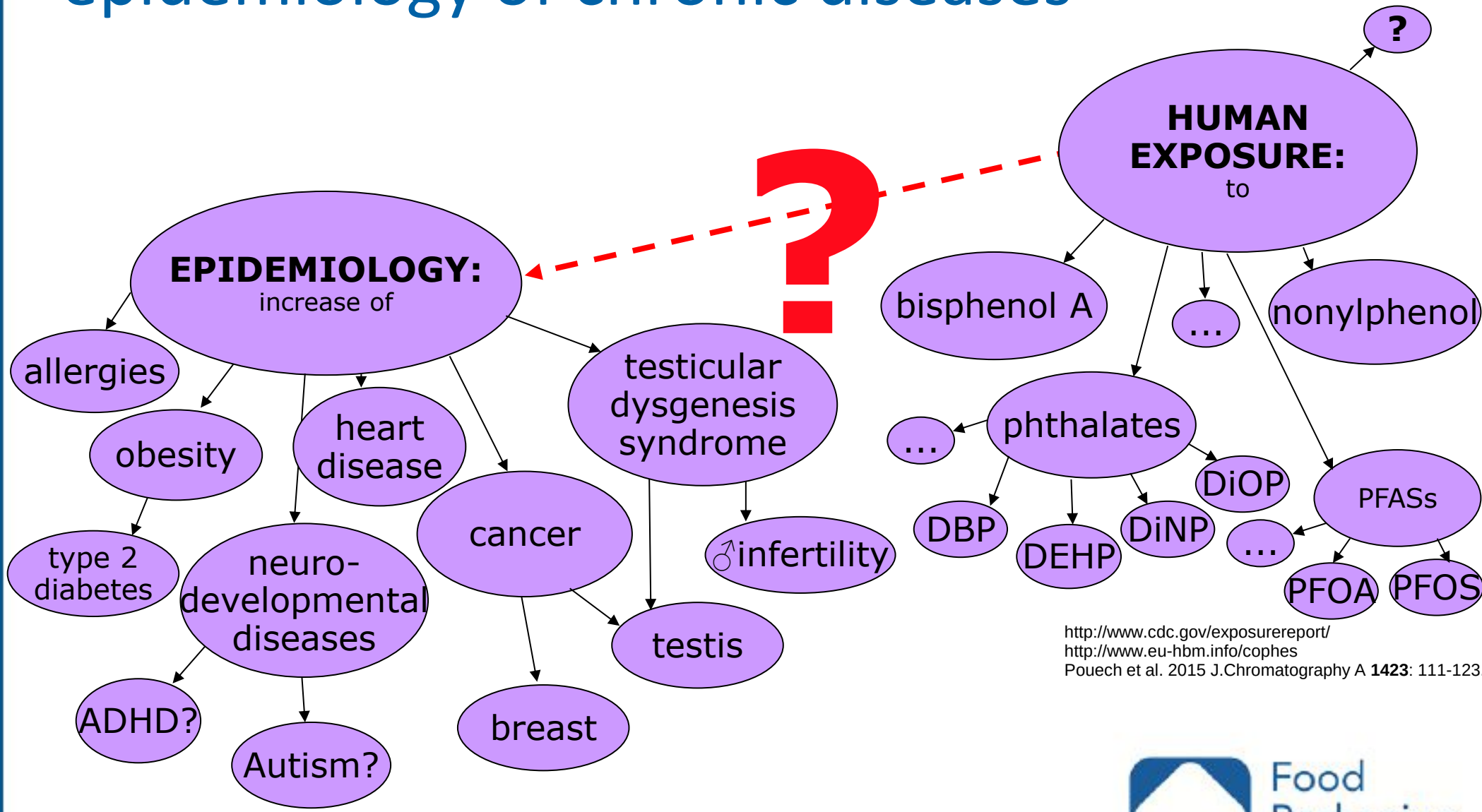
safe

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/

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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.

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EU Regulation


foto: Michael Coghlan @flickr

1. **ALL 17 FCMs:**
   <u>Framework Regulation 1935/2004, Article 3:</u>

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

2. **SPECIFIC MEASURES *harmonized* FOR FCMs:**
   <u>e.g. Plastics Regulation 10/2011:</u>

   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**."

