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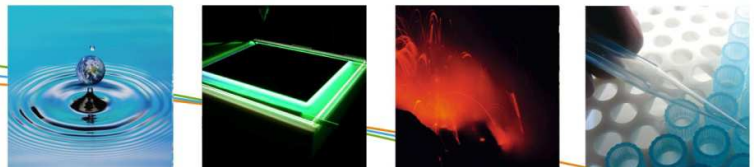Final report

Integrated Exposure for Risk Assessment in Indoor Environment (INTERA):

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CHAPTER 1   INTRODUCTION

Phthalates are used as plasticizers in polyvinyl chloride (PVC) plastics. Benefits of these additions are increased flexibility, transparency, durability, and longevity of the products.

Consequently, many consumer products and building materials contain one or more phthalates (e.g. packaging materials, toys, building materials, personal care products). As phthalates are not chemically bound to the plastics, they can leach, migrate or evaporate into indoor air, dust, foodstuff, other materials,…. As a result phthalates are ubiquitous in today's environment.

Due to their boiling points (Figure 1), most of the phthalates belong to the SVOC (semi volatile organic compound) category. These substances are essentially adsorbed to solids.
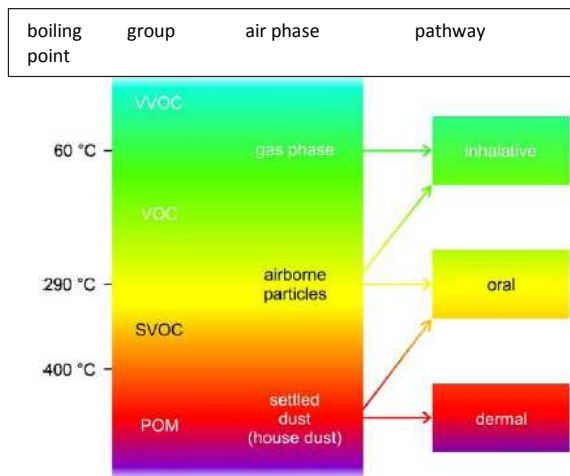
Figure 1: Classification of organic compounds using their boiling points, enrichment in indoor compartments and exposure pathways. VVOC: very volatile organic compound; VOC: volatile organic compound; SVOC: semi volatile compound; POM: particulate organic matter
(source: Wensing et al. (2005))

Given the diversity of phthalate containing sources in the indoor environment, their usage patterns and routes of exposure, an aggregate, multi-pathway exposure approach is needed for the evaluation of systemic health effects. Therefore, the INTERA phthalates case study is an excellent case study to test the INTERA methodology and tools (see main report and reports WP1 -4), where novelty lies in the approach to assess aggregate exposure in the indoor environment in a full chain (from source to dose) way, and in a way which deals with co-exposure via various sources and routes. A short overview of the data required to populate and run the phthalates case study within the INTERA methodology is given in Figure 2, and is detailed in the following sections.

INDOOR SOURCES/relevant pathways
- flooring materials: I, (O), (D)
- gloves: D
- adhesives, paints: D, I, (O)
- gloves: D
- personal care products: D, O, (I)
- textile: D
- toys: O, D
- others ???
- *(air, particles, soil): source/pathway*

between brackets: marginal or indirect source via transfer to air, PM, settled dust

oral pathway

Amount of phthalates in oral contact media at time of oral contact

type of oral contact: ingestion/mouthing

Ingestion:
- daily ingestion rate (soil/dust/PCP)

mouthing:
- product mouthed surface
- time of mouthing
- phthal release per area and time

oral dose

- body weight
- gastro-intestinal uptake

E internal, oral

dermal pathway

Amount of phthalates in products at time of dermal contact

source: mode of application/contact

instantaneous applications
- amounts used per application
- frequency of use

constant rate sources
- contact surface
- duration of contact
- weight per surface

Dermal dose

- body weight
- migration through skin

E internal dermal

inhalation pathway

type of available information

C_{air},
- gaseous phase
- PM phase

Emission - conc modelling
(building materials, hair spray, paints,):
- emission factor
- time of emission event
- frequency of emission event
- sorption on PM and settled dust

Inhalation dose

- body weight
- uptake

E internal, inhalation

E internal, aggregate

OR

(PB)PK modelling

Figure 2: Sources, pathways and concept to assess integrated exposure to phthalates in the indoor environment. I= inhalation; O= oral, D= dermal; PCP: personal care product, C_{air}: concentration in air; E: exposure (PB)PK= Physiologically based) pharmacokinetic modelling

This document is structured according to the case study methodology steps set out in the case studies guidance document (WP5) and as described in the INTERA main report Asikainen and et al. (2012).

CHAPTER 2   CASE STUDY STEPS

STEP 0: SELECTION OF PHTHALATES FOR INTERA CASE STUDY

Prior to the application of the methodology steps for the case studies (WP 5), there was a need to define which substances of the phthalates family the case study will focus on. After describing the groups of phthalates and its members, a decision tree was made and applied to select four substances to focus on. This exercise is described in the following paragraphs.

Phthalates: group of substances
Substances belonging to the phthalates group have the following phthalic acid diesters groups in common,
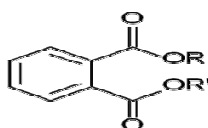
and they differ one from another in the R and R' groups in their backbone.
Often, phthalates are grouped into 2 classes: high molecular weight (HMW) phthalates (with more than 6 carbon atoms in their backbone) and low molecular weight (LMW) phthalates,:

- **HMW phthalates** (DINP(diisononyl phthalate), DIDP (diisodecyl phthalate), DPHP (di 2-propyl heptyl phthalate) , DIUP (diisoundecyl phthalate), and DTDP (ditridecyl phthalate)) represent just over 80% of all the phthalates currently being produced in Europe (ECPI, 2011). Risk assessments have shown positive results regarding the safe use of this group of substances. They all have been registered for REACH and do not require any classification for health and environmental effects, nor are they on the Candidate List for Authorisation (ECPI, 2012).

- **LMW phthalates** (DEHP di(2-ethylhexyl) phthalate), DBP (di-n-butyl phthalate), DIBP (diisobutyl phthalate), DMP (dimethyl phthalate) and BBzP (butylbenzyl phthalate)) represent about 10% of the European market (ECPI, 2012)). Risk assessments have led to their classification and labelling as Category 1B Reproductive agents. They have been registered under REACH but are included in the EU Candidate List based on their hazard classification and will therefore have to go through the REACH Authorisation process. These plasticizers will be phased out by the EU by February 2015 unless an application for authorisation is made before July 2013 and authorisation is granted.

The market share of MHW phthalates ('high' phthalates in Figure 3) has been steadily increasing over the last decade, in trade off of the LMW phthalates ('low' phthalates in the below graph) like DEHP. MHW are from a technical and economic perspective valuable substitutes for many applications in which DEHP used to be used.
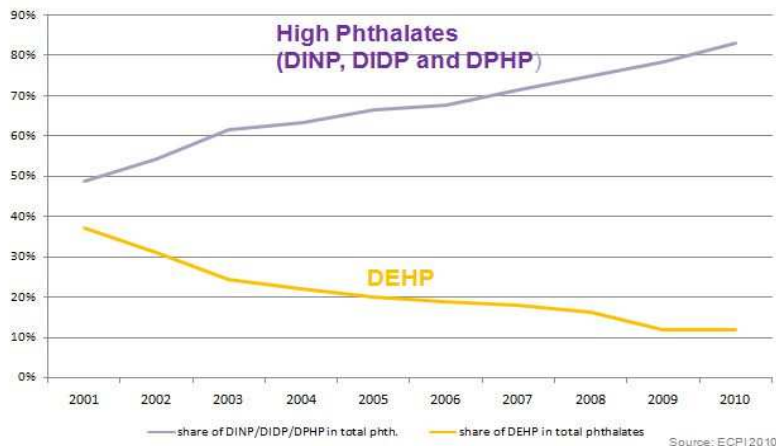
Figure 3: Share on phthalate market in EU

Besides this list of 10 high production phthalates, other phthalates are also used and encountered in the indoor environment (e.g. DNOP (Di-n-octylphthalate), DEP (diethylphthalate),ect., Wormuth et al. (2006); thought the focus in this case study is on the highest production volume list of ECPI (ECPI, 2012).

Selection of 4 phthalates to focus on in case study
Among the above list of 10 high production phthalate esters (i.e. DINP, DIDP, DPHP, DIUP, DTDP, DEHP, DBP, DIBP, DMP and BBzP) , a selection of 4 phthalates is made for focus in the INTERA cases study; hereto, the following criteria were applied:

> ***a.*** *coverage of both HMW and LMW phthalates (2 of each)*

> ***b.*** *substances with high production volumes*

Whereas at the end of the 1990s, 42 % of the consumption of plasticizers was for DEHP and 35 % for DINP and DIDP, the relative importance of these phthalates changed during the last ten years: DINP, DIDP and DPHP currently present ca. 65 % of the overall consumption of plasticizers in western Europe, and DEHP dropped to 16 % (ECHA, 2010). Based on production volumes, we selected DINP, DIDP and DPHP for the HMW group. For the LMW volume, DEHP is the highest production phthalates.

> ***c.*** *substances with known health effects and quantitative critical dose values (see also Step 1B)*

DIBP, DMP, BBzP, DEHP, DIDP, DINP: known health effects (systemic and/or local effects) & critical dose values

for DPHP, DIUP, DMP, DTDP: unclear health effects or lack of quantitative critical dose values

> ***d.*** *relevance of exposure in the indoor environment (see also in step 2 "identification of sources"):*
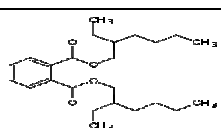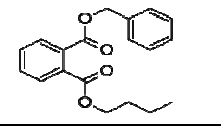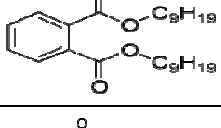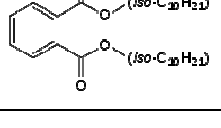
Wormuth et al. (2006) analyzed the contribution of various sources (indoor sources, dietary exposure,…) to the aggregate EU exposure in the EU population. Among the LMW phthalates, BBzP has the highest relative contribution from indoor sources; exposure to DIPB is dominated by dietary exposure (Wormuth et al., 2006). For DEHP, exposure is also dominated by dietary exposure; though, it is decided to retain this substance because of its high production volume compared to other LMW substances, and because it also causes local effects (due to inhalation). Both for DIDP and DINP, there is a significant contribution from indoor sources (Wormuth et al., 2006).

In conclusion, based on those criteria, we decided to focus the INTERA phthalates case study on the following 4 phthalates: for LMW group: DEHP and BBzP, for HMW group: DINP and DIDP.

<u>Description of some selected chemical properties of phthalates selected for this case study</u>

Table 1 details the structure, molecular weight and boiling point for each of the phthalates selected for the case study

Table 1:Name, abbreviation, CAS-nr , formula and molecular weight of 4 phthalates selected for the INTERA case study (source: Hutzinger, (2003)):

Abbreviation	Phthalate ester	CAS No	Structure	Molecular weight	Boiling point (C°)
DEHP	Di(2-ethylhexyl)phthalate	117-81-7		390.6	370
BB(z)P	Benzyl butyl phthalate	85-68-7		312.4	370
DINP	Diisononyl phthalate	28553-12-0 68515-48-0		418.6-432.6	244-254
DIDP	Diisodecyl phthalate	26761-40-0 68515-49-1		432.7-446.7	250- 257

2.1. STEP 1: DEFINE THE SCOPE OF THE CASE STUDY AND IDENTIFY LONG-TERM HEALTH ENDPOINTS RELATED TO EXPOSURE TO PHTHALATES

2.1.1. STEP 1A: DEFINE THE SCOPE OF THE CASE STUDY

An extensive amount on information and reports dealing with exposure to phthalates is published in the scientific literature and in the risk assessment reports under (EU) legislatory context. It would be an arduous task to reproduce, re-analyse or describe all existing information and scenarios using the INTERA methodologies and tools. Instead, we prefer to give firstly, a short summary of exposure data in indoor environments found in literature. Secondly, we'll apply the INTERA methodology and tools to answer a few dedicated questions:

1) <u>Can we reproduce the existing data on indoor phthalate exposure in the EU?</u>
   The INTERA predictions for exposure to phthalates in the EU through modeling via the INTERA platform will be compared with comparable, previous investigations made by Wormuth et al. (2007), Wormuth et al. (2006) and in the EU Risk Assessment Reports (RARs) ((ECB, 2003a; ECB, 2003b; ECB, 2007; ECB, 2008). Considering that these studies deal with multi-source and multi-pathway exposure to phthalates in the EU, they serve as a basis for validation of the INTERA outcomes.

2) <u>Can we validate the full chain approach of the INTERA tools:?</u>
   The above cited reviews on (indoor) exposure to phthalates in the EU study takes concentrations in air, dust and soil as a starting point (considered as "sources"). However, media such as air, dust and soil are rather '"pathways" than sources. Within the INTERA phthalate case study, the full chain approach (sources – emissions –air, dust) will be run, and, thus concentrations in air and dust (pathways) will be traced back to their sources (phthalate containing materials), and we'll verify the calculations by comparison with measured data.

3) <u>Can we stratify phthalate exposure according to geographical region in the EU?</u>
   The above cited reviews stratify phthalate exposure according to age and gender categories; not according to geographical region , except for a study by the Danish EPA (Danish EPA, 2009), which is based on Danish specific data. It will be investigated if we can find region specific data on phthalates concentrations, use patterns, and to what extent there is a geographical trend in phthalate exposure across the EU.

4) <u>What is the impact of the policy measures on restriction of use of phthalates in toys and child care products in term of aggregate exposure?</u>
   The use of phthalates in toys and childcare items has been restricted in the EU since December 1999. After January 2007, further restrictions on the use of phthalate plasticizers in toys came into effect throughout the EU (Directive 2005/84/EC). We'll run a scenario 'before restrictions' and 'after restrictions' to investigate the potential impact of such a policy on aggregate exposure to phthalates in children.

Thus, aim of the INTERA case study is not to repeat and recalculate all numerous and comprehensive previous exposure assessments on phthalates (Wormuth et al., 2006, EU RARs on phthalates, Danish EPA, 2009, ECHA, 2010), rather, we'll undertake a review of the existing exposure data, focus on the above four questions, and the test the INTERA case study methodology and tools for the selected phthalates.

2.1.2. STEP *1*B: IDENTIFICATION OF LONG-TERM HEALTH ENDPOINTS

An overview of long-term health effects and threshold values (systemic effects / local effects) for the selected phthalates is given in **Error! Reference source not found.**.

