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Plasticisers in the Regulatory Framework

AMI Polymers in Flooring

Berlin, 3./4. December 2019

Dr. Rainer Otter

1998: ~ 20 Years Ago: Toys and Childcare Articles

EU Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE)

Phthalate migration from soft PVC toys and child-care articles

Opinion expressed at the CSTEE third plenary meeting Brussels, 24 April 1998

L 315/46 EN Official Journal of the European Communities 9. 12. 1999

COMMISSION DECISION

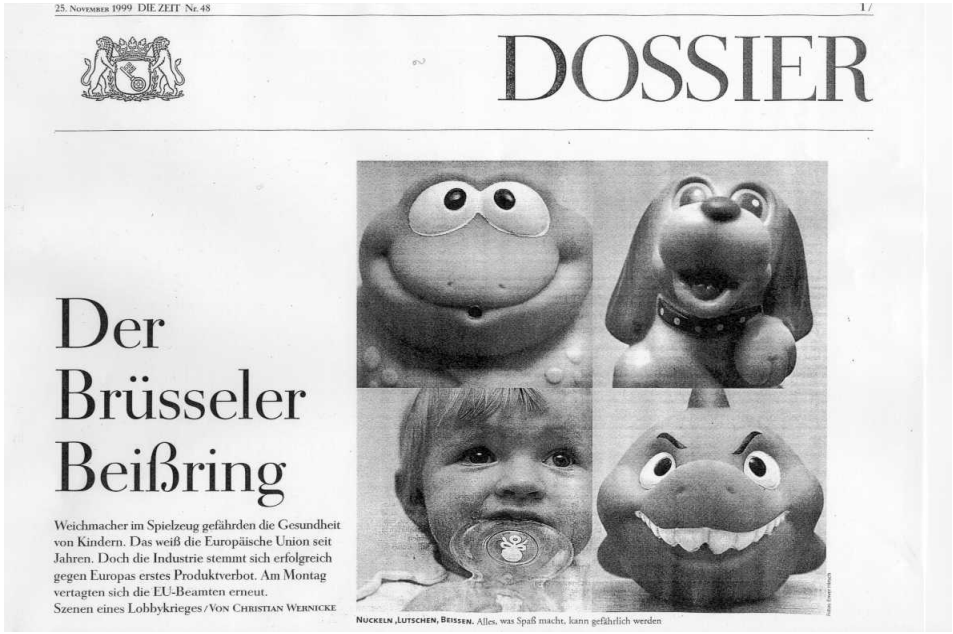
of 7 December 1999

adopting measures prohibiting the placing on the market of toys and childcare articles intended to be placed in the mouth by children under three years of age made of soft PVC containing one or more of the substances di-iso-nonyl phthalate (DINP), di(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), di-iso-decyl phthalate (DIDP), di-n-octyl phthalate (DNOP), and butylbenzyl phthalate (BBP)

(notified under document number C(1999) 4436)

(Text with EEA relevance)

(1999/815/EC)



25. November 1999 DIE ZEIT Nr. 48

DOSSIER

Der Brüsseler Beißring

Weichmacher im Spielzeug gefährden die Gesundheit von Kindern. Das weiß die Europäische Union seit Jahren. Doch die Industrie stemmt sich erfolgreich gegen Europas erstes Produktverbot. Am Montag vertagten sich die EU-Beamten erneut. Szenen eines Lobbykrieges / Von Christian Wernicke

Nuckeln, Lutschen, Beissen. Alles, was Spaß macht, kann gefährlich werden

The toy case has still a major impact on other, unrelated applications

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Plasticisers under Scrutiny

- Public perception: "***Plasticiser***" synonym to "***Problem***"
- Issue started with specific phthalates but spreading out to affect other chemicals
- Wide dispersive use of high production volume plasticisers
- Database for different plasticisers varies from poor to excellent
- Plasticiser content in soft PVC articles/consumer goods can be 30- 40 % (w/w)
- Plasticisers are physically bound in PVC
  - Leaching and migration depending on matrix
    - Mouthing of articles, e.g. toys
      - Dispute on duration of mouthing
      - Risk assessment with uncertainties
- Susceptible subpopulations used for scaremongering