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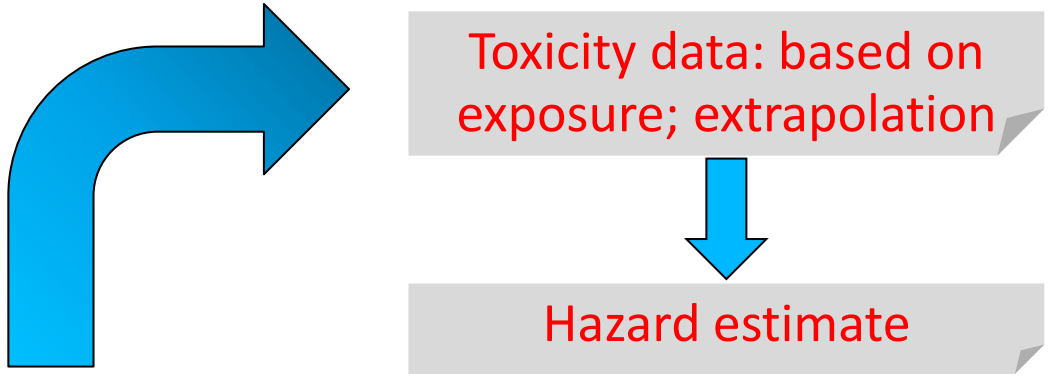
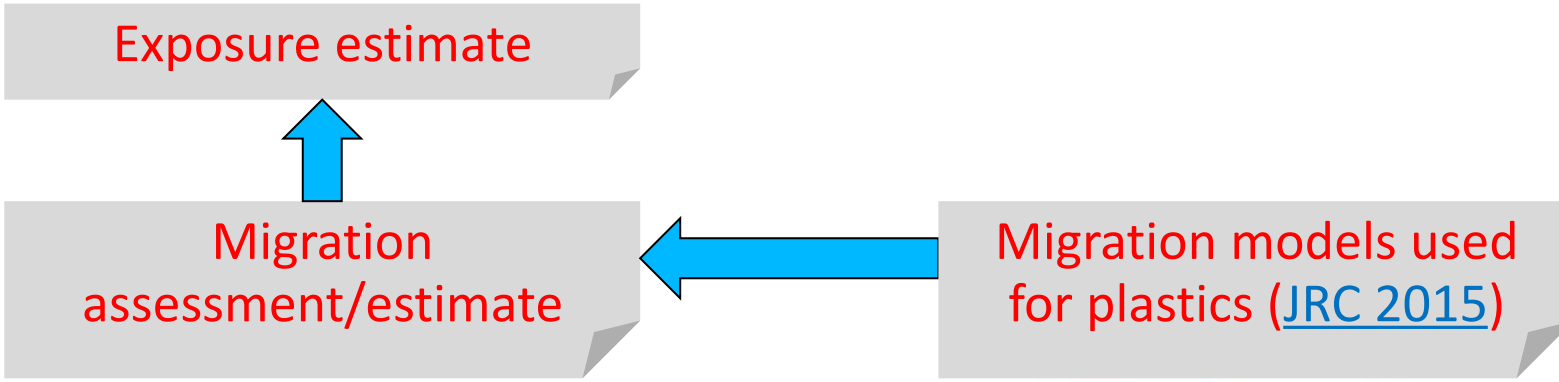
Chemical risk assessment for FCCs



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



EFSA scientific opinion RA for FCMs 2016

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„Only the dose makes the poison“ ?