Table 2: Systemic and local health effects associated with the four selected phthalates

	Systemic health effects			Local health effects (inhalation)		
Phthalate	Critical health effect	Threshold value systemic (µg/kg bw/day)	Reference	Health effect – local effects?	Threshold value local effect	Reference
DEHP	Reproductive effects Developmental effects	50 (20)* (25)**	CSTEE (1998); ECB (2008); EFSA (2005)	inhalation; increased asthma risk in children	?	Bornehag et al. (2004)
BBzP	Developmental effects	850 /200	CSTEE, (1998); ECB (2007); Wormuth et al. (2006)	Inhalation: increased incidence of rhinitis and eczema of children	?	Bornehag et al. (2004)
DINP	Developmental & reproductive effects	150	CSTEE (1998); EFSA (2005c)	_	°	°
DIDP	Developmental & reproductive effects	250/150	CSTEE (1998); EFSA (2005b); Wormuth et al. (2006)	_	°	°

*for infants 3-12 months
**for newborns (0-3 months) and women in childbearing age
?: no threshold value derived for local effects from the study of Bornehag et al. (2004)

DEPH, BBzP, DINP and DIDP have been reported to cause reproductive and or developmental systemic effects (CSTEE, 1998; ECB, 2003a; ECB, 2003b; ECB, 2007; ECB, 2008; EFSA, 2005a; EFSA, 2005b; EFSA, 2005c; Heudorf et al., 2007; Wormuth et al. 2006). In addition, there is concern about increased risk on asthma in children upon inhalation of DEHP (Bornehag and Nanberg, 2010; Bornehag et al., 2004). As a consequence, we focus the phthalate exposure investigations on 1) systemic dose and 2) inhalation dose.

2.2. STEP 2: IDENTIFICATION OF THE MAIN SOURCES OF EMISSION (PRODUCTS) IN RESIDENTIAL SETTINGS

2.2.1. USES OF PHTHALATES

The building and construction sector (e.g. roofing materials, hoses, flooring, ect.) represents about 60% of use of phthalates. Some application use specifically one or two phthalate (e.g. medical devices: DEHP; printing inks: DIDP; sealants: BBzP; adhesives: BBzP & DIDP); while many applications are not very specific in the type of phthalate which is used for the given application; especially in all purpose plastics, several types of a mixture of different phthalates are used (e.g. in flooring materials, wire and cable insulation, artificial leather & footwear, toys, etc.). The majority of these general applications in which DEHP used to be used is now being substituted by DINP & DIDP.

Each member of the phthalates family has one or more uses and application domains. For the four selected phthalates for this case study, the following major uses have been reported (ECB, 2003a ; ECB, 2003b; ECB, 2007; ECB, 2008; Heudorf et al., 2007; Koniecki et al., 2011; Wormuth et al., 2006) and are listed overleaf (**indoor relevant sources marked in bold**):

- DEHP: **building and construction materials, wallpaper, flooring, sealing, wire and cable insulation),** car interior (**vinyl upholstery), clothing (footwear, raincoats), food packaging, children's products (toys, grip bumpers)**, **gloves**, medical devices, **PCPs and cosmetics** (http://www.dehp-facts.com/)

- BBzP: **vinyl tiles**, food conveyor belts, **artificial leather**, automotive trim, traffic cones, **sealants, adhesives** (http://www.bbp-facts.com/)

- DINP: garden hoses, pool liners, **flooring tiles, tarps, toys, flexible PVC sheets, footwear,** swimming pools, **(+ majority of uses of DEHP)** (http://www.dinp-facts.com/)

- DIDP: **PVC plastics, covering on wires and cables, profiles, roofing sheets or pond linkers, artificial leather, toys, carpet backing,** pool liners, **non PVC end products: paints, printing inks, latex, adhesives (**http://www.didp-facts.com/**)**

The use of phthalates in toys and childcare items has been restricted in the EU since December 1999. The toys directive (Directive 2005/84/EC), which took effect since January 2007, stipulated further restrictions on the use of phthalate plasticizers in toys throughout the EU. Whereas current legislation limits DEHP and BBzP for all parts of toys and childcare articles, the restrictions on the use of DIDP and DINP phthalates are limited to (parts of) children's articles which can be placed in the mouth. This restriction define that these substances shall not be used, or as constituents of preparations, at concentrations of greater than 0,1 % by mass of the plasticized material, in toys and childcare articles.

DEHP and BBzP have both been registered under REACH but are included in the EU Candidate List based on their hazard classification and will therefore have to go through the REACH Authorisation process. These plasticizers will be phased out by the EU by February 2015 unless an application for authorisation is submitted before July 2013 and an authorisation granted. In general, it is expected that use of DEHP and BBzP will further decrease and be replaced by HMW phthalates.

2.2.2. SOURCES DOMINATING EXPOSURE TO PHTHALATES

The study of Wormuth et al. (2006) investigated the sources of exposure to phthalates in the European population. These authors reported a variety of phthalate sources present in residential settings. According with the study results the dominance of sources for exposure depended on 1) type of phthalate, and on 2) type of exposed population category: (Figure 4):

- DEHP:

    Indoor environment sources (dust, air, mouthing, PCP) contribute significantly to systemic DEHP exposure for infants and toddlers. The sum of these sources is about 50 % of systemic exposure. For other population groups, food (> 90 %) and not indoor sources dominate. This is in accordance with the lack of relationship between DEHP air and metabolites of DEHP in urine of pregnant women in the study of Adibi et al. (2008).

- BBzP:

    Mouthing, food and air dominate exposure to BBzP for infants and toddlers. For teenagers, spray paints (70 %) were reported as the dominant source. For adults, ingestion of food is main source (60%), followed by spray paints. The significant contribution of the inhalation pathway to systemic BBzP dose was also demonstrated in the study of Adibi et al. (2008) where a significant relationship was found between the concentration in air of BBzP and metabolites of BBzP in urine of pregnant women.

- DINP:

    Mouthing (toys) is the dominant source (> 90 %) for DINP for infants, toddlers and children. Ingestion of dust, indoor and outdoor air, and spray paints and gloves contribute more or less to the same extent to DINP exposure for teenagers and adults.

- DIDP:

    Mouthing (toys) and ingestion of dust are dominant sources for DIDP exposure for infants and toddlers. For teenagers and adults, food dominates exposure, although ingestion of dust, indoor air, gloves and spray paints cannot be neglected.
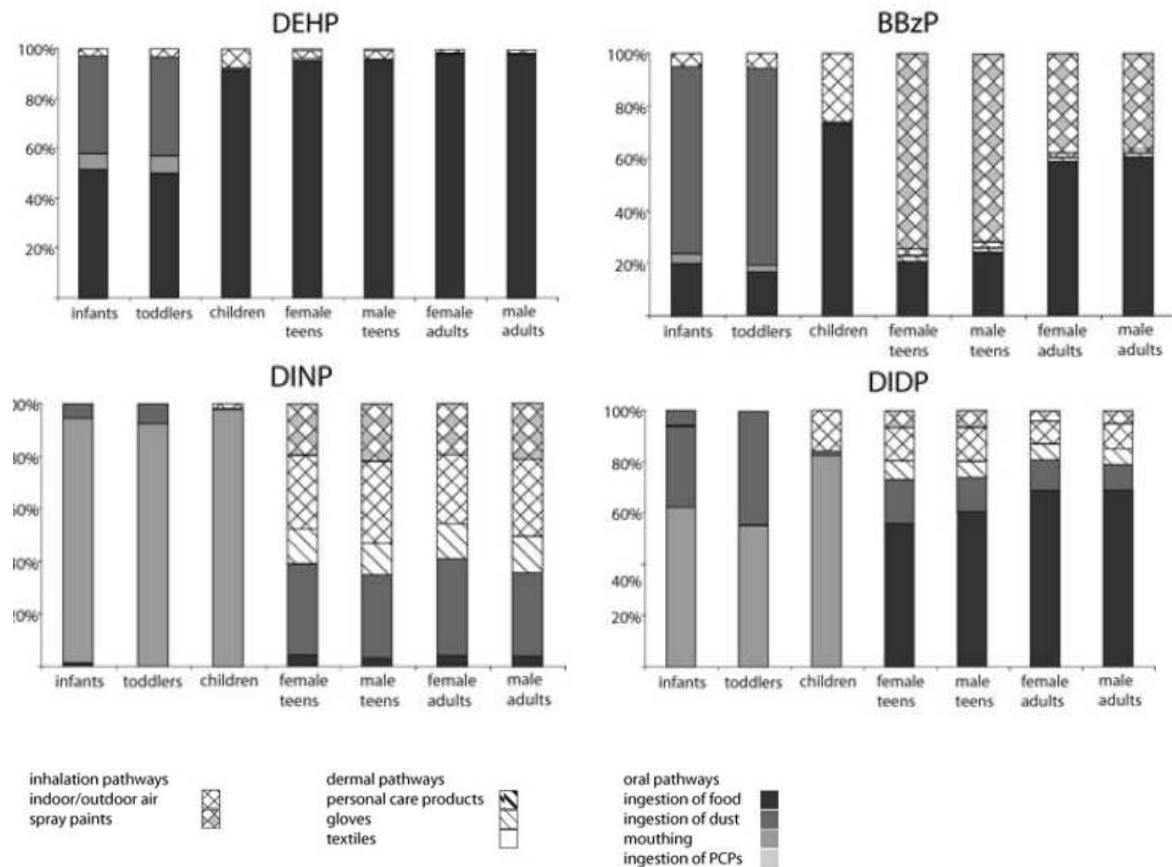
Figure 4: Contribution of different sources to the mean total daily internal exposure to 4 phthalates in seven age and gender groups in the European population (source:Wormuth et al. (2006))

Given that the publication of Wormuth et al. (2006) is based on data gathered before the restrictions on DINP, DIDP, BBzP and DEHP in toys and childcare products (restriction since 2007), it is likely that exposure via mouthing and dermal contact with articles (major source DINP and DIDP exposure) have dropped since then. However, it is yet difficult to assess quantitatively the impact of this regulation on actual exposure levels, since there is at present no information available on the compliance of producers and importers with restriction and the possible remaining levels in these categories of products (ECHA, 2010). Moreover, children might nowadays still be exposed to toys/childcare articles brought on the market before 2007, and to other articles not falling under

the restriction. For example, it appears that school children are exposed to DINP in some PVC containing school supplies, and in particular to non-toy erasers (Danish EPA, 2009).

Wormuth et al. (2006) used measured data on indoor and outdoor air, and soil and dust as starting point for the exposure assessment. However, they did not investigate what are the sources of phthalates in indoor and outdoor air or dust, soil; in other words, a full chain or mechanistic approach for source to exposure modeling is lacking. In contrast, in the RARs of the four selected phthalates, a source to dose approach was followed. For example, in the RAR of DEHP, modeling of emission from floor and wall covering materials to indoor concentrations was performed (ECB, 2008). However, other sources were not taken into account and the sorption of DEHP on particles was identified as being important in the RAR of DEHP; however, at the time of writing of the RAR of DEHP, an appropriate model describing sorption of DEHP on particles was lacking.

In addition to flooring and wall covering materials (as assessed as indoor sources contributing to indoor air concentrations of DEHP in the RAR of DEHP), other sources for air and dust phthalates concentrations include: wall paper, electric cables, refrigeration strips, electric wire, PVC flooring, PVC skirting (Afshari et al., 2004). Other sources of phthalates such as personal care products (PCP), textile, gloves as addressed as sources by Wormuth et al. (2006) could contribute as well, though these appeared to form perhaps minor sources for indoor air exposure (Wormuth et al.,2006). Phthalate containing sources with a high surface area such as vinyl flooring are generally considered to form the main sources of indoor phthalate levels. Phthalate emission rates for these identified sources are listed in step 3.

2.3. STEP 3A: EMISSION – INDOOR AIR MODELING

2.3.1. EMISSION RATES OF THE CONTAMINANTS OR RELEASES FROM CONSUMER PRODUCTS

An inventory of phthalate emission rates from consumer products is given Annex I, Table A 1. In addition the emission rate data collected were uploaded to the KMS database.

Hereto the following sources were consulted:
- Scientific literature (Web of Science searches)
- EU RARs on phthalates, Danish EPA (2009) report on phthalate exposure, ECHA report on DINP (2010)
- Databases on emission of chemicals from building materials (BUMA – database ((www.buma-project.eu)

It is remarked that the available data are hard to interpret in terms of representativeness of tested materials for the EU population in general, or to assess the geographical or other differences like socio-economic conditions in use of the materials across the EU.

Two types of consumer products causing phthalate emissions into indoor air were identified: 1) areal continuous sources (e.g. floor covering, carpets, cables,..) and 2) point instantaneous sources (e.g. spray paints).

2.3.1.1. AREAL CONTINUOUS SOURCES

In comparison to the numerous studies and large databases (e.g. BUMA) of (V)VOCs emissions from building materials, the number of studies investigating phthalate or other SVOC emissions from building materials is rather limited. This lack of scientific studies could be due to difficult analytical procedures (Afshari et al., 2004).

Moreover, building material test protocols (e.g. AgBB schema in Germany[1] and AFSSETT[2] scheme in France; and voluntary scheme's like Blue Angel[3], ect) do not provide any requirements on ceiling emission limits for phthalates.

Procedures to determine emission rate (for VOCs) are generally fixed at a 7 to 28 day testing period after the onset of the test, the latter defined as the moment when the material has been placed a controlled test chamber with a constant air flow (e.g. protocol AgBB and AFSSETT; protocol in prEN 15052 CEN/TC[4]). For volatile compounds, this covers the period of the highest emissions; after this initial release period, emission decrease steadily. In contrast, for SVOCs such as phthalates, emissions might increase after the initial period and reach quasi-static equilibrium concentrations above the initial concentrations. For example, DEHP emissions from flooring materials measured at a 35 day testing period were about 35 % of those at equilibrium reached around 150 days. These values were comparable for other DEHP releasing materials: floor material B: 43 %; wallpaper 53 %; skirting 32 %, electric cable 59 % and refrigerator strip 50 % at day 35 compared to quasi-static equilibrium (Afshari et al., 2004). Therefore, Afshari et al. (2004) propose to use a correction factor of 2.2 (based on mean value of 45 % for ratio day 35 / moment of equilibrium) for test results at day 35 to have an estimate of the quasi-static concentrations, relevant for long-term exposure assessment.

Emissions rates of DEHP appeared to not be affected by the relative humidity in the test environment (Clausen et al., 2007).

Whereas there is limited data on DEHP emissions found in the literature, emission rates of BBzP, DIDP and DINP from building materials or consumer products appeared to be non-existent in the literature.