Regulatory Testing

- Substance characterisation
  - Representative sample
- Information requirements
  - Physical-chemical properties
  - Ecotoxicological endpoints
  - Toxicological endpoints
  - Region specific chemicals legislations need to be considered
    - Adaptation of testing to meet regional requirements
- These data are required for compliance with chemicals legislations and approvals for use in specific applications, e.g. food contact, medical,…

REACH – Tiered Information Requirement Toxicology

Regulation (EU) 1907/2006 (REACH), Annex	VII	VIII	IX	X
t/a	≥ 1	≥ 10	≥100	≥ 1000
Skin irritation or corrosion (in vitro)	x	x	x	x
Eye irritation (in vitro)	x	x	x	x
Skin sensitization (LLNA)	x	x	x	x
Bacterial gene mutation (Ames)	x	x	x	x
Acute oral toxicity	x	x	x	x
Skin irritation in vivo		x	x	x
Eye irritation in vivo		x	x	x
Acute toxicity 2nd route (dermal/inhalative)		x	x	x
Cytogenicity study in mammalian cells		x	x	x
In vitro gene mutation in mammalian cells (HPRT)		x	x	x
In vivo mutagenicity (if indicated)		x	x	x
Reproduction toxicity (Screening OECD 421)		x	x	x
Information on Toxicokinetics		x	x	x
Short-term repeat dose toxicity (28d)		x	x	x
Repeat dose toxicity (90d)		x	x	x
Developmental toxicity (OECD 414)			x	x
Extended One-Generation Reproductive Toxicity (OECD 443)			x	x
Long-term repeat dose toxicity (≥ 12 months)				x
Mutagenicity studies (if indicated)				x
Carcinogenicity				x

Tiered information requirements exist also for physical-chemical data and for ecotoxicology

Testing proposals, Approval by ECHA

Regulation (EC) No 1272/2008 – Classification, Labelling and Packaging of Substances and Mixtures (CLP)

- Ensure a high level of protection of human health and the environment as well as the free movement of chemical substances, mixtures and certain specific articles, while enhancing competitiveness and innovation.
- Efficient functioning of the internal market for substances and mixtures
- A high level of human health and environmental protection should be ensured
- Approximation of legislation on the criteria for classification and labelling of substances and mixtures, with the goal of achieving sustainable development.
- Enterprises should benefit from the global harmonization
- Consistency between the rules for classification and labelling for supply and use and, on the other hand, those for transport.
- Facilitating worldwide trade while protecting human health and the environment

Regulation (EU) No 1272/2008 – Article 1 (Purpose and Scope)

- The purpose is to ensure a high level of protection of human health and the environment as well as the free movement of substances, mixtures and articles as referred to in Article 4(8) by:
- (a) harmonising the criteria for classification of substances and mixtures, and the rules on labelling and packaging for hazardous substances and mixtures;
- (b) providing an obligation for:
  - (i) manufacturers, importers and downstream users to classify substances and mixtures placed on the market;
  - (ii) suppliers to label and package substances and mixtures placed on the market;
  - (iii) manufacturers, producers of articles and importers to classify those substances not placed on the market that are subject to registration or notification under Regulation (EC) No 1907/2006

Regulation (EU) No 1272/2008 – Article 1 (Purpose and Scope)

- (c) providing an obligation for manufacturers and importers of substances to notify the Agency of such classifications and label elements if these have not been submitted to the Agency as part of a registration under Regulation (EC) No 1907/2006;
- (d) establishing a list of substances with their harmonised classifications and labelling elements at Community level in Part 3 of Annex VI;
- (e) establishing a classification and labelling inventory of substances, which is made up of all notifications, submissions and harmonised classifications and labelling elements referred to in points (c) and (d).

- Please note:

Neither 79 recitals nor 62 articles suggest that Annex VI of this regulation should be abused for company/trade organisation specific restriction lists

