



NEUROSOME



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H2020-MSCA-ITN-2017 GA - 766251

NEUROSOME: First training event

Heraklion, Crete, May 2019

NEUROSOME

Exploring The Neurological Exposome

Risk assessment of EDCs in Europe based on human biomonitoring data



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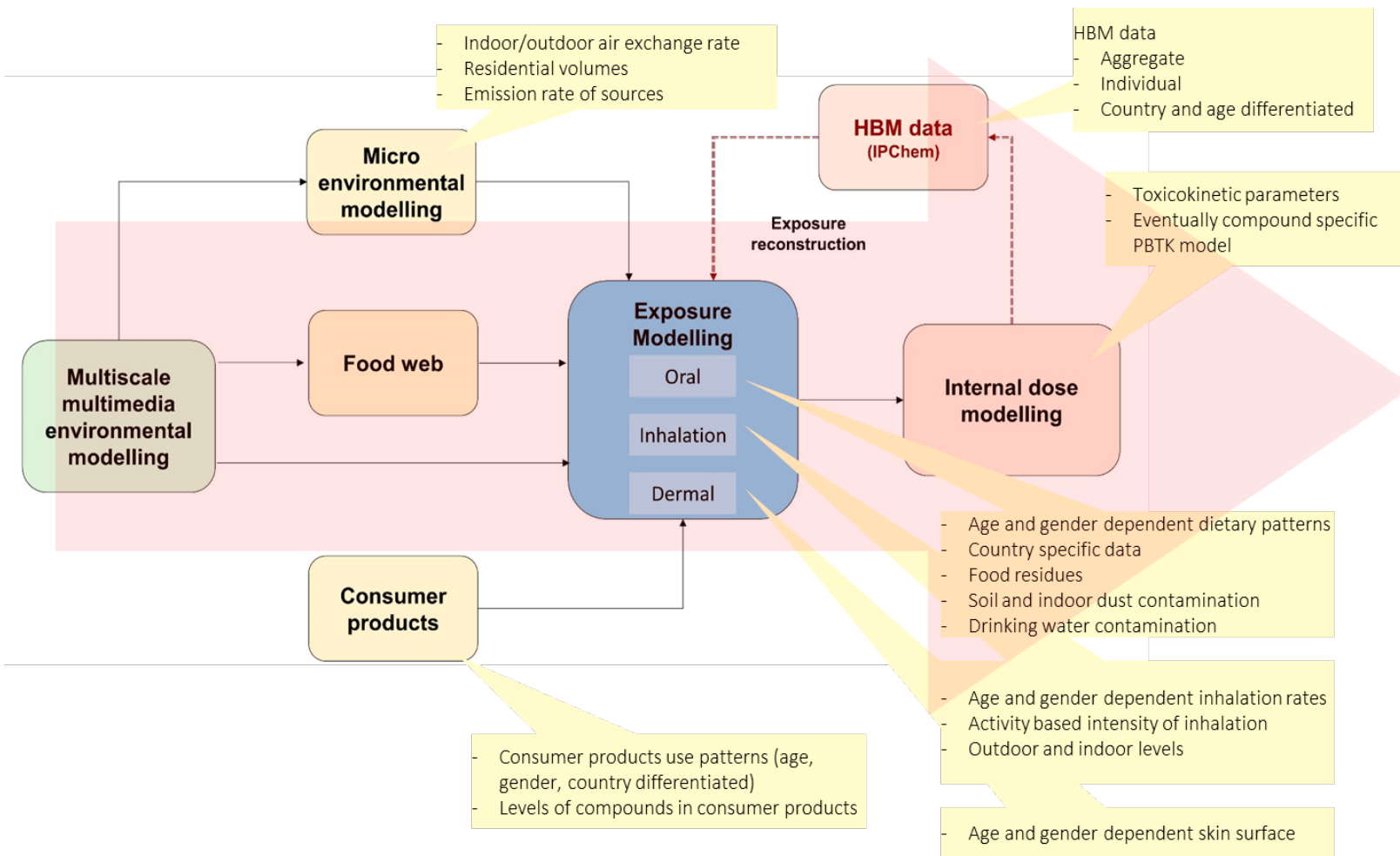
1. Introduction
2. Forward Modeling
3. Bisphenol A
4. Phthalates (DEHP, DINP) and DINCH
5. Flame retardants (TCEP)
6. Perfluorinated compounds (PFOA and PFOS)
7. Discussion



Human biomonitoring (HBM) offers unique opportunities in modern risk assessment, on condition that the biomonitoring data are properly interpreted, especially within the regulatory context.