2.3.1.2. POINT INSTANTANEOUS SOURCES

Spray paints generate aerosols that are inhaled by consumers. Emission rates are assumed to be related to concentrations of phthalates in spray paints. Data on concentrations are taken from the Swiss product register (BAG, 2004) and are on average 10 000 mg/kg DEHP, 3000 mg/kg DINP, 1667 mg/kg DIDP and 373333 mg/kg BBzP.

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[1] AgBB: Health-related evaluation of emissions of volatile organic compounds (VOC and SVOC) from building products, 2010. Available at: http://www.umweltbundesamt.de/produkte-e/bauprodukte/agbb.htm

[2] ANSES, Agence nationale de se´curite´ sanitaire de l'environment et du travail. Available at: http://www.afsset.fr

[3] http://www.blauer-engel.de/en/blauer_engel/index.php

[4] European prenormative stanstard for VOC emissions available at http://www.cen.eu/cen/pages/default.aspx

2.3.2. **U**SE PATTERNS OF PHTHALATE EMITTING CONSUMER PRODUCTS USED IN RESIDENCES

2.3.2.1. **A**REAL CONTINUOUS SOURCES

Emission factors (as listed above) are expressed as emission rates per unit surface area of products. Hence, information on usage of products and surface areas are needed to perform an exposure assessment. However, data on usage and surface areas of consumer products and building materials at household level are lacking.

Production and import/export data of e.g. floor covering materials do exist; however, these are of little use to assess population exposure to emission from building materials.

2.3.2.2. **P**OINT INSTANTANEOUS SOURCES

Emissions from sprays are assessed based on the following facts: a typical fingertip dispenser generates 25 mg of spray per minute; and the mean duration of spraying is 4 minutes; and spray paints are infrequently used by teenagers and adults (2 times per year, or 0.0055 per day) (Effting and van Veen, 1998)

2.3.3. **R**ESIDENCES VOLUMES

Data in KMS on residence volume are used for full chain calculations in for this case study.

2.3.4. **I**NDOOR-OUTDOOR AIR EXCHANGE RATES

Data in KMS on indoor-outdoor air exchange rates are used for full chain calculations in this case study.

2.3.5. **I**NDOOR CONCENTRATIONS

2.3.5.1. **M**ODELING APPROACH

This paragraph describes the state of the art in mechanisms and modeling approaches to estimate indoor concentrations in real indoor environments and exposure starting from phthalates emission test results.

All interior end use emissions are to the air compartment via volatilization mechanisms, except for flooring where abrasion may occur (Exxon Chemical Corporation 1997, cited in RAR DIDP, ECB, 2003a).

Emissions of DEHP from vinyl flooring are largely controlled by equilibrium between the material and the gas phase, external convective mass transfer, and also by strong partitioning to interior surfaces, including airborne and settled dust. These properties mean that it takes months to years for a compound like DEHP to reach equilibrium between dust and gas phase (Weschler and Nazaroff, 2010) and that variation in air exchange rates are expected to influence the emission rate of DEHP (Clausen et al., 2010).

In addition, results from emission studies in test chambers do not cover all factors in a real building. In a real building, large sinks such as furniture, curtains, doors, carpets and porous materials in wall and ceiling decrease the concentration of DEHP in the buildings and the re-emissions do the opposite. Consequently, the emission rate could be higher in a real building when compared with the results obtained in the chamber (Afshari et al., 2004). Liu et al. (2010) demonstrated that airborne DEHP consisted mainly of particle phase bound DEHP. This illustrated the need to take into account the transfer from the gaseous phase to particulate matter (PM) and settled dust in this case study.

Although needed for risk assessment and to develop control strategies, the mechanisms governing emissions and distribution of phthalates in the indoor environment are still not fully understood (Clausen et al., 2010). However, recent studies attempted to tackle this issue. For example, Xu et al. (2009) developed a (semi)mechanistic model that governed the release of DEHP from vinyl flooring and the subsequent interactions with interior surfaces, airborne particles, dust, and human skin. Subsequently, the oral, dermal and inhalation exposure to DEHP released for vinyl flooring was assessed. Xu et al. (2009) concluded that ingestion of dust was the dominant pathway in DEHP exposure related to vinyl flooring. This study was limited to one source (vinyl flooring) and one phthalate (DEHP); though, it consists of a promising approach that could perhaps be extended to other sources and other SVOCs.

The study of Xu et al. (2010) demonstrated the sensitivity of vinyl source characteristics (surface area, material-phase concentration of DEHP), of mass-transfer coefficients and ventilation rates on DEHP concentrations and resulting exposure. In addition, phthalates are sorbed strongly to surfaces, including airborne particles and settled dust. Hence, higher TSP (total suspended particles) levels in the indoor environment leads to increased sorption on particles, resulting in reduced gas concentration; consequently, inhalation exposure is lower than under conditions of low TSP levels, while oral and dermal exposure increase.

In their review paper, Weschler and Nazaroff (2010) gathered data on dust borne and airborne SVOC contents in thousand dwellings covering 66 SVOCs and used these data to test a simple equilibrium model for estimating the partitioning of an SVOC between the gas phase and the settled dust indoors. They demonstrated that, in central tendency, that a compound's octanol-air partitioning coefficient is a strong predictor of its abundance in settled dust relative to its gas phase concentration. However, the authors Weschler and Nazaroff (2010) emphasize that their approach should be used for median values from a collection of measurements made in multiple residences, and they anticipate that their approach would not be successful for predicting partitioning between the gas phase and settled dust in individual residences.

In the RARs of DEHP, BBzP, DINP and DIDP, the contribution of PM was addressed as 'likely significant'. However, in absence of a model, a pragmatic approach was used to estimate phthalate levels in PM in the RARs of these four phthalates: the phthalate concentrations in the PM phase were calculated as the 3-fold of the gaseous concentration. This factor 3 was based on a study Oie et al. (1997) who found that the exposure via the particulate air phase was 1-3 times greater than the vapour phase. This was also supported by the study of Wams (1987) who reported total air concentrations for phthalates exceeding the saturated vapour pressure by 100-fold.

In conclusion, the relevance of gaseous emission rates determined in test chambers forms a bottleneck in indoor exposure modeling since test chamber result reflect only gas phase concentrations and do not account for sorption to dust, which is of significant importance for phthalates. To cope with this, the computational platform includes a mechanistic model describing and predicting the partitioning of phthalates between gas and dust phase (see report WP 3).

2.3.5.2. MEASURED DATA

Besides full chain source to receptor modeling, one might also consider to bypass some parts of the full modeling chain, like the source to indoor concentration module, and use measured concentrations in air as starting point for the inhalation pathway. Hereto, an inventory of phthalates levels measured in the indoor air (gaseous phase + PM phase) of residences in the EU is made. These data might of course also be used for verification of full chain modeling results.

The inventory of phthalate indoor concentrations is given in Annex I, Table A2. The data is also available in the KMS database.
On this point, some data on various indoor environment (home, school, offices, daycare) are country-specific, allowing to assess geographical variations with the EU. This data was also entered into the KMS.

2.3.6. OUTDOOR CONCENTRATIONS

Data on phthalate concentrations in the outdoor air are scarce. These data demonstrate that phthalate levels in outdoor air are several orders of magnitude lower than in the indoor air (for DEHP and BBzP) or were not detected in the outdoor air (for DIDP and DINP) (Wormuth et al., 2006) The inventory of phthalate indoor concentrations is given in Annex I, Table A3.

2.4. STEP 3B: DERMAL EXPOSURE

For phthalates, two types of sources, having a distinct exposure mechanism for dermal exposure are identified:

- sources with instant application applications (e.g. PCP)
- sources with exposure through migration (e.g. articles like toys, textile, gloves)

Whereas some tools (e.g. ECETOC TRA) use rather generic models to describe dermal exposure for articles with constant rate resources via migration, Wormuth et al. (2006) describe and use product-specific dermal exposure models for assessing phthalate exposure via those type of products.

In the context of INTERA methods and tools, it was preferred to use generic models, as the models are aimed to be used also for other purposes and products than the ones within this case study. Two models, according to exposure mechanisms are used; firstly a generic model to assess exposure to sources with instant application to the skin (e.g. personal care products and cosmetics) (see 2.4.1), and secondly, a model accounting for unavoidable exposure to sources via the mechanism of migration from the source to the skin (see 2.4.2).

2.4.1. SOURCES WITH INSTANT APPLICATIONS

The dermal exposure to phthalates in personal care products (PCPs) can be mathematically described as (Koniecki et al., 2011):

$$\text{Exposure } (\mu g/kg\,bw/d) = C(\mu g/g) \times AF(g/use) \times FD(\text{time}/d) \times RF \times A(\%)/bw(kg)$$

With C: concentration of phthalates in products,
AF: amount of product applied
FD: frequency of use of products
RF: retention factor: default value to account for rinsing off and dilution of finished products by application to wet skin or hair
A: percutaneous absorption

This equation was applied in the calculations for case 1 which was performed using Microsoft Excel, outside the computational platform (see below).
An inventory of C, AF, FD, RF and A factors found in literature is given in Annex I, Table A4.

The use of DEHP and BBzP in PCP is banned in the EU since 2007 under the Cosmetics Directive (76/768/EC, and amendement in 2004/93/EC). The presence of traces such as DEHP is allowed under the cosmetic directive, provided that such presence is technically unavoidable in good manufacturing practice. In practice, traces of DEHP might be present due to leaching from the containers.

The study of Wormuth et al. (2006) focused on the EU market (based on a review of literature data, period before 2005), while the study by Koniecki et al. (2011) was focused on the Canadian market; the latter might not be fully transferable to the EU situation. Information on analysis method, detection limit, number of samples investigated are lacking in the paper of Wormuth et al. (2006) while this information was reported by Koniecki et al. (2011).

In addition, among all product types, it was only a minority of products that phthalates were above the detection limit (0.5 µg/g) for DEHP. The phthalates BBzP, DIDP and DINP were not included in the survey of phthalates in cosmetics and personal care products of Koniecki et al. (2011).

In Table A4 of Annex I, only PCPs where one or more of the 4 case study phthalates were found in the study of Wormuth et al. (2006) are listed. In other investigated PCPs (i.e. shampoo, skin care, nail care, make-up, baby shampoo, baby lotion, creams, oils) in the Wormuth et al. (2006) study, no detectable levels of BBzP, DEHP, DINP and DIPD were reported.

Koniecki et al. (2011) mention that among the parameters in the above equation, the percutaneous absorption parameter is a parameter that is not easy to determine and highly variable. As a conservative approach, Koniecki et al. (2011) used a percutaneous absorption factor of 5 % for all phthalates, except for subungual penetration (nail polish) (penetration rate of 0.6 % per 24 h).

2.4.2. SOURCES WITH EXPOSURE THROUGH MIGRATION

There are several models in the literature describing dermal exposure through contact with consumer products, each having their own set of required input parameters, and application domain. For example, Wormuth et al. (2006) developed a specific model for each product type (one for toys, textile, gloves, paints, adhesives, particles), and product- specific input parameters (e.g. for toys: concentration in toys, density of toy, thickness of toy, while for textile: weight of textile… Other models are more generic (e.g. 2 models described in the RAR of DEHP).

Irrespective of the model, the following factors are required to determine the exposure:

- S: skin contact area (cm²)
- t : time of contact (h/day)

- DAR: dermal absorption rate (µg/cm²/h) or
  - release factor (µg/cm^2/h) X absorption through the skin (% of external dose)

The generic model for dermal exposure to sources via migration can be described as:

$$dermal\ exposure\ \left(\mu\frac{g}{day}\right) = DAR \times S \times t$$

The various models described in the literature differ mainly in the way how the dermal absorption rate is calculated:

- either based on experimental measured release factors or absorption rates;
- either based on modeling tools starting from concentrations in products, weight, density,ect.

An inventory is made for the above described generic factors (see Annex I, Table A5). The Danish EPA report (2009) addresses dermal exposure to DINP and DEHP present in the labels of two mittens (DINP concentration: 7.8 % - 8. 6%; DEHP concentration: 0.04 – 14.7 %). No DINP appeared to be released from the mittens following a fluid saliva extraction (3h), while releases of DEHP in the range of 0.01 – 0.68 µg/g were measured (the latter corresponding to the material in 14. 7 %). The potential dermal exposure from baby changing mats/cushions was assessed based on migration rate of DINP from baby changing mat of 6.6 µg/200 cm² (during 4h, and taking into account a dermal absorption fraction of 0.05 %, and rescaling for time a baby is placed on a changing mat during one day (10 minutes for a 2 years-old baby).

As mentioned above, we revealed two types of studies and used models for addressing dermal exposure to phthalates via the mechanism of migration. The first group of studies, including RAR reports, study of Müller et al. (2003) used generic, product aspecific models (like equations above), often in combination with conservative estimates for dermal migration rates and contact times to address dermal exposure to products via migration. For example, Müller et al. (2003) (and the RARs) performed a dermal exposure assessment not covering one specific dermal exposure scenario for children, but instead a generic scenario covering different sources/pathways to dermal exposure. Herein, it was assumed that the release rate from these sources is equal to the DEHP release rate from vinyl flooring. Dermal contact duration to phthalate containing products was estimated on 2h/day in the EU RARs, and as 3h/day by Müller et al. (2003).

The second type of studies (e.g. Wormuth et al.,2006) uses product-specific models and contact times.

Not surprisingly, the first group of models results in vast more conservative and thus higher dermal exposure values than the latter one. For example dermal exposure – expressed as yearly averaged uptake - via use of paints for adults is 3.4 10^{-3} µg/kg bw/day for DEHP, 3.4 10^{-4} µg/kg bw/day for DINP and DIDP and 0.032 µg/kg bw/day for BBzP) (Muller et al.,2003), and similar data in RARs. These values are higher than contributions via air. Dermal exposure to DEHP for children is estimated on 1 µg/kg bw/d; and for DINP and on 0.15 µg/kg bw/d for DIDP (Müller et al.,2003). In contrast, in Wormuth et al. (2006), dermal exposure is insignificant for all 4 phthalates and sources (except via gloves for DIDP and DINP for some age categories).

One child-specific scenario for dermal contact to phthalates is dermal exposure via toys. In previous risk assessments, analyses of dermal exposure to phthalates are based on the situation before the

restrictions. By lack of experimental data for toys, migration rates from toys were in most cases (in the RARs and Müller et al.,2003) assumed to be based on equal as the rates for flooring materials. However, since the content of flooring materials (up to 40 % phthalates) is more than 100 –fold above allowed concentrations in toys, this extrapolation is no longer valid. Based on the concentration of DEHP (0.04 %) in mittens being low and its corresponding release rate (< 0.01 µg/g in a 3h saliva fluid test), it is more likely that exposure to DEHP via toys corresponds to the latter value, and thus can be neglected for toys brought on market after the ban.