Overview: Classification and Labelling of Phthalates

Phthalate	Abbrev.	CASNo or EU	C (linear/side)	C&L HH	ED
Dimethyl-	DMP	131-11-3	1	No	No
Diethyl-	DEP	84-66-2	2	No	No
Dipropyl-	DPrP	131-16-9	3	Repro 2*	No
Diisobutyl-	DIBP	84-69-5	3:1	Repro 1B	Yes
Dibutyl-	DBP	84-74-2	4	Repro 1B	Yes
Benzylbutyl-	BBP	85-68-7	4/6c	Repro 1B	Yes
Diisopentyl-	DIPP	605-50-5	4:1	Repro 1B	Yes
Dipentyl-	DPP	131-18-0	5	Repro 1B	Yes
Dihexyl-	DHxP	84-75-3	6	Repro 1B	Yes
Dicylohexyl-	DCHP	84-61-7	6c	Repro 1B	Yes
Di(2-ethylhexyl)-	DEHP	117-81-7	6:2	Repro 1B	Yes
Diheptyl-	DHP	3648-21-3	7	Repro 2*	No
Dioctyl-	DOP	117-84-0	8	No	No
Diisononyl-	DINP	28553-12-0	9	No	No
	DINP	68515-48-0	8-10(C9rich)	No	No
Di(2-propylheptyl)-	DPHP	53306-54-0	7:3	No	No
Diisodecyl-	DIDP	26761-40-0	10	No	No
		68515-49-1	9-11(C10rich)	No	No
Diundecyl-	DIUP	85507-79-5	10-12(C11rich)	No	No
Ditridecyl-	DTDP	68515-47-0	12-14(C13rich)	No	No

*) C&L Inventory

Structure/Activity Relations of Phthalates

- Only specific substances **within the active cluster** show toxicity to reproduction in rats
  - Straight carbon backbone C3 to C6 and total C ≤ 8
  - Respective monoester is the active toxicant
    - Most sensitive endpoint:
      Testicular toxicity leading to impairment of fertility in the rat
    - Developmental toxicity at higher dose levels
    - Members of the active cluster do meet the ED criteria of WHO
      - Hormonal changes resulting in adverse effects

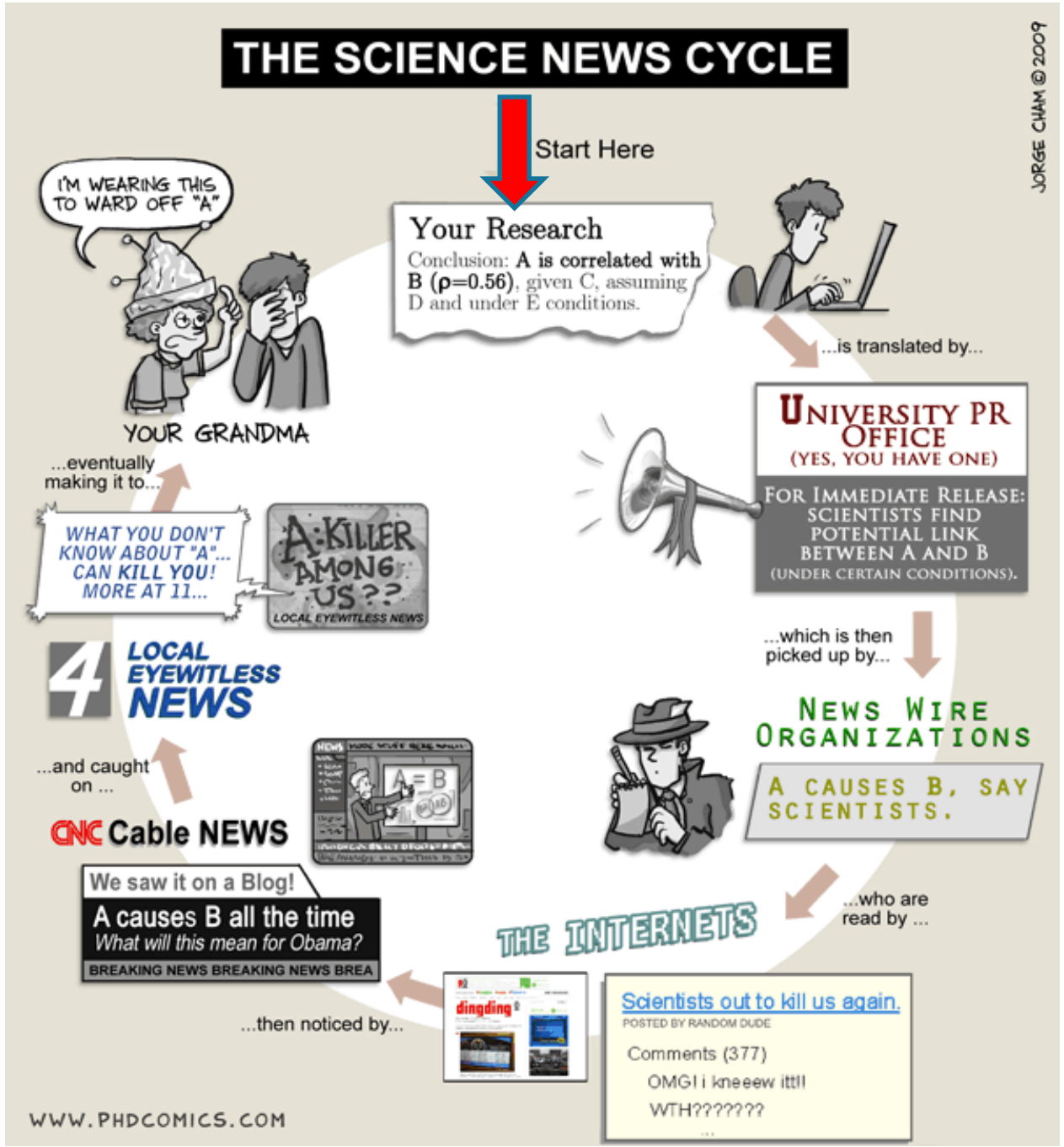
Regulatory Programs (Examples)