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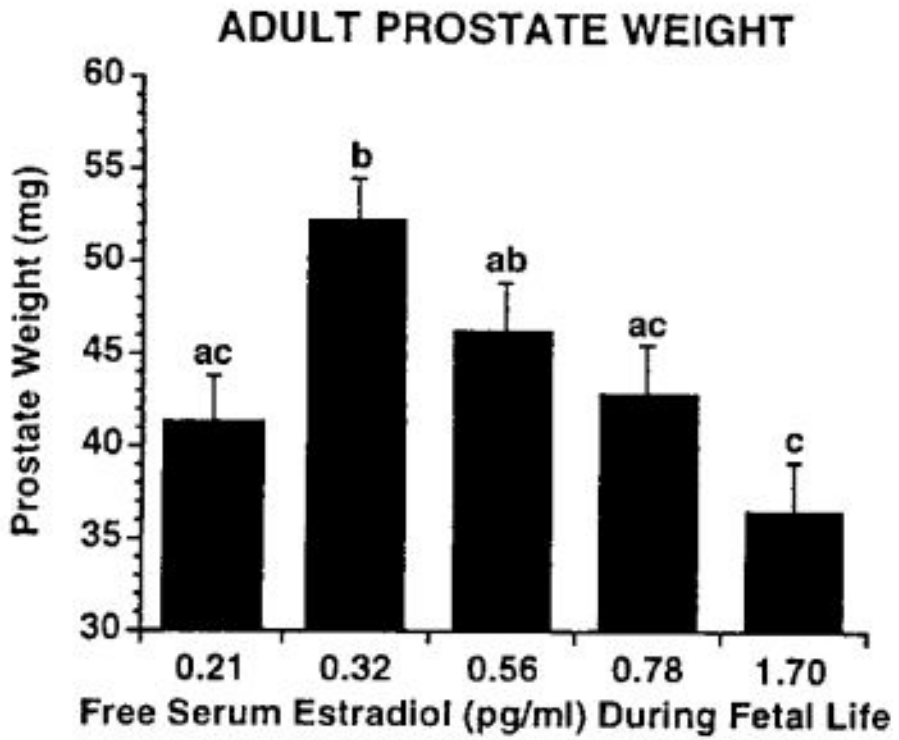
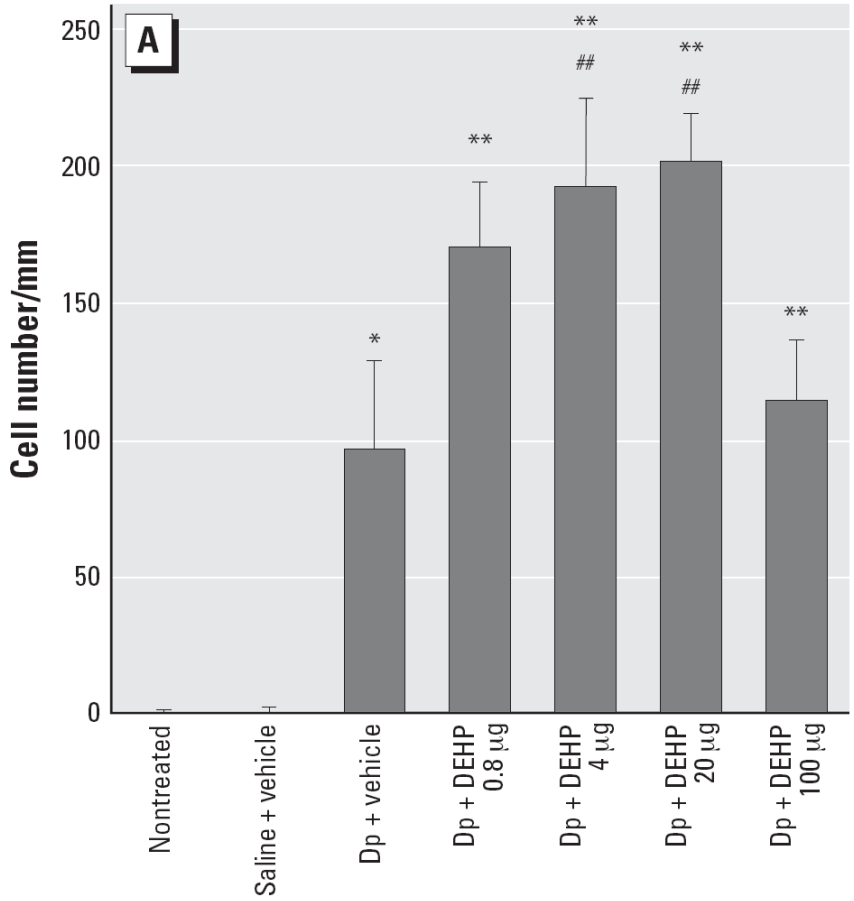
Typical hormone dose-response is *non-monotonic*