However, in addition to that, children are also in dermal contact with a variety of other phthalate containing articles like flooring material, packaging material, textile, plastic table-cloths,…., However, both 1) product specific dermal release data are unavailable (e.g. DEHP release from toys in EU RARs is based on DEHP release from PVC flooring material), and 2) data describing children's contact to specific products are scarce (duration, frequency and contact surface area)).

In contrast, Wormuth et al. (2006) did apply a product-specific approach for dermal contact to toys, gloves, textile, PCPs, paints & adhesives and particles. In their analysis, dermal exposure to DINP and DIDP via gloves appeared to be significant (though lower than 5 % of aggregate dose), while dermal exposure to toys and textiles was negligible. For DEHP and BBzP, dermal exposure to none of the products (toys, gloves, textiles) led to a significant contribution of aggregate exposure.

2.4.2.1. DERMAL CONTACT AREA

Surface areas for dermal contact from the KMS are applied. Herein, age and gender specific data are available, and differentiation for the various parts of the body. This is more detail than what is used in the RARs (where a skin surface factor of 100 cm² was applied), and comparable to the approach taken by Wormuth et al. (2006) who applied a skin surface area for hands of 121 cm² (infants), 295 cm²(toddlers), 463 cm² (children), and 900 cm² (adults).

2.4.2.2. DERMAL CONTACT TIME

Among the various assessments in literature, there is quite a range in assumptions on dermal contact time with gloves. In the EU-RAR, a contact duration for 2h/day was assumed (surface hand contact of 840 cm²); whereas Wormuth et al. (2006), simulated a 'mean' and 'max' scenario based on respectively daily dishwashing events with gloves of 0.63 (mean) – 5 (max), and duration per event of 11 minutes (mean) – 60 min (max). The data is also available in the KMS database.

2.5. STEP 3C: ORAL EXPOSURE

Dietary exposure dominates the oral exposure pathway for DEHP, BBzP and DIDP, especially for adults. For infants and toddlers, ingestion of dust and mouthing are main exposure routes for DEHP, BBzP and DEHP. For DINP, oral exposure is dominated by mouthing and ingestion of PCP (for infants, toddlers and children), and food is only a minor pathway.

However, it is out with the scope of INTERA to deal with oral exposure via the diet. This pathway is not addressed in the INTERA methodology and computational modeling platform, and would require inclusion of modeling transfer from the environment to food, from packaging and contact materials to food, food consumption patterns, ect.

Nevertheless, if one wants to use the oral exposure estimates from indoor sources in health risk assessment for systemic effects, especially when considering aggregate doses and PBPK modeling one must be aware that the 'background' (= other sources than indoor, thus food) should be added up to the indoor-related oral exposure estimates.

Indoor related sources for oral exposure to phthalates are:

- Mouthing (children): mainly toys, but also other objects (e.g. school supplies, erasers)
- Ingestion of dust
- Ingestion of PCPs (children)

2.5.1. MOUTHING

Oral exposure via mouthing is calculated as:

$$oral\ exposure\ mouthing = leaching\ \left(^{\mu g}/_{cm^2.h}\right) \times time\ mouthing\ \left(\frac{h}{day}\right) \times surface\ mouthing\ (cm^2)$$

2.5.1.1. LEACHING

An inventory of leaching of DEHP from toys (sucking) is given in Annex I, Table A6.

The references from which the data in Annex 1, Table A6 were drawn do not in general report on phthalate concentrations in the toys (or the materials used as proxy for toys); though, it can be derived from the data the majority pertain to phthalate containing toys/materials.

Though, it should be accounted for that not all toys on the market contain phthalates, as demonstrated by Ragosti and Worsoe (2001) (see paragraph below), and this must have been further decreased since the Toys regulation (Directive 2005/84/EC)came into force.

Rastogi (2001) have measured the concentration of toys in the Danish market. In 2001, 20 products of toys intended for children < 3 years were collected from Danish retail outlets. The plastic parts of the products were analyzed for their phthalate contents (DEHP, DINP and DIDP). For DEHP, for 10 of the 20 samples DEHP was detected, in 7 DIDP was detected and in 9 toys, DIDP was detected. A Nordic investigation (Throne-Holst, 2001) demonstrated that DINP was found in 15 out of 18 investigated products, and DEHP was found in 12of the 18 products.

Since majority of data were gathered (and used in EU RARs and Wormuth et el.,2006) before the restrictions on DINP, DIDP, BBzP and DEHP in toys and childcare products (since 2007), it is likely that exposure to mouthing and dermal contact with articles (major source DINP and DIDP exposure) have dropped since then. However, it is presently difficult to assess quantitatively the impact of this regulation on actual exposure levels, since there is at present no information available on the compliance of producers and importers with restriction and the possible remaining levels in these categories of products (ECHA, 2010). Moreover, children might nowadays still be exposed to toys/childcare articles brought on the market before 2007, and to other articles not falling under the restriction. For example, it appears that children are exposed via mouthing to DINP in some PVC containing school supplies, and in particular to non-toy erasers (Danish EPA, 2009).

2.5.1.2. MOUTHING TIME AND SURFACE MOUTHING

For calculation of the individual oral exposure to DEHP from these leaching values, a maximum exposure of 3 hr/day (mouthing time) and a mouthing area of 10 cm^2 for a child (8 kg) were assumed in the RARs of DEHP, DINP, BBzP and DIDP. In the (Wormuth et al., 2006) study, a differentiation in mouthing time is made between infants (mean – max: 92 min – 292 min/day), toddlers (mean – max: 69 – 350 min/day), and children (mean – max: 3.2 – 55 min/day). No differentiation in mouthing time between girls and boys were found in the literature.

2.5.2.   INGESTION OF DUST

Oral exposure via ingestion of dust is calculated as:

$$oral\ exposure\ dust\ ingestion\left(\frac{\mu g}{day}\right) - Cdust\left(\frac{\mu g}{g}\right) \times dust\ ingestion\ rate\left(\frac{g}{day}\right)$$

2.5.2.1. CONCENTRATIONS IN DUST

An inventory of phthalate levels in settled indoor dust is given in Annex I, Table A7.

Alternative to the exposure assessment starting from measured levels in settled dust, full chain modeling starting from emissions – over settled dust to intake is also considered in the INTERA modeling approach.

2.5.2.2. INGESTION RATES OF DUST

Infants and toddlers are known to incidentally ingest small amounts of dust and soil daily.

In the study of Wormuth et al. (2006), intake rates of house dust of 50 mg/day (infants and toddlers), 10 mg/day (children), and 1 mg/day (teenagers and adults) were applied.
The US-EPA Exposure factor handbook for children (US-EPA, 2008) recommend indoor dust ingestion values of 30 mg/day (infants 6-12 months) to 60 mg/day (children 1-6 years).

2.5.3.   INGESTION OF PCPS

2.5.3.1. CONCENTRATIONS IN PCP

Phthalates concentrations measured in PCPs (Annex I, Table A4) could be used as input for the calculation of exposure to phthalates through ingestion of PCPs.

2.5.3.2. INGESTION RATES OF PCP

No sound scientifically based data on ingestion rates of PCP could be found in the literature. Wormuth et al. (2006) filled this data gap by assuming a worst case assumption, namely intake rates of 50 mg/day (infants, toddlers, children, female teenagers and adults) or 25 mg/day (male teenagers and adults).

Ingestion of phthalates via ingestion of PCPs was not addressed in the RARs of DEHP, BBzP, DIDP and DINP. Moreover, in the study of Wormuth et al. (2006), ingestion of PCPs appeared to be insignificant for these four phthalates. Hence, this intake route could be neglected in further calculations in the INTERA phthalate case study.

2.6. STEP 4: EXPOSURE MODELLING

2.6.1. TIME/ACTIVITY DATA

Time activity data is included in the KMS and was used in the case study.

2.6.2. USE FREQUENCIES

Use frequencies of sources provoking exposure are addressed in steps 3A-3C (see 2.3, 2.4 and 2.5)

2.6.3. USE PATTERNS

Here, some 'typical' or specific use pattern for a set of exposed population groups, addressing their specific use pattern for groups of consumer products were constructed. This is partly addressed in steps 3A-3C (see 2.3, 2.4 and 2.5), and further the delineation of selected scenarios is described in section 2.6.4.

Exposure modeling for the following groups of exposed populations were performed, based on specific time/activity pattern, use frequencies and patterns of those population groups (parameters described in step 3):
- Infants + toddlers
- children
- adults

2.6.4. EXPOSURE MODELLING

Exposure modelling is performed by means of the approaches and data mentioned in steps 1-4, by means of manual calculations using Microsoft Excel. For a few selected scenarios (see below), the exposure modeling was run in parallel via the computational platform. The parallel runs aimed to validate the computational platform.

Exposure modeling for four cases were run to address the dedicated questions set out in the scope of this case study, namely;

1) **Case 1:** assessment of indoor phthalate exposure in the EU ("can we reproduce the existing data on indoor phthalate exposure in the EU ?")
2) **Case 2**: validation of intermediate blocks of the full chain model (" can we validate the full chain approach of the INTERA tools")
3) **Case 3**: stratification of phthalate exposure according to geographical region in the EU
4) **Case 4**: impact the policy measures on restriction of use of phthalates in toys and child care products

2.6.4.1. CASE 1: ASSESSMENT OF INDOOR PHTHALATE EXPOSURE IN THE EU

Hereto, exposure scenario's for 4 age categories were constructed, and fed with age-specific parameterization for exposure modifiers for all relevant routes and sources, and physiological properties. The calculations are based on a mix of realistic parameters (central estimates) if available, and (conservative) assumptions if we lack data.

Error! Reference source not found. lists the sources and routes considered for each age group. It is noticed that the majority of sources/routes addressed in step 1-4 are used in calculations. Though, some specific and not every-day uses (e.g. spray paints) were not addressed here, because this is outside the scope of the current assessment where we aim to make a relevant, daily average exposure assessment.

Error! Reference source not found. lists the parameters selected for use in the calculations, and **Error! Reference source not found.** lists the selected phthalate exposure concentrations and release rates in different media.

Table 3: Exposure scenario's under investigation for the EU population (case 1)

	oral exposure			inhalation exposure	dermal exposure			
	toys	dust	PCP	air (indoor/outdoor)	dust	gloves	toys	PCP
Infants	X	X	(X)	X	X		X	(X)
Toddlers	X	X	(X)	X	X		X	(X)
Children	X	X	(X)	X	X		X	(X)
Adults		X	(X)	X	X	X		(X)

(X): PCPs were initially considered to be included, though these exposures appeared to be insignificant based on a first screening of phthalate concentration levels in PCP (see above)

Parameter selection

The parameters used for the exposure calculations are based on a selection made from the patchwork of above mentioned databases (reported in step 1-4) and from the common values applied across the 3 case studies (see Asikainen et al., 2012). When making the selection, we aimed to assess 'typical', contemporary exposure to phthalates, and tried to select the values corresponding to the mean, typical population in the EU, based on recent data on typical use patterns, median and mean concentrations….

Since there is only for a few parameters (mainly on indoor dust concentrations and on physiological parameters) geographical specific data, it is preferred not to make differentiation across EU regions at this stage.

The variation of exposure across the EU – for those parameters with available data for differentiation) will be shown in case 3.

When more than one data point of equal quality was available (e.g. for indoor air), the average of those values was taken forward. Though, in some cases, when there was deficit in the data or no information on representativeness of the data for the EU population; assumptions were made. For

example, the data gap on indoor concentrations for BBzP, DIDP and DINP in schools and offices, were filled by assuming similar concentrations in these locations as in residential environments.

Table 4: Selected exposure modifiers used in calculations of selected scenarios

exposure modifiers	infant (0-1 year)	toddler (1-3 year)	child (3- 8 year)	adult (>18 year)	source
body weight (kg)	7,525	13,34	19,5	70	Asikainen et al., 2012
daily average inhalation rate (m³/day)	3,56	4,95	7,88	15,0	(Brochu et al., 2007)
body surface - hands (cm²)	190	380	570	1240	Asikainen et al., 2012
mouthing time (min/day)	92	69	3,2	-	Wormuth et al 2006
daily dust ingestion rate (mg/day)	50	50	10	1	Wormuth et al 2006
time-activity					Asikainen et al., 2012
fraction time home	0,96	0,96	0,63	0,55	Asikainen et al., 2012
fraction time school/work	-	-	0,33	0,34	Asikainen et al., 2012
fraction time outdoor	0,04	0,04	0,04	0,10	Asikainen et al., 2012
dermal contact time dust (h/day)	16	16	16	16	(Holmes et al., 1999)
dermal dust hand loading (mg/cm² hand)	0,06	0,06	0,06	0,01	(Holmes et al., 1999)
dermal contact time toys (h/day)	2	2	2,00	-	Muller et al., 2003
dermal contact time gloves (min/day)	-	-	-	6,9	Wormuth et al 2006

*raw data from source were often recalculated to match the age categories of this case study

Table 5: Selected phthalate exposure concentrations & release rates in different media

Parameter	unit	DEHP	DIDP	DINP	BBzP
leaching from toys	µg/cm²/h	2,64	5	8,3	0,12
indoor settled dust	mg/kg	717	34	129	126
PCP	mg/kg	0	0	0	0
indoor air - home	ng/m³	126	20	37	19
indoor air - office	ng/m³	300	-	-	-
indoor air - school	ng/m³	195	-	-	-
outdoor air	ng/m³				
dermal uptake rate from toys	µg/cm²/h	0,07	0,024	0,04	0,05
oral uptake rate (all groups)	-	0,55	0,83	0,83	0,73
inhalation uptake rate - adults	-	0,75	0,75	0,75	0,75
inhalation uptake rate - children	-	1	1	1	1
dust - dermal uptake rate - infants, toddler, children	-	0,01%	0,01%	0,01%	0,07%
dust - dermal uptake rate - adults	-	0,01%	0,00%	0,00%	0,04%

(references: see in data collection step (step 1- 4) and in tables in Annex I).

For dermal and oral exposure to toys, it is acknowledged that oral and dermal release rates as found in literature (based on data before 2007) and used in the calculations might overestimate release from toys nowadays brought in the market. The impact of restrictions of phthalates in toys will be demonstrated in **case 4**.