- **EU**
  - REACH (Regulation (EC) No 1907/2006)
    - Dossier Evaluation by ECHA
    - CLP (Regulation (EC) 1272/2008)
    - Substance Evaluation in the context of the Commission Rolling Action Plan (CoRAP)
    - Public Activities Communications Tool (PACT) / Risk Management Option Analysis (RMOA)
    - Endocrine Disrupting Properties (ED)
    - Persistence, Bioaccumulation or Toxic Properties (PBT)
    - Authorisation and Restriction Issues
- **US**
    - National Toxicology Program: CERHR Monographs
    - EPA IRIS (Integrated Risk Information System)
    - California EPA / Proposition 65
    - Consumer Products Safety Commission (CPSC)
- **Australia**
  - NICNAS evaluations

Academic Research

- Academic research depends significantly on public funding
  - Number of publications in scientific journals is used as measure of scientific productivity and impacts funding
  - Declaration “no conflict of interest” is ambiguous
  - Peer review process deteriorated
  - New business models of journals
    - Page fee model
    - Pre-peer review online publication
    - Payed, non-peer reviewed publications
    - Predator journals as an emerging topic related to junk science
- Emotional and non-targeted “**my science ⇔ your science**” discussion
- Media may use the opportunity for a good story

	Industry/CRO Study	Academic Study
Guideline	Yes	No
GLP	Yes	No
Good Scientific Practice	Yes	Variable
Qualified Staff	Yes	Variable
Historical Control Data	Yes	No
Regulatory Expericence	Yes	No
Alleged Conflict of Interest	Yes	No



Academic Funding Dilemma – How to Get a Bigger Slice of the Cake

- Cry for money by creating an issue
  - Undertake simple in vitro testing using concentrations exceeding the solubility in the test system or
  - Use test concentrations that exceed achievable tissue levels (measured/PBPK model) by 10^3 to 10^6
  - Disregard toxicokinetics and ignore saturation of metabolism and excretion in animal studies
  - Disregard published data and risk assessments and claim lack of published data
  - Complain about lack of independent studies to propagate own simple in vitro studies
  - Complain about lack of independent animal studies
    Question: where is the qualified lab and who is going to pay?

Regulatory Processes ⇔ Media and Market

- Regulatory processes take time and resources
- Notifications, regulatory working lists, any information on regulatory activities or scientific publications, especially those spread by media result in **immediate** market reactions
- Some of these media promoted studies are ambiguous and do result in a waste of resources
  - REACH dossier update requires that all the evidence must be evaluated
    - Use or disregard of a study needs to be justified
  - Information requests by customers, distributors and downstream users

Fact based regulatory view  Emotional scaremongering with hypothetical risks

ED Issue – The Circular Approach

- The only official list relevant to REACH chemicals is the REACH Candidate List
  - Substances included via Article 57(f)- endocrine activity resulting in adverse effects
  - WHO definition (2002)
    - "An endocrine disruptor is an exogenous substance or mixture **that alters function(s) of the endocrine system and consequently cause adverse health effects** in an intact organism, or its progeny, or (sub)populations."