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

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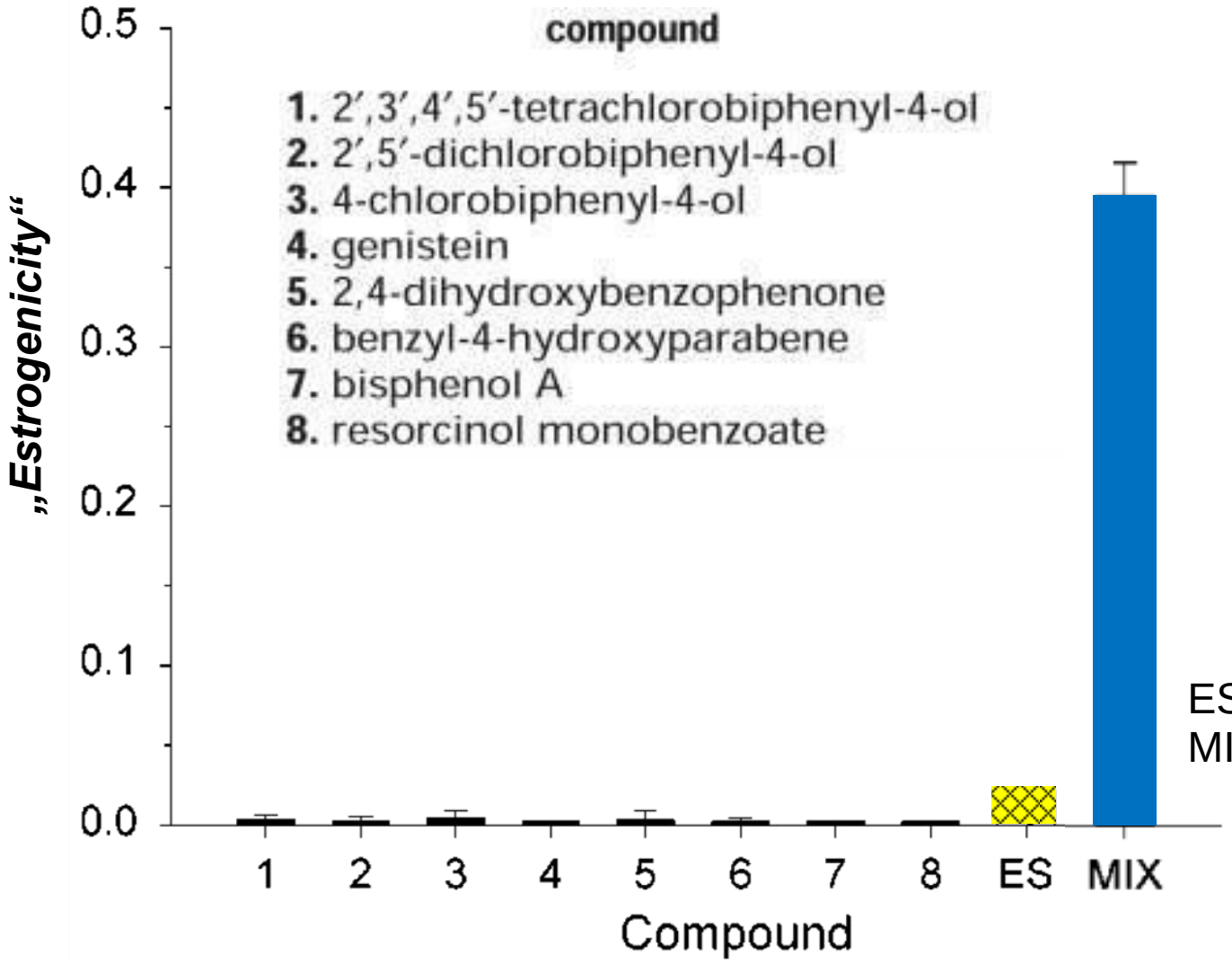
Mixture Toxicity: „Something from Nothing“



ES: estimate
MIX: actual mixture

Silva, E. et al. (2002) Env Sci Technol 36(8):1751-1756.