There was a gap in data on dermal uptake rate BBzP from toys. Hereto, we calculated the BBzP dermal uptake rate based on the corresponding value for DEHP from PVC products (40 % DEHP), and correcting for the ratio BBzP content in toys (based on estimates from children clothes) (max. value of 2 % BBzP, Danish EPA, 2009) vs. DEHP in the tested PVC product, and corrected for the ratio of dermal uptake rate of DEHP vs. BBzP in cosmetics, according to a similar data gap filling method handled by Wormuth et al. (2006).

Whereas the intention was to investigate dermal and oral exposure to phthalates via PCP, the analyses of the database on concentration of DEHP, DIDP, DINP and BBzP (see above) showed that typical concentration were below the detection limit, so exposure via this pathway could be neglected and, is therefore not addressed in this case study.

In all of the above mentioned scenarios, the measured concentrations in indoor and outdoor air were preferred over the emission - source to indoor concentrations. These most likely better reflect reality then if we would have started from emission sources to indoor concentrations, especially given the lack of knowledge of use patterns and emission strengths of materials present in the indoor environment. In addition, the validation of the emission to indoor concentration module of the INTERA computational platform will be tested in **case 3.**

Calculations for **case 1** are based on INTERA methodology, based on calculations in Microsoft Excel, outside the computational platform. Results are presented in section 2.10.1.

2.6.4.2. CASE 2: VALIDATION OF INTERMEDIATE BLOCKS OF THE FULL CHAIN MODEL

The emissions-to-indoor- dust pathway calculations of the computational tool were verified by comparison with measured house dust.

Hereto, a scenario was run assuming a room volume of 122 m³ and floor area of 49 m², air exchange rate (AER) of 1.29 (data for Bulgaria) and full coverage of the floor area with vinyl flooring material. Three emission rates covering ranges of emissions found in literature (0.21, 0.65 and 7 DEHP µg/m²/h) were used in the calculations. Other model parameters were kept constant across the three scenarios.

Results are presented in section 2.10.2

2.6.4.3. CASE 3: STRATIFICATION OF PHTHALATE EXPOSURE ACCORDING TO GEOGRAPHICAL REGION IN THE EU

In the data collection exercise of exposure modifiers, emission and concentration data, we tried to differentiate across regions in the EU. However, few data (mainly on indoor dust concentrations and physiological parameters) allowed a differentiation across the EU.

Stratification on indoor exposure to settled indoor dust are demonstrated using the INTERA visualization tool. Output is presented in section 2.10.3.

2.6.4.4. CASE 4: IMPACT OF RESTRICTIONS OF DEHP IN TOYS AND CHILD CARE ARTICLES

By lack of recent data, the above calculations in case 1 rely on dermal and oral release rate from toys measured before the restrictions since 2007. These data (oral release of factor of 2.64 µg/cm²/h) are according to Muller et al. (2003) and Rastogi (2001) representative for concentrations of phthalates in toys on the Danish market at the time of writing of these reports. Among 20 products of toys for children in the age 0-3 years, 10 samples were positive for DEHP, ranging between 0.6 – 302 mg DEHP/g (mean: 130 mg DEHP); in 9/20 samples DINP was detected (range: 4-361 mg/g; mean:130 mg/g); in 7/20 samples DIDP was detected.

The impact of the policy measure of the restriction of DEHP to maximum levels of 0.1 % in toys since 2007 was assessed. By lack of measured data, it was assumed that the release of DEHP from toys is proportional to the total content of DEHP in the toys. So, the extrapolation of oral release rate of 2.64 µg DEHP/cm²/h for a toy with a content of 130 mg DEHP/g results in an assumed release rate of 0.02 µg DEHP/cm²/h for content of max. 0.1 % DEHP.

The dermal release rate of 0.07 µg/cm²/h for an 'average' toy of 130 mg/g DEHP could be extrapolated to a release rate of 0.0005 µg/cm²/h for a toy in compliance with the toys Directive.

Two scenario's were run, a scenario before the restrictions (i.e. scenario based on toys with 130 mg DEHP/g) and a scenario where all toys are assumed to be compliant to the Toys Directive (< 0.1 %). Other exposure routes and modifying factors (inhalation of air, dust) were kept constant across the 2 scenarios.

Calculations for **case 4** are based on INTERA methodology, using the tools of the computational platform. Results are presented in section 2.10.4.

2.7. STEP 5: INTERNAL DOSE MODELLING

Two approaches might be considered for internal dose modeling to phthalates
- PBPK modeling
- Conversion from external to internal dose by means of uptake, absorption factors.

2.7.1. PBPK MODELING

PBPK modeling has not been used to any extent to study exposure to phthalates (Lorber et al., 2010). Cahill et al. (2003) attempted to model human exposure to DEHP and DBP using a generalized pharmacokinetic model but was finding the simulation problematic for DEHP.

Besides the attempt of Cahill et al. (2003) to apply a PBPK model for phthalates, Lorber et al. (2010) developed a "simple" pharmacokinetic (PK) model to characterize exposure of Americans to DEHP. Lorber et al. (2010) name their model a "simple PK model" in that it considers a minimal amount of body compartments, rate constants and other required inputs. Specifically, parameters describing overall dissipation or loss from the body or tissue being modeled, and parameters describing the volume of mixing (in blood, urine, or body fat) are all that are required. In contrast, PBPK models require parameterization of numerous metabolism rate constants or transfer coefficients between body tissue and organs.

The simple PK models do not provide information on target organ dose and cannot address potential health impacts (Lorber et al., 2010). However, with the proliferation on human biomonitoring studies, these simple models provide a valuable means to tie external dose to measurements in body fluids/tissues.

According to these authors, the structure and approach described in their paper can easily be extended to other phthalates with the proper data.

The computational platform is fed these recent advances in PBPK modeling for DEHP (see report WP 3).

2.7.2. CONVERSION FROM EXTERNAL TO INTERNAL DOSE BY MEANS OF UPTAKE, ABSORPTION FACTORS.

Wormuth et al. (2006) calculated internal phthalate doses by scaling the external dose for each intake route with the appropriate absorption/uptake factor:
The inventory of uptake rates used to convert external exposures to internal doses (based on data of Wormuth et al. (2006)) is listed in Annex I, Table A8.

These authors applied source and age specific absorption factors. In contrast, others (Muller et al., 2003; Danish EPA, 2009; RARs on phthalates) applied the generic defaults for absorption through the various pathways: 5 % for dermal route, 100 % for oral route and 100 % for inhalation.
Case 1 is based on calculations using the absorption factors of Wormuth et al. (2006), by lack of a PPBK model for phthalates other than DEHP in the modeling platform at the time of execution of this case study.

In case 4, the PBPK model for DEHP is tested, and for one scenario (scenario before restrictions) run in parallel with the approach using absorption factors.

2.8. STEP 6: ADDRESSING THE DEFICITS IN DATA AND INDICATIONS TO ADDRESS THE DEFICITS

2.8.1. GEOGRAPHICAL VARIABILITY

- *deficit*: Relevance of data in relation to geographical distribution. Apart from measurements of phthalates indoor air, there was lack geographical differentiation in exposure data (concentrations, emissions, use patterns, etc.)
- *how was this deficit addressed*? Exposure was assessed for the EU population as a whole, without regional differentiation (except for case 3). Selection of EU – representative data were based on expert judgment of most appropriate dataset (recent data, large dataset, scope of dataset..), and if more than one database was available of equal quality, the average of the different values was taken forward as the EU average value.
- *suggestions to fill this gap*? (new) data collection in function of geographical location

2.8.2. MARKET REPRESENTATIVENESS OF ARTICLES

- *deficit*: Representativeness of data found in literature (emissions, concentration, leaching). Some (older) data gathered in our review might be no longer representative for the current market in the EU given, in 2 views: 1) representativeness of tested

product/brand for its wider category, and 2) in view of the ongoing substitution of certain phthalates in certain applications, and the restrictions in certain uses since 2007.
-   *how was this deficit addressed*? It was assumed that tested brand were representative for its broader category, and, it was (qualitatively) suggested that the predicted exposure, based on older data, are likely to overestimate nowadays exposure given the restrictions in use since 2007.
-   *suggestions to fill this gap*? new data gathering: monitoring of phthalates contents and releases on products brought on the market nowadays

2.8.3.   USE PATTERNS OF BUILDING MATERIALS

-   *deficit*: information on use patterns of building materials
-   *how was this deficit addressed*? for the EU wide assessment, the use of these data were bypassed by information in concentrations indoor air; for the full chain test case, a realistic worst case assumption on use of phthalate containing building materials (i.e. full floor coverage with phthalate containing PVC flooring)- was made
-   *suggestions to fill this gap*? new data gathering – market analysis/survey of materials used in residential settings.

2.9.   STEP 7: EXECUTION OF EXPOSURE CALCULATIONS

2.9.1.   EXPOSURE PREDICTIONS MADE BY MANUAL CALCULATIONS

Exposure predictions for case 1 (for DEHP, DIDP, DINP and BBzP) were run using calculations in Microsoft Excel.

2.9.2.   EXPOSURE PREDICTIONS MADE BY THE COMPUTATIONAL PLATFORM

Exposure predictions for case 4 (for DEHP) and case 2 (for DEHP) were run using the INTERA computational platform.

2.10.   STEP 8: REPORTING AND INTERPRETING THE OUTPUTS

2.10.1.   CASE 1: ASSESSMENT OF INDOOR PHTHALATE EXPOSURE IN THE EU

The predicted aggregate uptake (i.e. internal dose taking into account different absorption factors for different exposure routes) for DEHP, DIDP, DINP and BBzP, expressed per kg bodyweight, is more than 10 fold higher for infants (0- 1 years) than for adults (Figure 5).

This is not surprising given, firstly, the particular mouthing behaviour (toys, other materials), secondly, the higher unintentional ingestion of house dust among infants, which are the main drivers for exposure for infants and toddlers, and thirdly, the relative higher external exposure relative to body weight. Whereas mouthing and ingestion of soil and dust are the main pathways for DEHP exposure to children, dermal exposure via the use of gloves is the main sources for indoor DEHP exposure to adults.

The distribution of exposure routes and sources for DEHP, DINP and DIDP and BBzP for infants (0-1 year) is shown in Figure 6. Whereas mouthing dominates exposure to DINP, DINP, and DEHP, this pathway is less important for BBzP, where dermal exposure to materials and oral ingestion of soil and dust are the dominant sources for infants.

 The distribution of exposure routes of adults strongly differs from the one for children. For adults, dermal exposure (through the use of gloves) is the main pathway while mouthing is negligible for this population group (Figure 7).
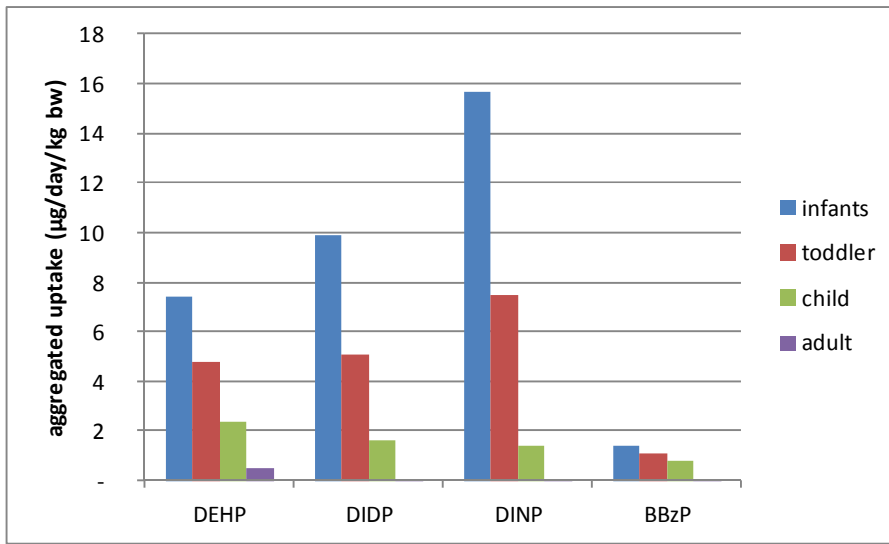
Figure 5: Aggregated exposure to DEHP, DIDP, DINP and BBzP via indoor sources for infants (0-1 year), toddlers (1-3 year), children (3-8 year) and adults (> 18 year) in the EU
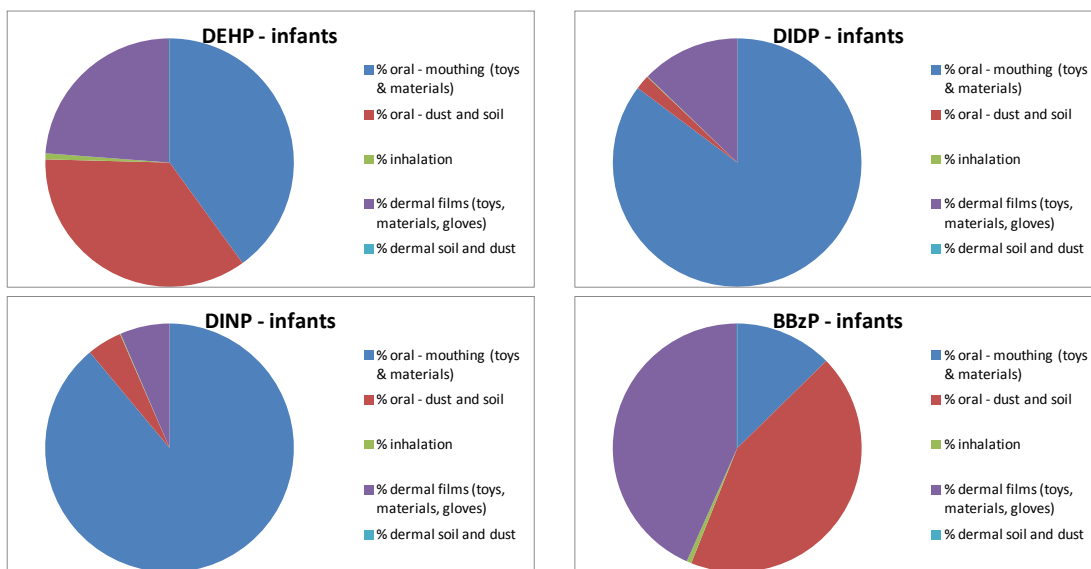
Figure 6 Contribution of indoor sources and routes to DEHP, DIDP, DINP and BBzP exposure in infants.
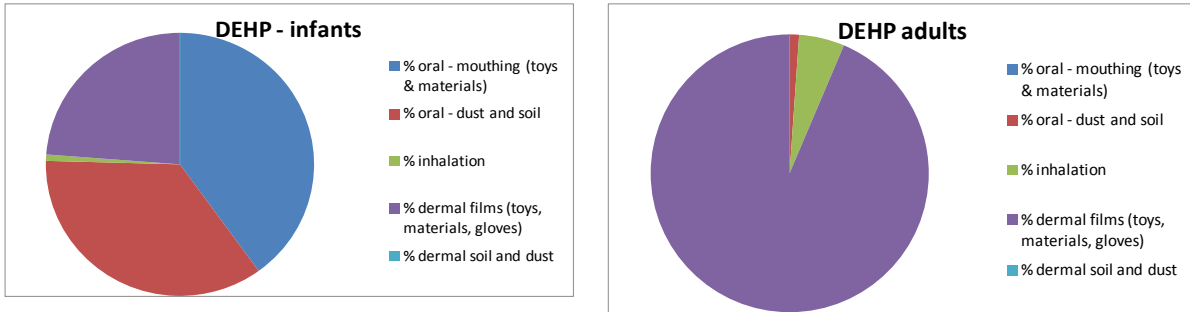
Figure 7: Comparison of DEHP exposure contribution from sources between infants and adults

This **case 1** was set up to address the question whether we reproduce the existing data on indoor phthalate exposure in the EU using the INTERA methodology.