- More than 10 lists known, e.g. Danish ED list, ChemSec etc. refer back to the BKH list from 2000 and seem to be ambiguous due to data quality and verification issues
  - The listed substances need further, in-depth evaluation and listing per se is not a proof of ED
  - These lists are a data collection exercise with recycling and cross-referencing of lists, i.e. not a reliable source of information

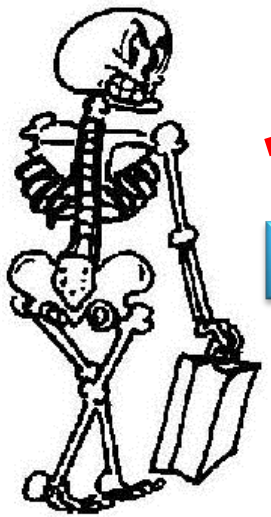
C&L Results in Substitution of old Plasticisers by New Products

Regulation (EU) No 1907/2006, Annex XVII, 51 and 52

Hexamoll® DINCH

Dir 67/548/EC C3-C8 Phthalates

Toxic



Danger

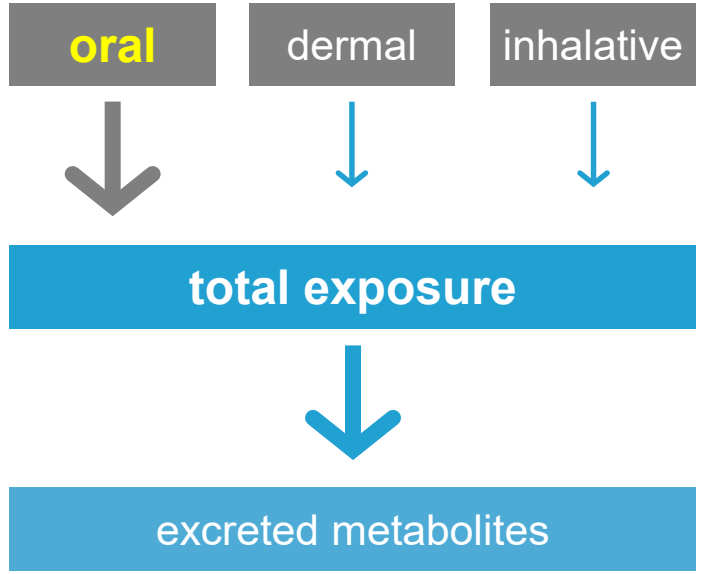
Regulation (EC) No 1272/2008 (CLP)

- **Cyclohexanoate, i.e. different structure**
- **Non-hazardous (CLP)**
- **Approvals for different applications**

Exposure Data for Plasticisers

Human Biomonitoring (HBM)

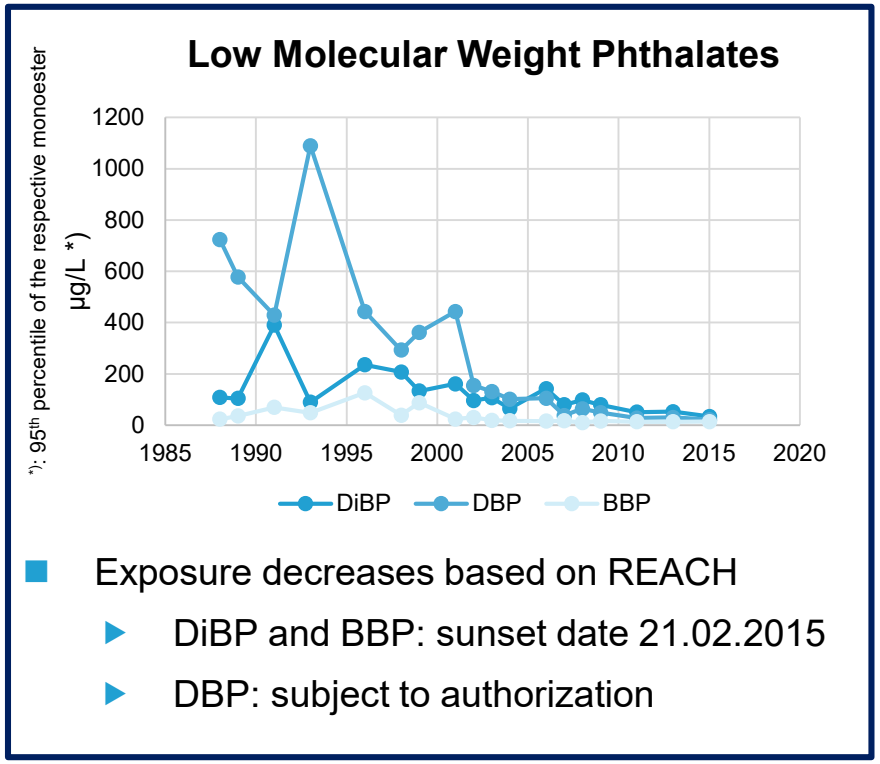
- Development of analytical methods for plasticisers
- Plasticisers are degraded in the human body
  - Degradation products (metabolites) are excreted into urine
  - Conversion factors (Fue) for calculation of external exposure are established based on human volunteer studies
  - Determination of actual human exposure
- Risk assessment based on robust exposure data
  - **Risk = Hazard x Exposure**
- Independent regarding route of exposure:
  total exposure = Σ (oral + dermal + inhalative)