A major advantage of HBM data is that they provide an integrated overview of the body burden to xenobiotics that an individual is exposed to; hence they serve as a very good approximation of aggregate exposure.

The aim of this study was to derive EU-wide external exposure estimates by HBM data using the INTEGRRA computational platform that includes a generic PBTK model coupled with exposure reconstruction algorithms, for the compounds of interest (i.e. bisphenol-A (BPA), phthalates (DEHP (Di-ethylhexyl Phthalate), DiNP (Diisononyl Phthalate) and DnBP) and DINCH (Di(isononyl)cyclohexane-1,2-dicarboxylate), emerging flame retardants (TCEP) and perfluorinated compounds (PFOA (Perfluorooctanoic Acid) and PFOS (Perfluorooctyl Sulfonate))).

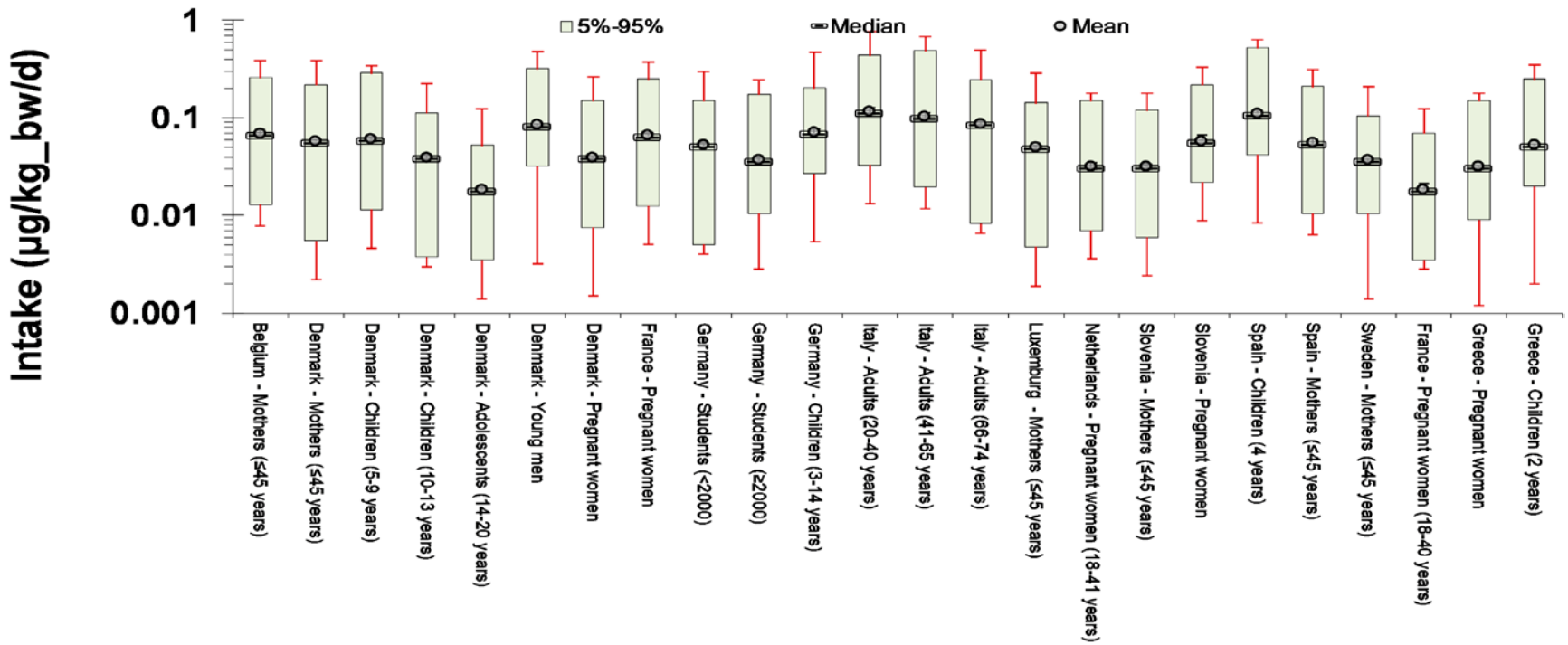




Bisphenol A (BPA)