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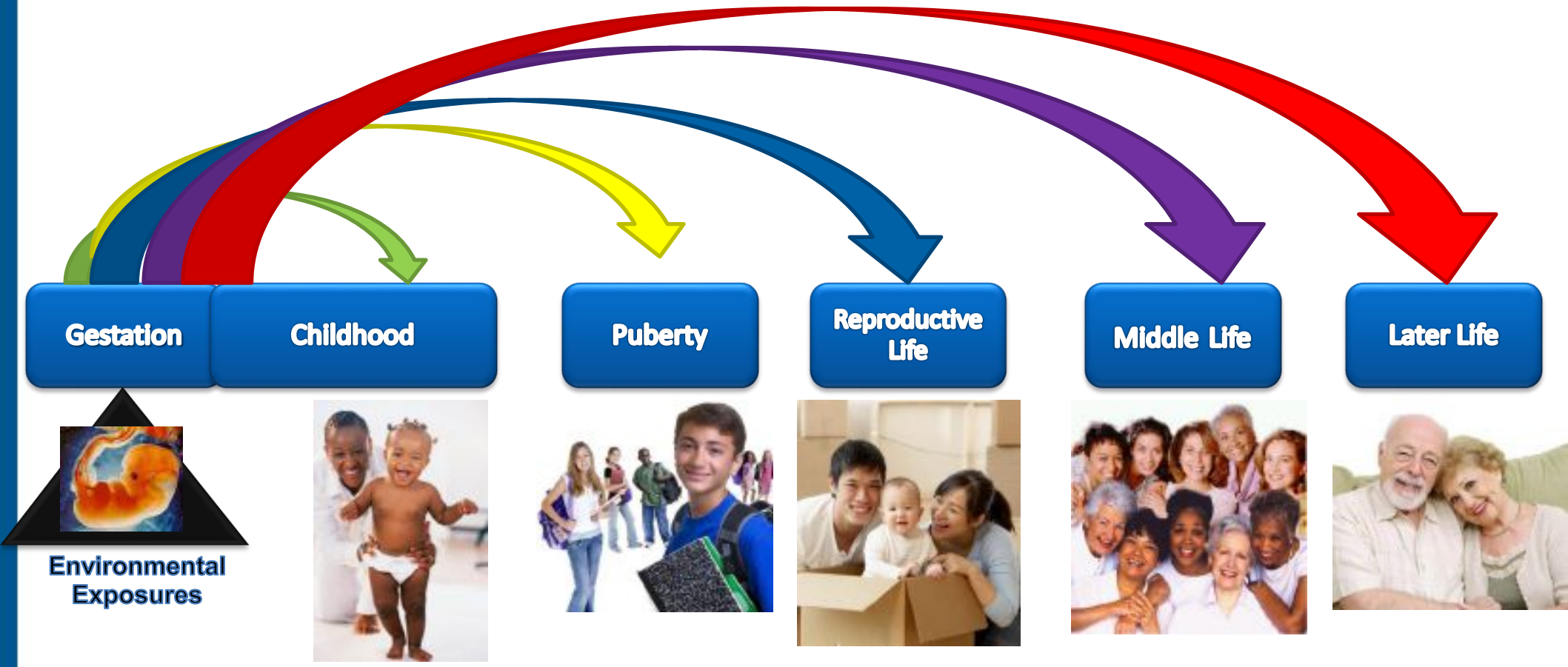
Developmental Exposure Can Lead to Disease Throughout Life



Developmental Origins of Disease Hypothesis (DOHAD)

from Jerry Heindel, NIEHS

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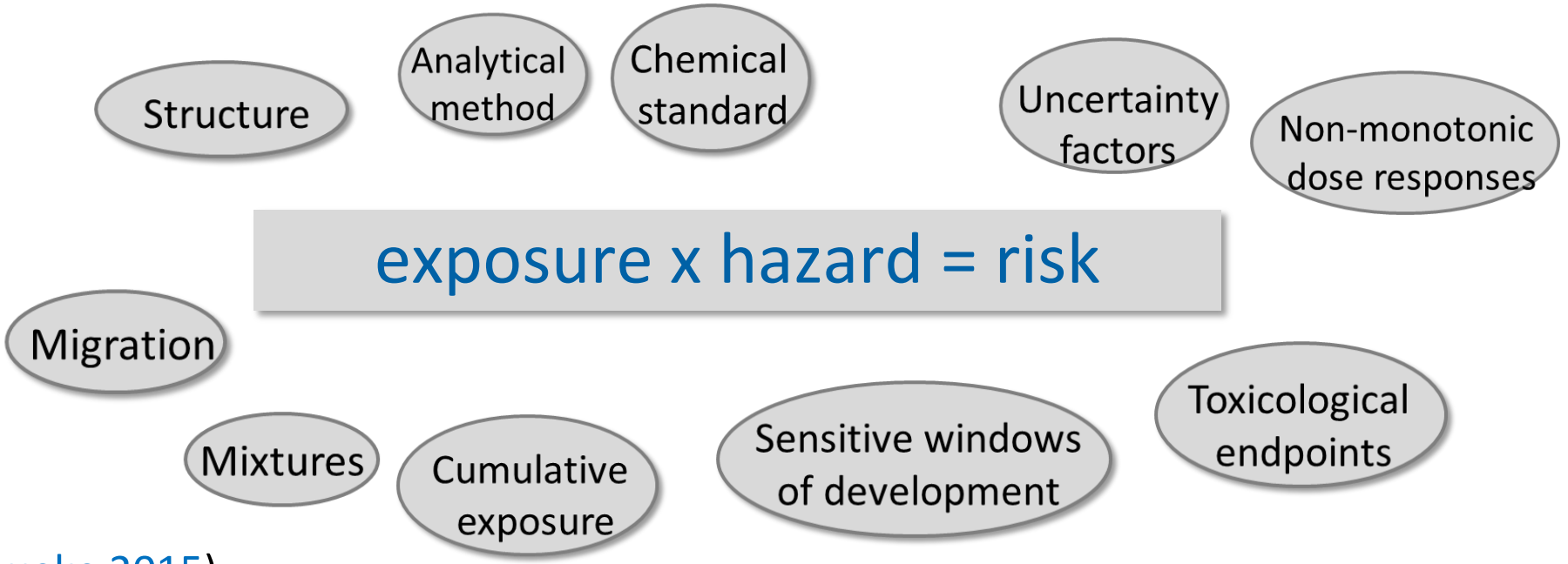
Challenges for risk assessment of food contact chemicals (FCCs)