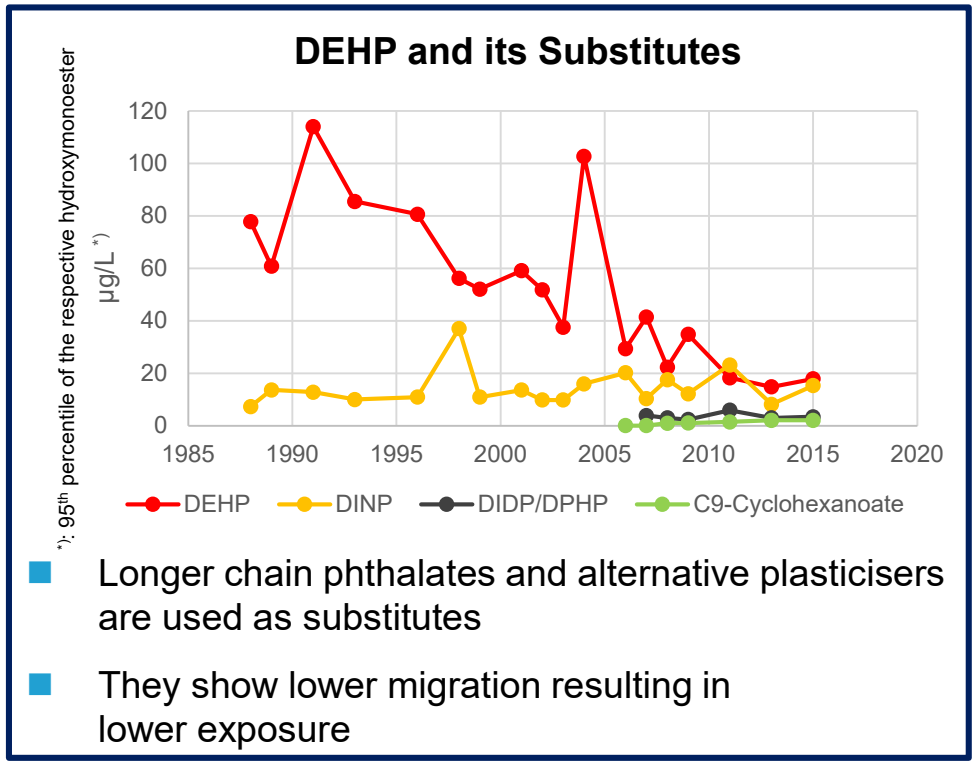
Environmental monitoring

- Methods for monitoring plasticisers in soil, sediment, plants and air established

Effectiveness of the Substitution Process mirrored by Exposure Trends in the General Population



- Exposure decreases based on REACH
  - DiBP and BBP: sunset date 21.02.2015
  - DBP: subject to authorization



- Longer chain phthalates and alternative plasticisers are used as substitutes
- They show lower migration resulting in lower exposure

Data source: Koch HM et al., Int J Hyg Environ Health. 2016, doi: 10.1016/j.ijheh.2016.11.003

- HBM reflects changes in use pattern based on regulatory developments and subsequent market trends
- Exposure to substitutes well below safety limits

Indoor Exposure

- Plasticiser concentration in house dust is not correlated with urinary metabolites