- Bisphenol A (BPA) is a chemical compound used in massive amounts in the production of synthetic polymers and thermal paper.
- BPA exhibits moderate acute toxicity to vertebrates.
- Recently, intensive investigations have shown teratogenic, carcinogenic and particularly estrogenic mechanisms of BPA action.



BPA intake levels based on HBM data

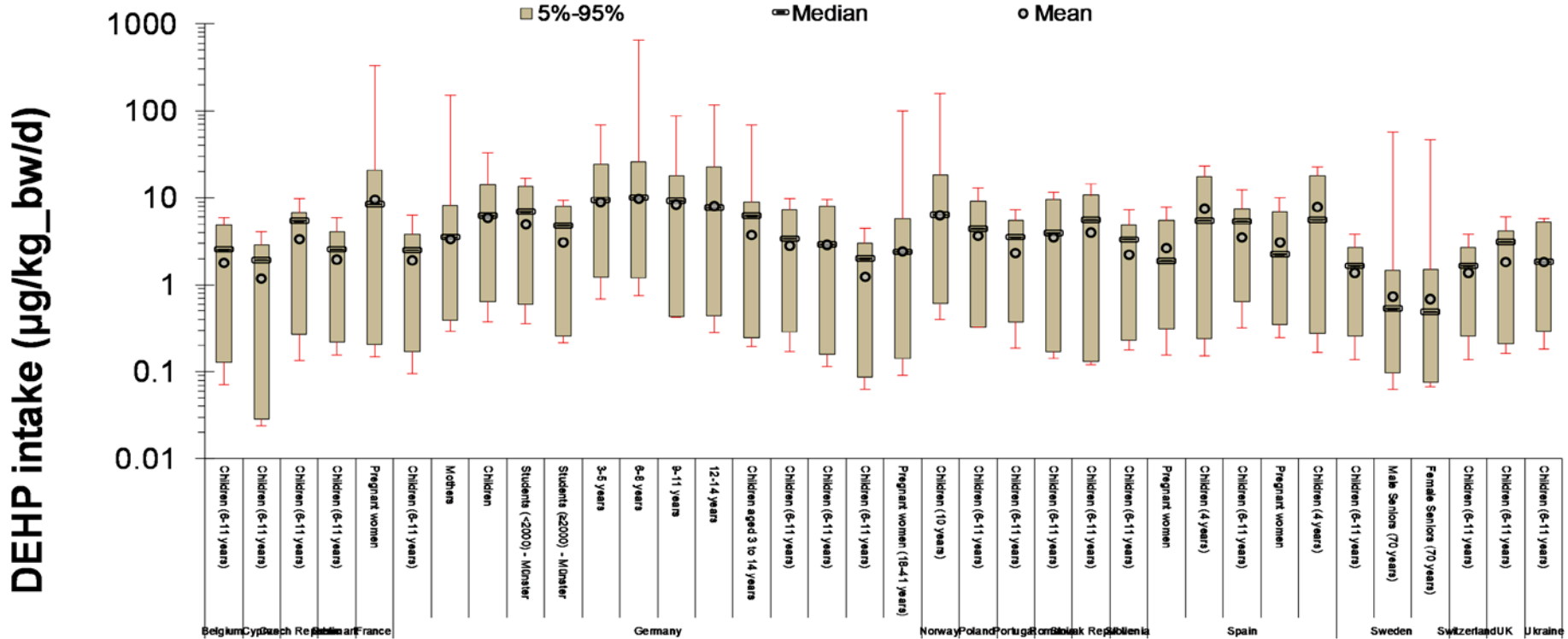
EFSA TDI: 0.77 µg/kg bw•d



- Some phthalates (DEHP, DINP) affect the development of the male reproductive system
- DINCH has been used in Europe since 2002 as a plasticizer to replace phthalates such as DEHP and DINP.
- At high doses, thyroid hyperplasia and signs of renal toxicity have been reported in rats and several oxidative metabolites of DINCH have been identified in DINCH-dosed rats.