The most recent and complete study for comparison is the one of Wormuth et al.(2006). Exposure predictions made by Wormuth et al.(2006) are shown in Figure 8.
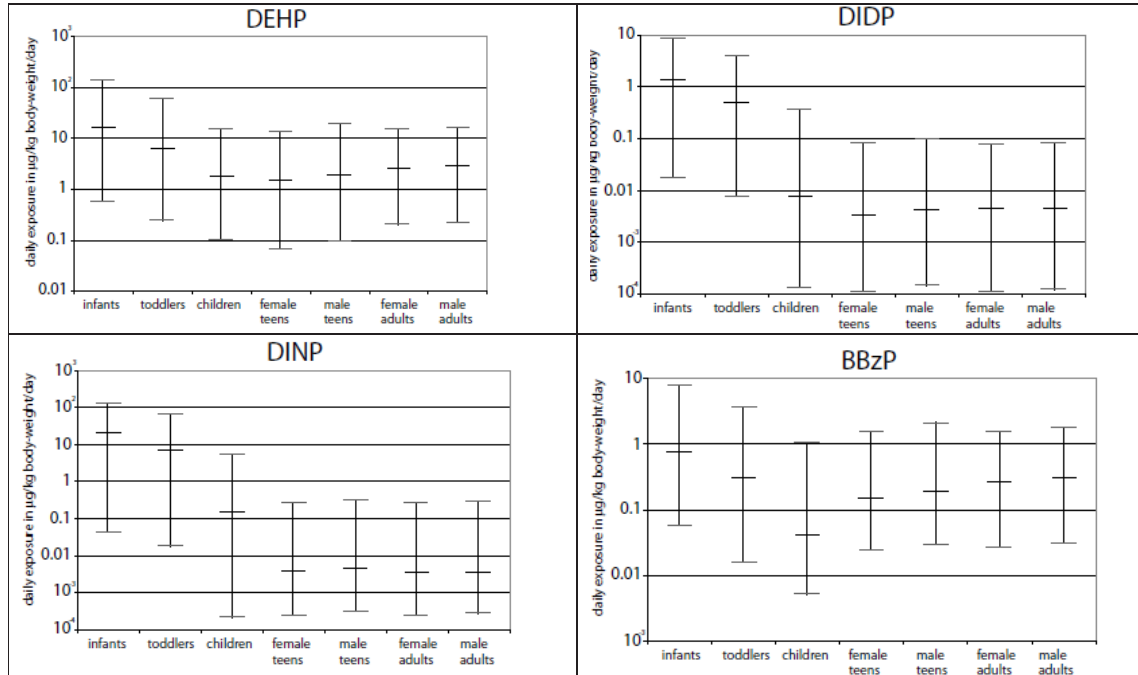
Figure 8: Daily internal exposure to phthalates estimated by Wormuth et al.(2006). Min, mean and maximal exposure are shown.

For DIDP and DINP, the predicted values for aggregate exposure, and trends over the age groups, match reasonably well with the predictions made previously by Wormuth et al. (2006). In addition, the dominance of indoor sources (mouthing and ingestion of dust) compared to non-indoor related exposure routes (dietary exposure) Wormuth et al. (2006) confirms this match.

For BBzP exposure to adults, our predictions are lower than those of Wormuth et al. (2006) (i.e. around .0.5 µg/day/kg bw on average). The discrepancy with our results can be explained by the fact that Wormuth et al. (2006) did consider the use of spray paints by adults in their scenario, while this (very infrequently used) source is not considered in our scenarios. In addition to the dominance of BBzP exposure by spray paints by Wormuth et al. (2006), dietary exposure was

included in their study (see Figure 4), while it does not belong to the aspect of indoor exposure which is the focus of the current study.

For BBzP exposure to infants, the INTERA calculations seem to result in a higher contribution from dermal exposure than assessed by Wormuth et al. (2006). The use of a generic model and defaults in the INTERA assessment versus the use of product-specific dermal exposure models probably serve as a basis for this discrepancy.

For DEHP, the INTERA exposure predictions for infants are in agreement with the ones of Wormuth et al.(2006). Analogously to for BBzP, discrepancy between the 2 assessments is stronger for older age categories. Here again, discrepancy for older age groups is explained by the fact that dietary exposure dominates DEHP exposure for adults, while for infants, mouthing and ingestion of food do play a major role.

By lack of probabilistic tools of the INTERA computational platform at the time of execution of this case study, no assessment of variability of exposure was made in this case 1 assessment, and hence, no comparison with variability in phthalate exposure made Wormuth et al. (2006) could be made at this stage.

2.10.2. CASE 2: VALIDATION OF INTERMEDIATE BLOCKS OF THE FULL CHAIN MODEL OF THE COMPUTATIONAL PLATFORM

Concentrations predicted in settled dust for the 3 scenarios (emissions for materials of 0.21, 0.65 and 7 µg/m²/h - which represent the range of emission strengths of DEHP found in literature) are shown in Figure 9.
The predictions were run in the INTERA computational platform and the graph shown in Figure 9 was produced using the INTERA tools of the visualization platform.

After an initial equilibrium phase (about 24-48h), steady state concentrations of 135, 410 and 4400 µg DEHP/g dust were predicted using the modeling platform.

These predictions were compared with measured data on phthalate levels in settled dust. The conditions of the scenario used for modeling is not fully comparible with the conditions of the environments where measurements took place. Thus, a real 'validation' of the outcome , which would require identical conditions for modeling and measurements, is not possible. Though , ithe comparison could serve a a 'reality' check, i.e. are the predictions within realistic ranges, or do the predictions and measurements fall in the same order of magnitude?

These values seem to be realistic when comparing to DEHP concentrations measured in real indoor environments in the EU, which are in the range of 210-1050 µg DEHP/g dust.

Thus, is not surprising that the ranges of measured versus predicted concentrations do not perfectly match, given the fact that the predicted values represent rather a theoretical situation (where 100 % of the floor is covered with a high emitting vinyl floor, in absence of other materials like furniture which could act as a sink/source of DEHP), and the measured data reflect real indoor environments where we lack information of presence of DEHP sources in the indoor environment.

Nevertheless, these results confirm the performance of this part of the computational modeling tool.
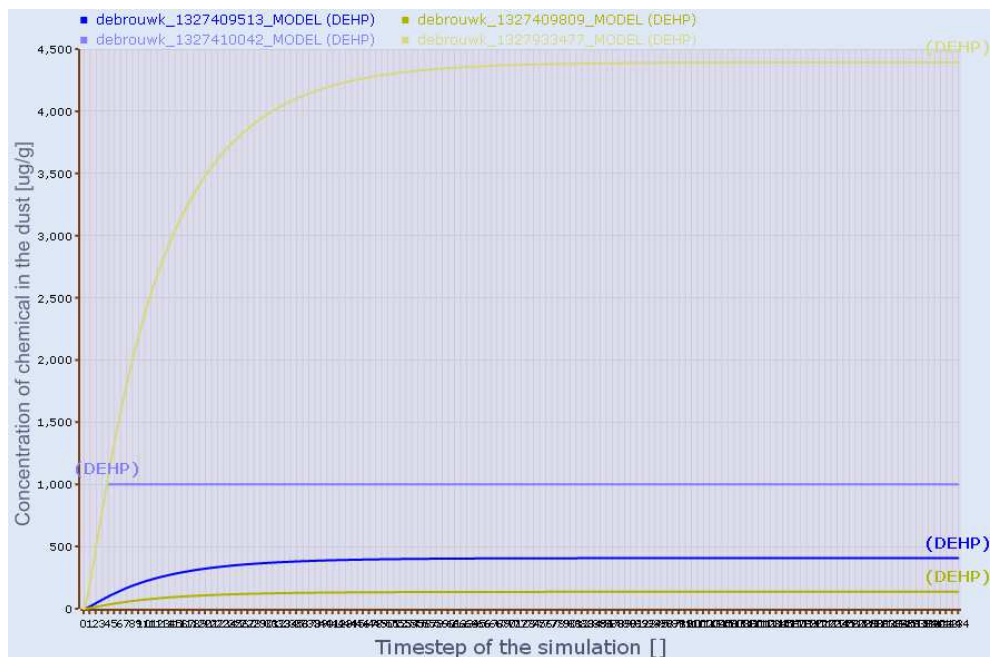
Figure 9: prediction of DEHP accumulation (0-64 hours) in indoor settled dust for 3 DEHP emission rates.

2.10.3. CASE 3 : STRATIFICATION OF PHTHALATE EXPOSURE ACCORDING TO GEOGRAPHICAL REGION IN THE EU

During the data inventory phase, only a very limited number of the data could be apportioned to one or more specific regions or countries in the EU. Apart from measurements of phthalates in dust, there was a lack of geographical differentiation in exposure data (concentrations, emissions, use patterns), and therefore, stratification of aggregate exposure to indoor exposure in the EU for different regions/countries was not possible.

Instead, for the limited data we have, i.e. the data on DEHP concentrations in dust, a representation of the geographical distribution exposure across the EU was made using the INTERA visualization tool for mapping geographical information.
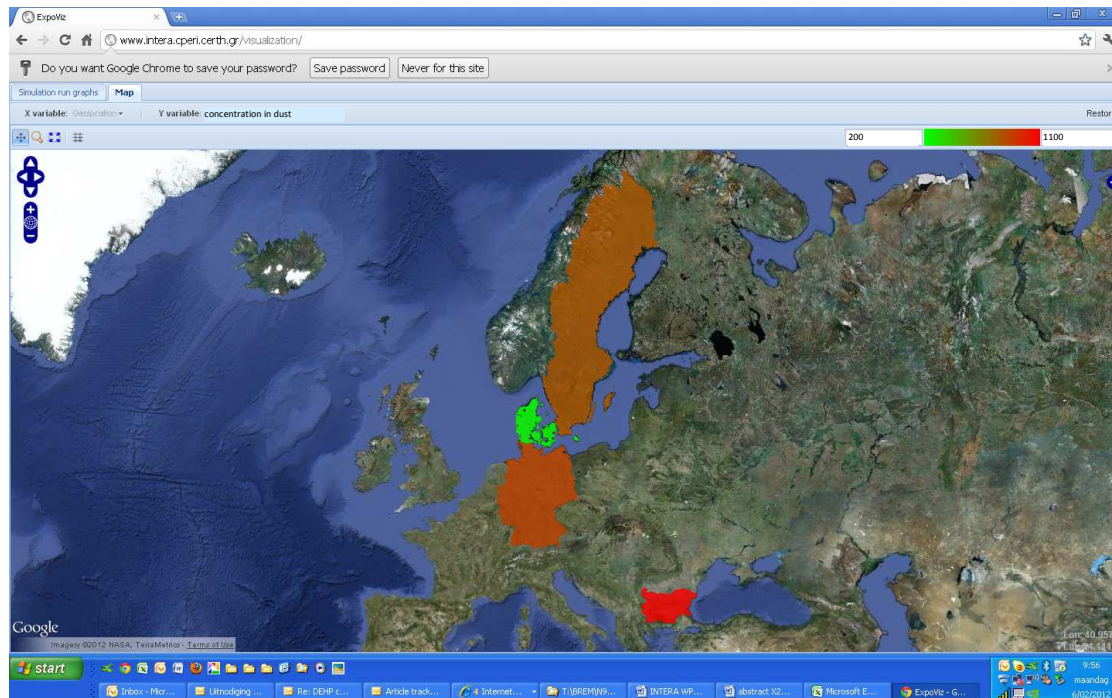
Figure 10: Geographical distribution of DEHP in dust across the EU

2.10.4. CASE 4: IMPACT OF RESTRICTIONS OF DEHP IN TOYS AND CHILD CARE ARTICLES

Two scenarios were run, i.e. a scenario before the restrictions (cfr. scenario's under case 1) and a scenario where all toys are assumed to be compliant to the Toys Directive (Dir. 2005/84/EC) (< 0.1 % DEHP). Other exposure routes and modifying factors (inhalation of air, dust, etc.) were kept constant across the 2 scenarios. The (theoretical) impact of the restrictions on aggregate exposure (as generated by the computational platform in terms of total amount taken up by the body and concentrations of metabolites of DEHP in urine are shown in Figure 11 and Figure 12.
In terms of total amount taken up by the body (Figure 11), a difference in uptake between the 2 scenarios by factor 6 is predicted. Analogously, concentrations of metabolites MEHP, 5-OH MEHP and 5-oxo MEHP are about factor 4- 6 lower in the scenario where compliance to 0.1% DEHP in toys is assumed versus the scenario before the ban (Figure 12).