- Plasticiser content in house dust is not mirrored by indoor air concentrations

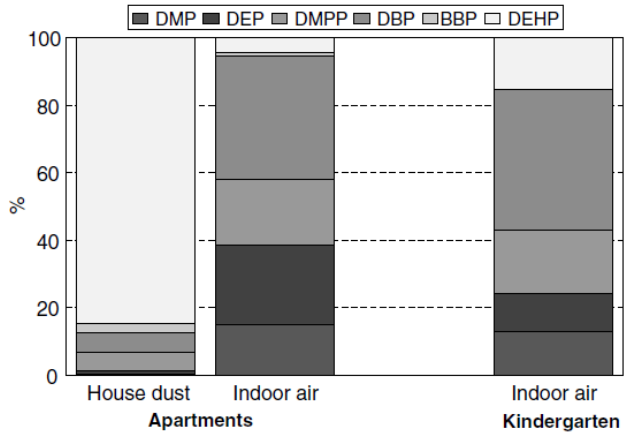
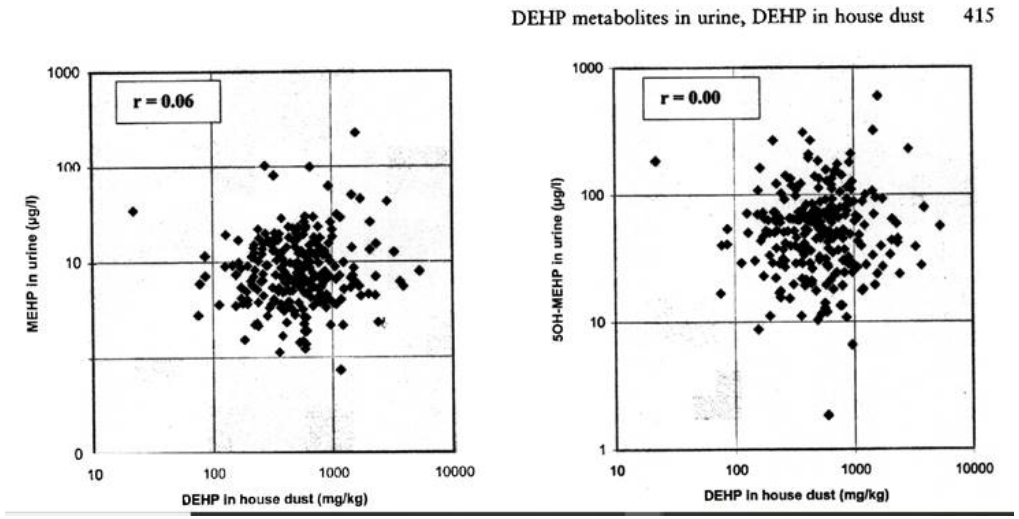


Fig. 2 Median contribution of single phthalates to the total content in indoor air and in household dust (only samples where household dust was also examined)

source: Fromme et al. (2003), Indoor Air 13, 1-8



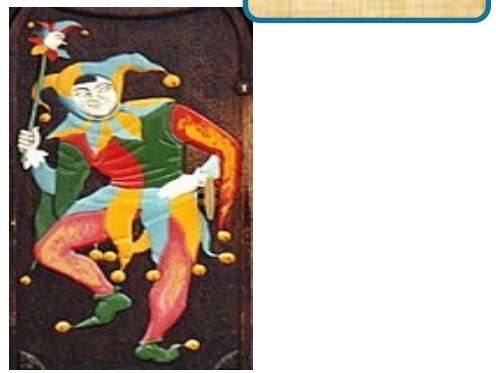
Source: Becker et al. (2004), Int. J. Hyg. Environ. Health 207, 409-417

- Plasticiser uptake by the oral route (food) is the most relevant source for human exposure for the high molecular weight phthalates
  - This may change in the near future due to the PAE restrictions

Summary

- The dispute on plasticisers is ongoing, but…

- Human biomonitoring, e.g. HBM4EU and NHANES enable robust risk assessments
  - More and reliable data regarding exposure levels are becoming available
    - Sources contributing to exposure are decreasing
      - By regulatory measures
      - By substitution with (new) high molecular weight plasticisers
        - HMW PAEs result in much lower exposure



- Wild speculations, hypotheses and scaremongering can be objected by undisputable, robust data

- Applications like e.g. flooring and wall covering are supported by scientifically robust and reliable data supporting the conclusion of no risk for the intended uses

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