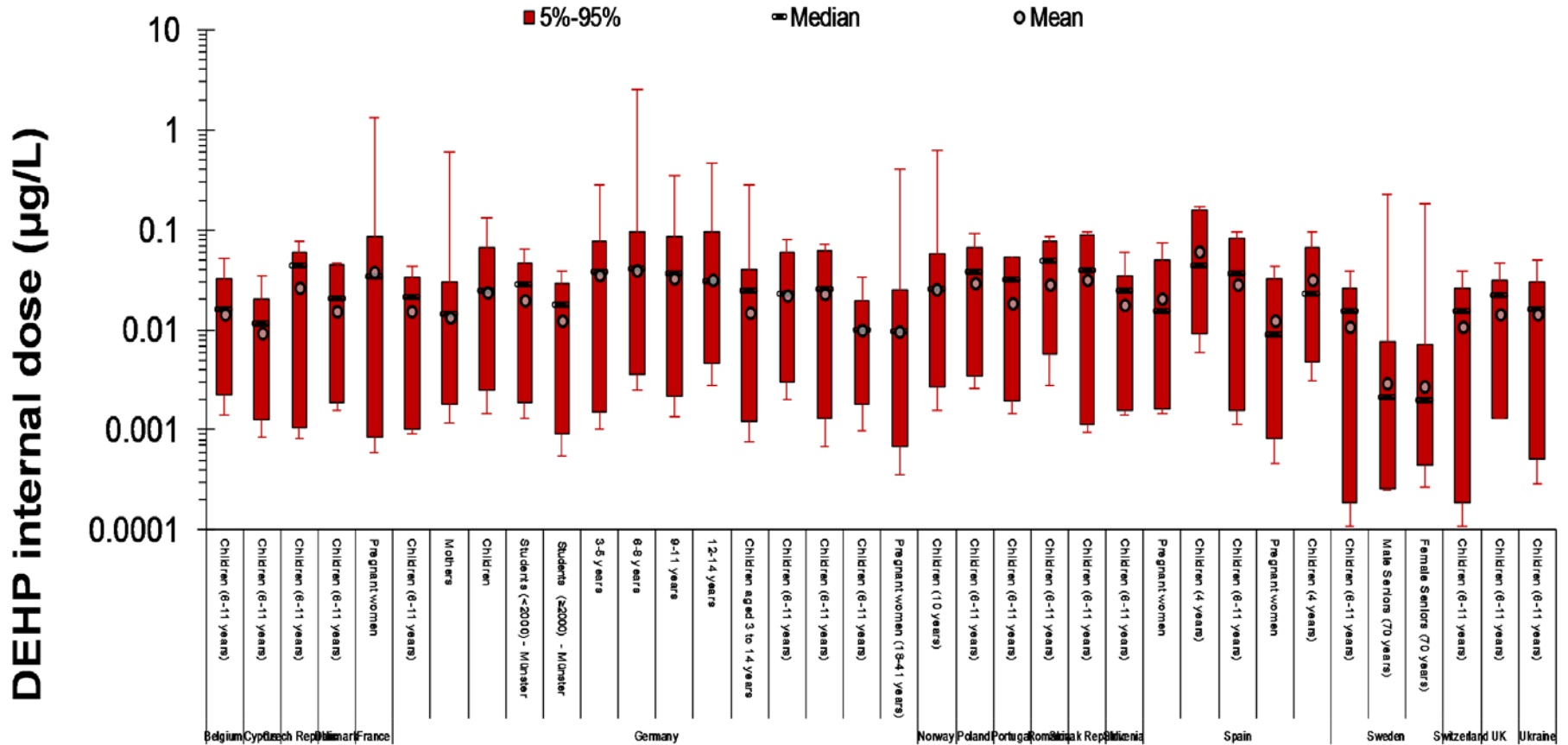
DEHP Intake based on HBM data



DEHP Intake based on reconstructed intake from HBM data