Figure 11 and Figure 12 have been generated using the tools of the INTERA visualization starting from the results obtained through the application of the INTERA computational platform.
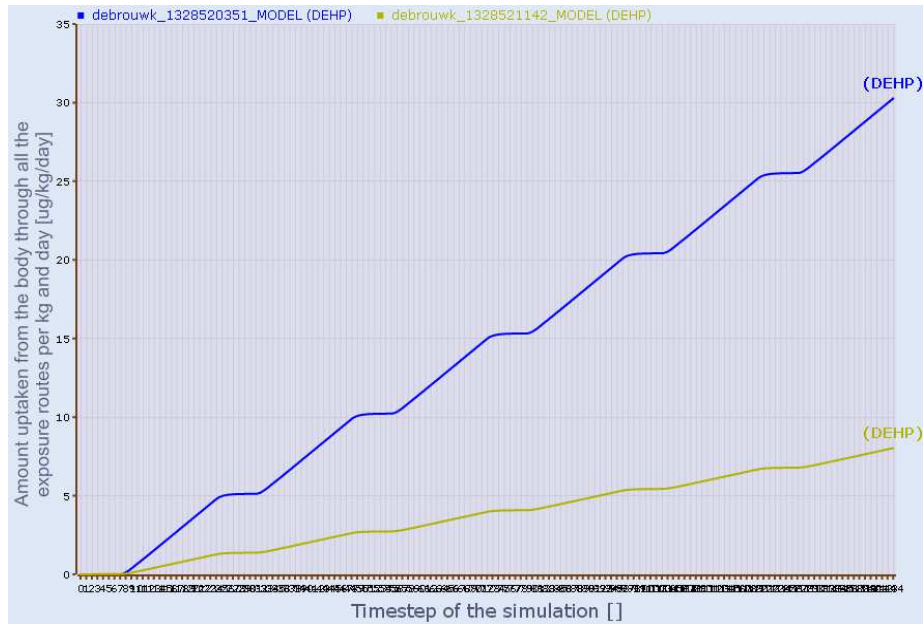
Figure 11: predicted amount of DEHP taken up from the body of an infant (0-1year) during 1 week for 2 contrasting scenarios: 1) scenario 1 exposure before DEHP restrictions in toys and childcare articles (blue line), and 2) scenario 2: exposure under the assumption of fully compliance to DEHP restrictions in toys and childcare articles (green line)
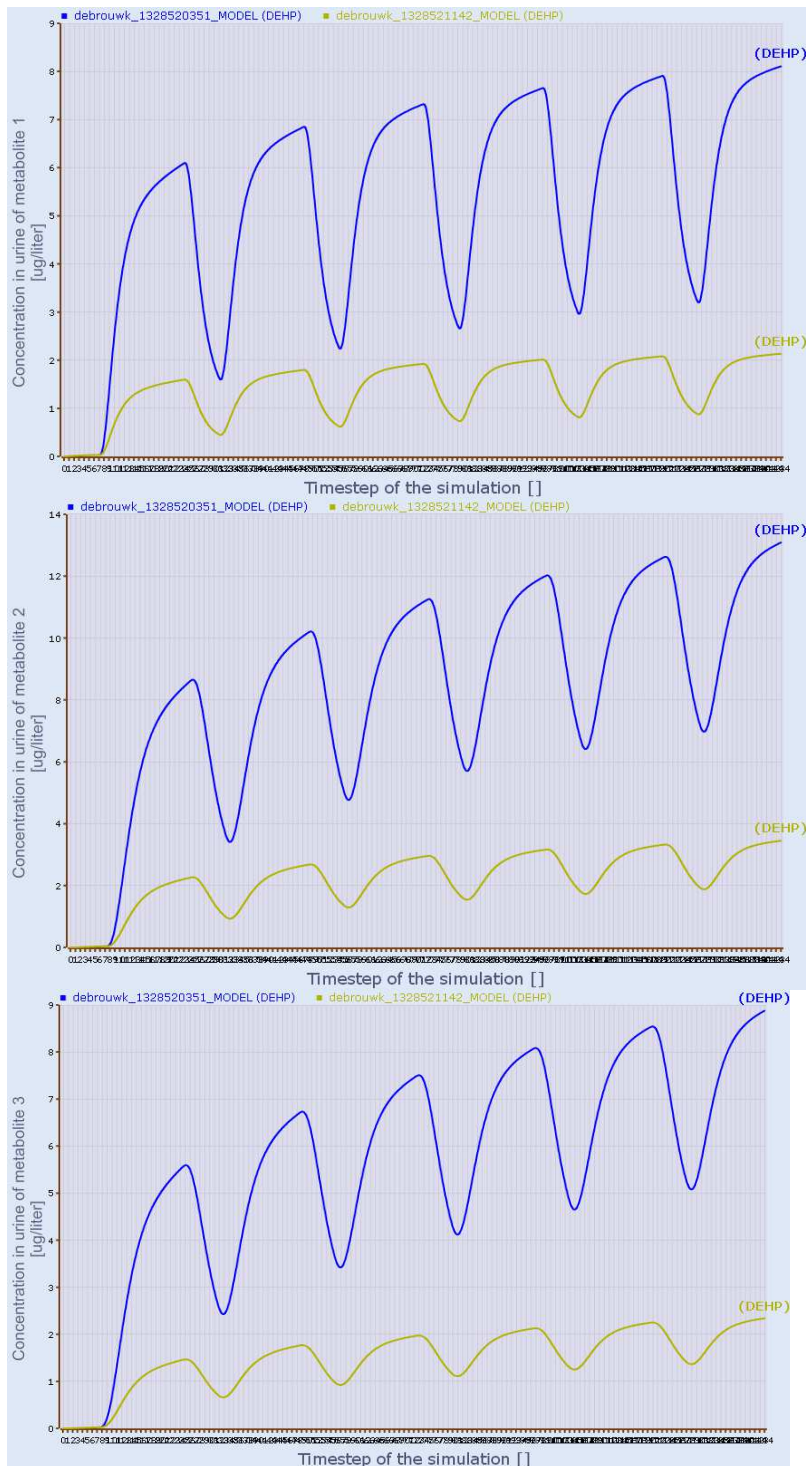
Figure 12: predicted concentrations of DEHP metabolites in urine of an infant (0-1year) during 1 week for 2 contrasting scenario's: 1) scenario 1: exposure before DEHP restrictions in toys and childcare articles (blue line), and 2) scenario 2: exposure of DEHP under the assumption of fully compliance restrictions in toys and childcare articles (green line). Upper graph: DEHP metabolite 1 (MEHP), middle graph: metabolite 2 (5-OH MEHP); lower graph: metabolite 3 (5 oxo MEHP)

At this stage, it is too early to be able to confirm by means of biomonitoring data whether this decrease is within realistic ranges of not. Indeed, phasing out of DEHP rich toys and other articles to which children might experience oral and dermal contact is in practice most likely a rather slow process. In addition, variability within the population might mask the time trend of DEHP exposure and policy measures.

Nevertheless, comparison of predicted concentrations of DEHP metabolites in urine might be helpful to support the outcomes of the DEHP PBPK module of the computational platform.

Wittassek et al. (2011) recently made a review of phthalate metabolisms in urine. Whereas the majority of data pertain to older age groups or susceptible groups of infants, with a specific DEHP exposure source (neonates), the exposure profile of the 19 children (1-3 years) of the study of Brock et al. (2002) are, among the available datasets, to closest to the group of children on which current scenario's are based. As a result, there was a relatively good match between the predicted MEHP concentration in urine for 0-1 years infants (2 and 8 ng/ml for respectively after and before DEHP restrictions) and the measured MEHP in urine in 1-3 year old toddlers (mean: 4.6 ng/ml), providing a satisfactory preliminary validation of the PBPK model implemented in the INTERA platform. The finding that the predictions (before ban situation) are a bit above the measured data are not very surprising since the aggregate dose for the infants (0-1 years) are higher than for the age category 1 – 3 years, which is the age category of the children in the study of Brock et al. (2002). However, one should keep in mind that MEHP measured concentrations in urine integrate all exposure sources and routes, while our predictions only account for indoor sources (thus excluding contribution from dietary intake).

Unfortunately, concentrations of other major DEHP metabolites, i.e. metabolites 5-OH MEHP and 5 oxo-MEHP in urine of young children have not been published.

Metabolites 5-OH MEHP and 5 oxo- MEHP have been measured in urine of older age groups (general population), and median concentrations among these studies ranged in Europe between 14 and 52 ng/ml for 5-OH MEHP and between 8 and 36.5 ng/l for 5 oxo-MEHP. Apparently, in all of the studies where the 3 metabolites were measured, the concentrations of 5OH-MEHP were about 2 – 7 higher than MEHP concentrations. Similarly, concentrations of 5-oxo MEHP were about 2-4 fold higher than MEHP concentrations. In contrast, predictions made by the PBPK module of the computational platform resulted in concentrations of MEHP at nearly the same level of concentrations 5 OH MEHP and 5-oxo MEHP.

In summary, using the INTERA computational tool, a potential reduction in DEHP body burden and concentrations of DEHP metabolites were predicted for shifting from a situation where children are commonly exposed to DEHP rich toys and products, to a new situation where the use of DEHP in toys is restricted. The predicted levels of DEHP metabolites were in line with measured data; though some additional biomonitoring data would be needed to confirm the relative dynamics of the metabolites of DEHP in urine.

CHAPTER 3   DISCUSSION AND CONCLUSION

3.1.   USEFULNESS OF INTERA METHODOLOGY AND TOOLS IN THE PHTHALATE CASE STUDY

In the phthalates case study, the methodology and three online tools (the KMS, computational platform and visualization platform) developed within the INTERA project were used.

At the stage of the execution of the cases study, the tools were still under development, and refined based on the outcome of the case studies. Some calculations were run using the online tools, however, others were not performed using the online tools, but instead, manually performed in Microsoft Excel using the INTERA methodology, which, in analogy to the tools, involves aggregating sources and routes relevant for indoor exposure.

The first of the three INTERA tools, i.e. the INTERA KMS was useful for the case study in that respect that generic and region specific data on body weight, skin area, volumes or rooms, AER could be used. On the other hand, at the onset of the case study, no phthalate specific data (e.g. concentrations, emission rates, etc) were available in the KMS. During the execution of the phthalate case study, the data were fed into the KMS. As a learning lesson for future case studies for which the INTERA tools might be used, a user should not expect from the KMS a ready for use, up to date database on substance/product specific data. Instead, one should regard the KMS as a starting point, and add new, quality checked data. The possibility to do that was build up into the KMS to make it flexible for the future needs and wider usage. The strength and completeness of the KMS will depend on these updates (and its quality) from users of the tool.

The second set of tools, i.e. the computational tools was experienced as a powerful tool to calculate aggregate exposure to contaminants from indoor sources, especially for complex scenarios and substances with complex interactions with dust, and when one wants to model up to concentrations of metabolites in the human body. As a learning lesson from the phthalate case study, one should always try to verify (intermediate) model predictions by means of measured, independent data. Verification of sub modules of the INTERA computational platform were helpful in giving confidence in the output, or were very helpful in identifying bugs and needs for model corrections or improvement. Especially when running the platform for a substance not previously assessed by means of the computational tool, some verification of predictions would be essential.

The third set of tools, i.e. the visualization tools was experienced a useful tool for comparison of outcomes of different scenarios and for displaying geographical trends in exposure.

In summary, the results of this case study demonstrate the use of the INTERA tools for indoor exposure assessment for chemicals with multiple sources and pathways, and complex dynamics between gas phase and settled phase in the indoor environment.

3.2.   SUMMARY OF THE PHTHALATE CASE STUDY

Given the multitude of phthalates originating from sources in the indoor environment, their usage patterns and routes of exposure, an aggregate, multi-pathway exposure approach is needed for the evaluation of systemic health effects.

The phthalate case study, focused on four phthalates, namely on DEHP, BBzP, DINP and DIPD, aimed applying the INTERA methodology and tools to answer 4 dedicated questions:

- Can we reproduce the existing data on indoor phthalate exposure in the EU?
- Can we validate the full chain approach of the INTERA tools:?
- Can we stratify phthalate exposure according to geographical region in the EU?
- What is the impact of the policy measures on restriction of use of phthalates in toys and child care products in term of aggregate exposure?

To address the first question, an inventory of concentrations of phthalates in consumer products, air, dust, etc in the EU was made based on a literature screening, and fed into the KMS, and exposure predictions made using the INTERA methodology.

Indoor exposure to DEHP, BBzP, DINP and DIDP in the EU population, split up into several subpopulations, were modeled using the INTERA methodology and tools.

The average aggregate exposure to DEHP in the indoor environment was more than 10 -fold higher for infants than for adults (infants: 7.4 µg/day/kg bw ; adults: 0.5 µg/day/kg bw). Similar differences in aggregate exposure between age groups were found for BBzP, DIDP and DINP.

Infants exposure to DEHP in the indoor environment was dominated by oral exposure via mouthing to toys and other plastic objects (40 %) and by unintentional ingestion of dust (35 %). Dermal contact to objects contributed to about 24 %, while dermal contact with dust was negligible; inhalation contributed marginally (0.7 %) to the systemic dose for DEHP.

For adults, indoor exposure to DEHP was dominated by exposure via dermal contact with gloves.

Predictions were verified by means of independent data at various stages of the modeling chain. There was a good match between predicted and measured concentrations in settled house dust. In addition, predictions of metabolites of DEHP in urine (MEHP: 2-8 ng/ml) fell in the same order of magnitude as average data from biomonitoring studies in literature (MEHP in urine children average: 4.5 ng/ml).

By lack of geographical specific data on phthalate concentrations in consumer articles, in use patterns and emission rates, it was not possible to stratify exposure or to identify geographical trends in phthalates exposure across the EU.

The potential impact of restrictions of DEHP in toys and children articles was estimated by comparison of a situation with a child was supposed to be exposed via the dermal and oral pathway exclusively to toys rich in DEHP (13 %) v before the ban, versus a similar scenario where a child was exclusively exposed to toys compliant with the restrictions in DEHP (0.1%). The expected DEHP body burden appeared to be 4 fold lower for the restriction scenario compared to the situation before the ban.