- 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

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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))

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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)

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Arch Toxicol
DOI 10.1007/s00204-017-1931-z

GUEST EDITORIAL

Safeguarding human health using *in silico* tools?

Melissa Van Bossuyt[1,2] · Els Van Hoeck[1] · Tamara Vanhaecke[2] · Vera Rogiers[2] · Birgit Mertens[1]

Received: 28 December 2016 / Accepted: 12 January 2017

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

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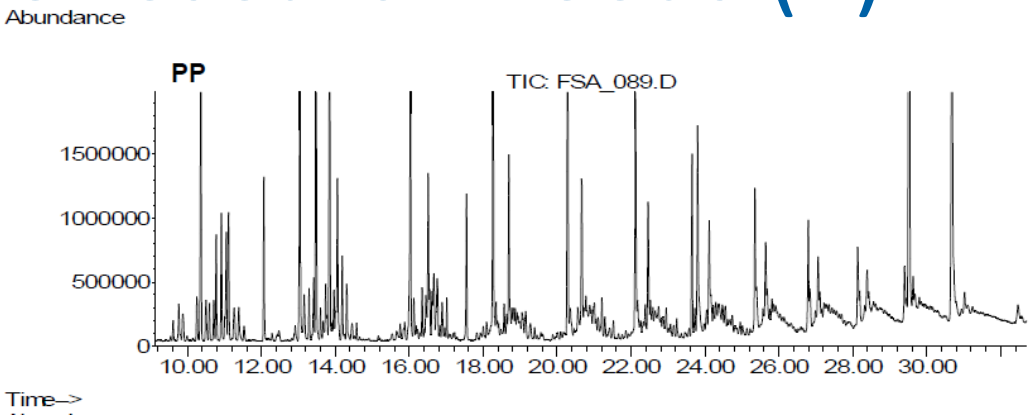
The way forward: some research needs (1)



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.)

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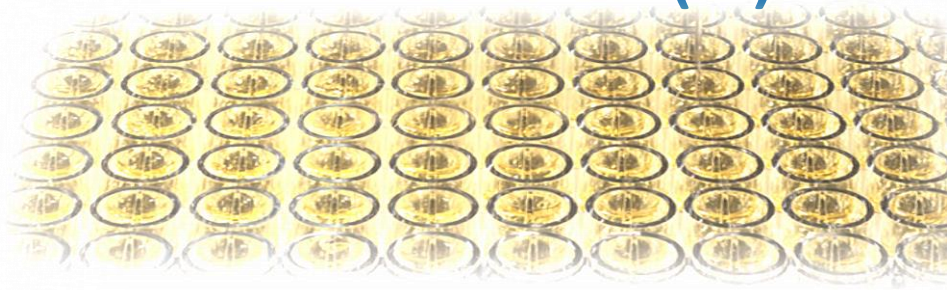
The way forward: some research needs (2)



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)

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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

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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!





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