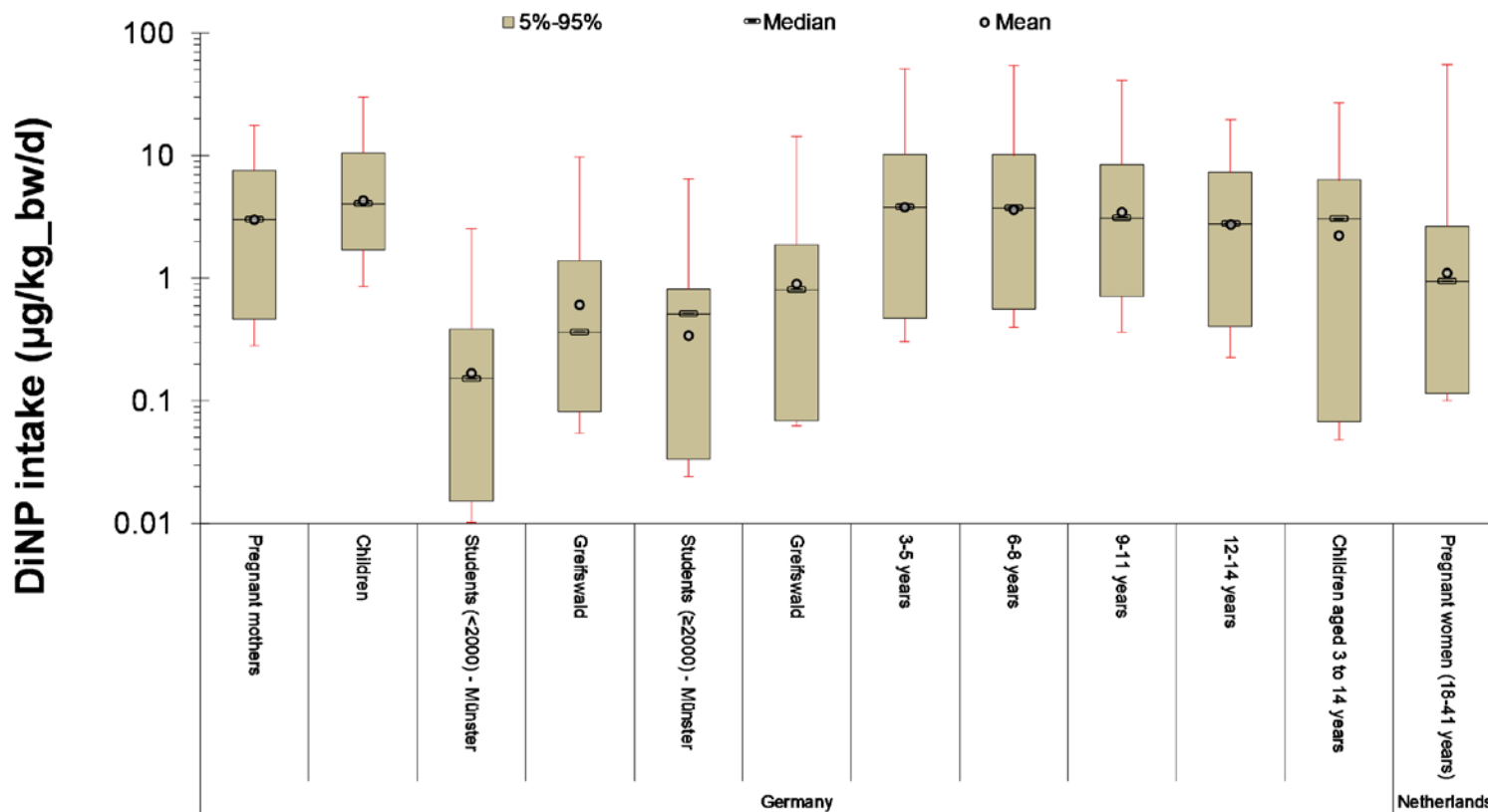
DEHP Internal Dose based on HBM data



DEHP Internal dose based on reconstructed intake from HBM data