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Table A 9: Air emission rates of materials for DEHP, BBzP, DINP and DIDP

phthalate	phase	material/product	emission rate	unit	testing period/circumstances	reference
DEHP	gaseous, volatilisation	PVC flooring and wall covering	0,00018	µg/m²/s	?	RAR DEHP, 2001
DEHP	gaseous, volatilisation	PVC flooring and wall covering	0,0003	µg/m²/s	?	RAR DEHP, 2002
DEHP	gaseous, volatilisation	vinyl flooring	1,4	µg/m²/h	modelling at day 500	Xu et al., 2009
DEHP	gas phase	poly olefine wax	0,0072	µg/m²/h	150 days	Ashafari et al,2004
DEHP	gas phase	wallpaper	0,108	µg/m²/h	150 days	Ashafari et al,2004
DEHP	gas phase	refrigarator strip	0,36	µg/m²/h	150 days	Ashafari et al,2004
DEHP	gas phase	electric wire 6 mm	0,432	µg/m²/h	150 days	Ashafari et al,2004
DEHP	gas phase	electric wire 11mm	0,234	µg/m²/h	150 days	Ashafari et al,2004
DEHP	gas phase	PVC flooring	0,216	µg/m²/h	150 days	Ashafari et al,2004
DEHP	gas phase	PVC skirting	0,504	µg/m²/h	150 days	Ashafari et al,2004
DEHP	gas phase	wallpaper	0,14	µg/m²/h	14 days	Uhde et al., 2001
DEHP	gas phase	wallpaper	1	µg/m²/h	14 days	Uhde et al., 2001
DEHP	gas phase	vinyl flooring	3	µg/m²/h	> 700 days; flow rate 1000 ml/min	Clausen et al., 2010
DEHP	gas phase	vinyl flooring	7	µg/m²/h	> 700 days; flow rate 3000 ml/min	Clausen et al., 2010
DIDP	-	wall covering	< DL		14 days	Uhde et al., 2001
DINP	-	wall covering	< DL		14 days	Uhde et al., 2001
DIDP	-		no data			RAR DIDP 2003a
DINP	-		no data			RAR DINP 2003
BBzP	-		no data			RAR BBzP, 2007

Table A 10: Measured concentrations phthalates in indoor environments in the EU

phthalate	phase	concentration	unit	residence type	statistic	No. samples	country	reference
DEHP	total airborne conc (gas + particle phase)	126	ng/m³	apartment	median	30	Germany	Fromme et al., 2008
DEHP	total airborne conc (gas + particle phase)	368	ng/m³	apartment	P95	30	Germany	Fromme et al., 2008
BBzP	total airborne conc (gas + particle phase)	19	ng/m³	apartment	median	30	Germany	Fromme et al., 2008
BBzP	total airborne conc (gas + particle phase)	57	ng/m³	apartment	P95	30	Germany	Fromme et al., 2008
BBzP	?	1	ng/m³	office		1	US	Weschler et al.,1984, cited in RAR BBzP
BBzP		20	ng/m³	office		1	US	Weschler et al.,1984, cited in RAR BBzP
DIDP	?	5-20	ng/m³	sport hall, kindergarten, home carpet and flooring store, laboratory, grenhouse, underground park	range	23	Belgium	Research Institute for Chromatography, 2000 (cited in RAR DIDP)
DINP	?	7-36	ng/m³	sport hall, kindergarten, home carpet and flooring store, laboratory, grenhouse, underground park	range		Belgium	Research Institute for Chromatography, 2000 (cited in RAR DIDP)
BBzP	gaseous phase	35	ng/m³	homes	median, night-time sampling		California	California EPA, 1992, cited in RAR BBzP
BBzP	gaseous phase	90	ng/m³	homes	P90, daytime sampling		California	California EPA, 1992, cited in RAR BBzP
BBzP		75	ng/m³	apartment	P95	59	Germany	Fromme et al., 2004
BBzP		26	ng/m³	kindergarten	P95	18	Germany	Fromme et al., 2004
				car interior				
DEHP		470	ng/m³	homes; based on calculations from emissions				Muller et al,2003
DEHP	? (gas + PM?)	110	ng/m³	classroom, winter	single value	1	Denmark	Clausen et al. 1999
DEHP	? (gas + PM?)	280	ng/m³	classroom, spring	single value	1	Denmark	Clausen et al. 1999
DEHP	? (gas + PM?)	195	ng/m³	classroom, average winter-spring	single value	1	Denmark	Clausen et al. 1999
DEHP	? (gas + PM?)	1050	ng/m³	daycare, winter	single value		Denmark	Clausen et al. 1999
DEHP	? (gas + PM?)	160	ng/m³	daycare, spring	single value		Denmark	Clausen et al. 1999
DEHP	? (gas + PM?)	605	ng/m³	daycare, average winter-spring	single value	1	Denmark	Clausen et al. 1999
DEHP	? (gas + PM?)	300	ng/m³	offices	average	4	Denmark	Clausen et al. 1999

Table A 11: Concentrations phthalates in outdoor air

phthalate	min	median	mean	max	ref
DEHP	46	200	304	615	ref. cited in Weschler et al., 2006
BBzP	0	0	1,1	6	ref. cited in Weschler et al., 2006
DINP	0	0	0	0	ref. cited in Weschler et al., 2006
DIDP	0	0	0	0	ref. cited in Weschler et al., 2006

Table A 12: Concentrations, application factor, frequency and absorption of phthalates in personal care products.

	phtal	C			n in database	AF		FD	RF	A	reference
		µg/g				g/use	g/use	time/d	-	%	
type		median	mean	max	detected in X/Y analysed samples	female adults	babies				
fragrance	DEHP	ND		521	3/30	0,61		3	1	5%	Koneicki et al., 2011
hair spray	DEHP	ND		1,6	1/11	5		1	0,1	5%	Koneicki et al., 2011
hair mousse	DEHP	ND		ND	0/7	5		1	0,1	5%	Koneicki et al., 2011
hair gel	DEHP	ND		ND	0/6	5		1	0,1	5%	Koneicki et al., 2011
deodorant	DEHP	ND		ND	0/18	0,5		1	1	5%	Koneicki et al., 2011
nail polish	DEHP	ND		1045	2/20	0,25		0,28	1	5%	Koneicki et al., 2011
lotion	DEHP	ND		ND	0/29	8		1	1	5%	Koneicki et al., 2011
skin cleanser	DEHP	ND		30	1/20	2,5		2	0,1	5%	Koneicki et al., 2011
baby lotion	DEHP	ND		15	1/25		1,4	0,14	1	5%	Koneicki et al., 2011
baby oil	DEHP	ND		ND	0/19		1,3	1,57	1	5%	Koneicki et al., 2011
diaper cream	DEHP	ND		ND	0/31		1,4	1,72	1	5%	Koneicki et al., 2011
baby shampoo	DEHP	ND		ND	0/23		0,51	0,27	0,01	5%	Koneicki et al., 2011
deodorant	DEHP		8,6	8,6	1/1 (?)						Wormuth et al., 2006
deodorant	DINP		ND	ND	?	1,3					Wormuth et al., 2006
deodorant	DIDP		ND	ND	?	1,3					Wormuth et al., 2006
deodorant	BBzP		ND	ND	?	1,3					Wormuth et al., 2006
perfumes	DEHP		15	130		0,7					Wormuth et al., 2006
perfumes	DINP		ND	ND		0,7					Wormuth et al., 2006
perfumes	DIDP		ND	ND		0,7					Wormuth et al., 2006
perfumes	BBzP		8	29		0,7					Wormuth et al., 2006
hair styling	DEHP		17	41		7,5					Wormuth et al., 2006
hair styling	DINP		ND	ND		7,5					Wormuth et al., 2006
hair styling	DIDP		ND	ND		7,5					Wormuth et al., 2006
hair styling	BBzP		16	46		7,5					Wormuth et al., 2006
perfumes	BBzP			110							Greenpeace, 2005
perfumes	DEHP			167							Greenpeace, 2005
perfumes	DINP			26							Greenpeace, 2005
perfumes	DIDP			36							Greenpeace, 2005

Table A 13: Determinants for dermal contact to phthalates via contact with materials via the mechanism of migration

d	phthalate	release value	dermal absorption rate	% abs	dermal contact time	contact area	body weight (kg)	exposure (internal dose)	references
		µg/cm²/h	µg/cm²/h		h/day	cm²			
toys	DEHP	6,6		5,00%	3	100	8	12,375	RAR DEHP
toys	DEHP		0,24		3	100	8	9	
toys	BBzP								not adressed in RAR
toys	DIDP		0,024		3	100	8	0,9	RAR DIDP
toys	DINP		0,024		3	100	8	0,9	RAR DINP
toys									
gloves	DINP		0,024		2	840	60	0,672	RAR DINP
clothing	DINP		not quantitively adressed						RAR DINP
footwear	DINP		not quantitively adressed						RAR DINP
gloves	DIDP		0,024		2	840	60	0,672	RAR DIDP
clothing	DIDP		not quantitively adressed						RAR DIDP
footwear	DIDP		not quantitively adressed						RAR DIDP
films	BBzP		1,68						Wormuth et al. 2006

Table A 14: Phthalate leaching rates from toys and contact materials (mouthing behaviour)

	leaching rate			source
	mean (or range)	max	unit	
phthalate				
DEHP	4193		µg/dm²/24h	Ref in RAR DEHP
DEHP	1790 - 2130		µg/dm²/6h	Ref in RAR DEHP
DEHP	30 -720		µg/cm²/h	Ref in RAR DEHP
DEHP	10,5 - 652,9		µg/dm²/6h	Ref in RAR DEHP
DEHP	200 - 1000		µg/dm²/h	Ref in RAR DEHP
DEHP	< 4 - 10		µg/dm²/24h	Ref in RAR DEHP
DEHP	< 100		µg/dm²/h	Ref in RAR DEHP
DEHP	< 50 - 180		µg/dm²/24h	Ref in RAR DEHP
DEHP	793		µg/dm²/3h	Ref in RAR DEHP
DEHP	0,074		µg/cm²/h	Ref in RAR DEHP
DEHP	2,64		µg/cm²/h	Steiner et al., 1998 (cited in Muller et al, 2003)
DINP	13,8		µg/dm²/min	Ref in RAR DEHP
DINP	89		µg/dm²/min	Ref in RAR DEHP
DINP		53,4	µg/cm²/h	Könneman, 1998 (cited in Muller et al,2003)
DINP	8,3		µg/cm²/h	Steiner et al., 1998 (cited in Muller et al, 2003)
DINP	59,6		µg/cm²/h	Chen, 1998 (cited in Muller, 2003)
BBzP	0,01 -611		µg/dm²/24h	Ref in RAR BBzP
BBzP	611		µg/dm²/24h	Ref in RAR BBzP
BBzP	< dl		in 15 products	Ref in RAR BBzP
DIDP	0,9-4,6		µg/cm²/h	Ref in RAR DIDP
DIDP	< dl - 0,084		mg/kg/6h	Ref in RAR DIDP
DIDP	nd		µg/dm²/6h	Ref in RAR DIDP
DIDP	< 0,1		mg/dm²/h	Ref in RAR DIDP
DIDP	0,11		mg/kg/6h	Ref in RAR DIDP
DIDP	5		µg/cm²/h	Ref in RAR DIDP
BBzP	0,12	0,002	µg/cm²/h	ref in Wormuth et al. 2006
DEHP	0,05	0,236	µg/cm²/h	ref in Wormuth et al. 2006
DINP	0,206	0,359	µg/cm²/h	ref in Wormuth et al. 2006
DIDP	0,162	0,277	µg/cm²/h	ref in Wormuth et al. 2006

Table A 15: Phthalate concentrations in indoor settled dust in the EU

phthalate	conc (mg/kg)	value for	nr samples in database	location	country	ref
DEHP	970	median of db	29		germany	Butte et al., 2008
DEHP	703	median of db	30		germany	Fromme et al., 2008
DEHP	600	median of db	65		germany	Kersten and Reich, 2003
DEHP	480	median of db	278		germany	Nagorka et al,.2005
DEHP	604	median of db	30	households	germany	Abb et al., 2009
BBzP	28	median of db	29		germany	Butte et al., 2008
BBzP	29,7	median of db	30		germany	Fromme et al., 2008
BBzP	19	median of db	65		germany	Kersten and Reich, 2003
BBzP	13	median of db	278		germany	Nagorka et al,.2005
BBzP	15,2	median of db	30	households	germany	Abb et al., 2009
DIDP	31	median of db	65		germany	Kersten and Reich, 2003
DIDP	60	median of db	278		germany	Nagorka et al,.2005
DIDP	33,6	median of db	30	households	germany	Abb et al., 2009
DINP	72	median of db	65		germany	Kersten and Reich, 2003
DINP	80	median of db	278		germany	Nagorka et al,.2005
DINP	129	median of db	30	households	germany	Abb et al., 2009
DEHP	210	median of db	497	homes	Denmark	Langer et al. 2010
DEHP	500	median of db	498	daycare	Denmark	Langer et al. 2010
BBzP	4,2	median of db	151	homes	Denmark	Langer et al. 2010
BBzP	16,4	median of db	151	daycare	Denmark	Langer et al. 2010
BBzP	340	median of db	177		Bulgaria	Kolarik et al,2008
DEHP	1050	median of db	177		Bulgaria	Kolarik et al,2008
DEHP	770				Sweden	Bornehag et al.2005
BBzP	135				Sweden	Bornehag et al.2005
DEHP	858		23	homes	Denmark	Clausen et al. 2003
DEHP	3214		15	schools	Denmark	Clausen et al. 2003
DEHP	515		252		Germany	Becker et al.2004

Table A 16: Uptake rates to convert external exposure to phthalates to internal doses

		child			adult				
		min	mean	max	min	mean	max		ref
oral uptake rates [fraction of applied dose]									
	BBzP	0,67	0,725	0,78	0,67	0,725	0,78		Wormuth et al., 2006
	DEHP	0,153	0,552	0,95	0,153	0,552	0,95		Wormuth et al., 2006
	DINP	0,75	0,825	0,9	0,75	0,825	0,9		Wormuth et al., 2006
	DIDP	0,75	0,825	0,9	0,75	0,825	0,9		Wormuth et al., 2006
dermal uptake rate (cosmetics) [fraction of applied dose]									
	BBzP	0,011	0,0143	0,017	0,0057	0,0071	0,0086		Wormuth et al., 2006
	DEHP	0,001	0,0021	0,003	0,0007	0,0011	0,0014		Wormuth et al., 2006
	DINP	0,001	0,0013	0,002	0,0004	0,0006	0,0009		Wormuth et al., 2006
	DIDP	0,001	0,0016	0,002	0,0006	0,0008	0,001		Wormuth et al., 2006
dermal uptake rate (soil and dust) [fraction of applied dose]									
	BBzP	0,000566	0,000707	0,000849	0,00283	0,000354	0,000424		Wormuth et al., 2006
	DEHP	0,0000707	0,000106	0,000141	0,0000354	0,000053	7,07E-05		Wormuth et al., 2006
	DINP	0,0000424	0,0000636	0,0000849	0,0000212	3,18E-05	4,25E-05		Wormuth et al., 2006
	DIDP	0,0000566	0,0000778	0,000099	0,0000283	3,89E-05	4,95E-05		Wormuth et al., 2006
dermal uptake rate (sources via migration) [µg/cm²/hr]									
	BBzP		0,48			0,24			Wormuth et al., 2006
	DEHP		0,07			0,03			Wormuth et al., 2006
	DINP		0,04			0,02			Wormuth et al., 2006
	DIDP		0,05			0,03			Wormuth et al., 2006
inhalation uptake rate (fraction of applied dose)									
	BBzP		1			1			Wormuth et al., 2006
	DEHP		1			1			Wormuth et al., 2006
	DINP		1			1			Wormuth et al., 2006
	DIDP		1			1			Wormuth et al., 2006