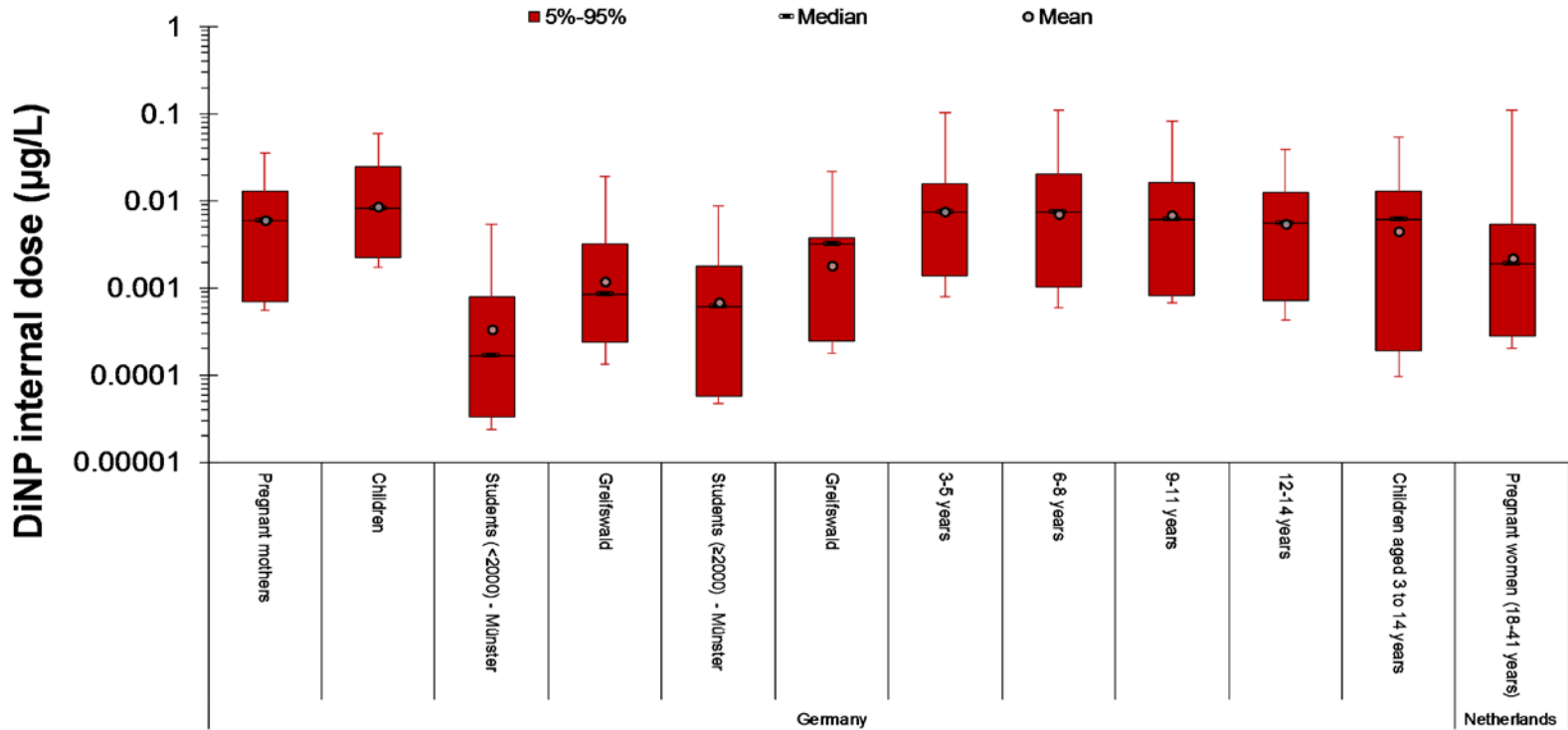
DINP Intake based on HBM data



DiNP Intake based on reconstructed intake from HBM data



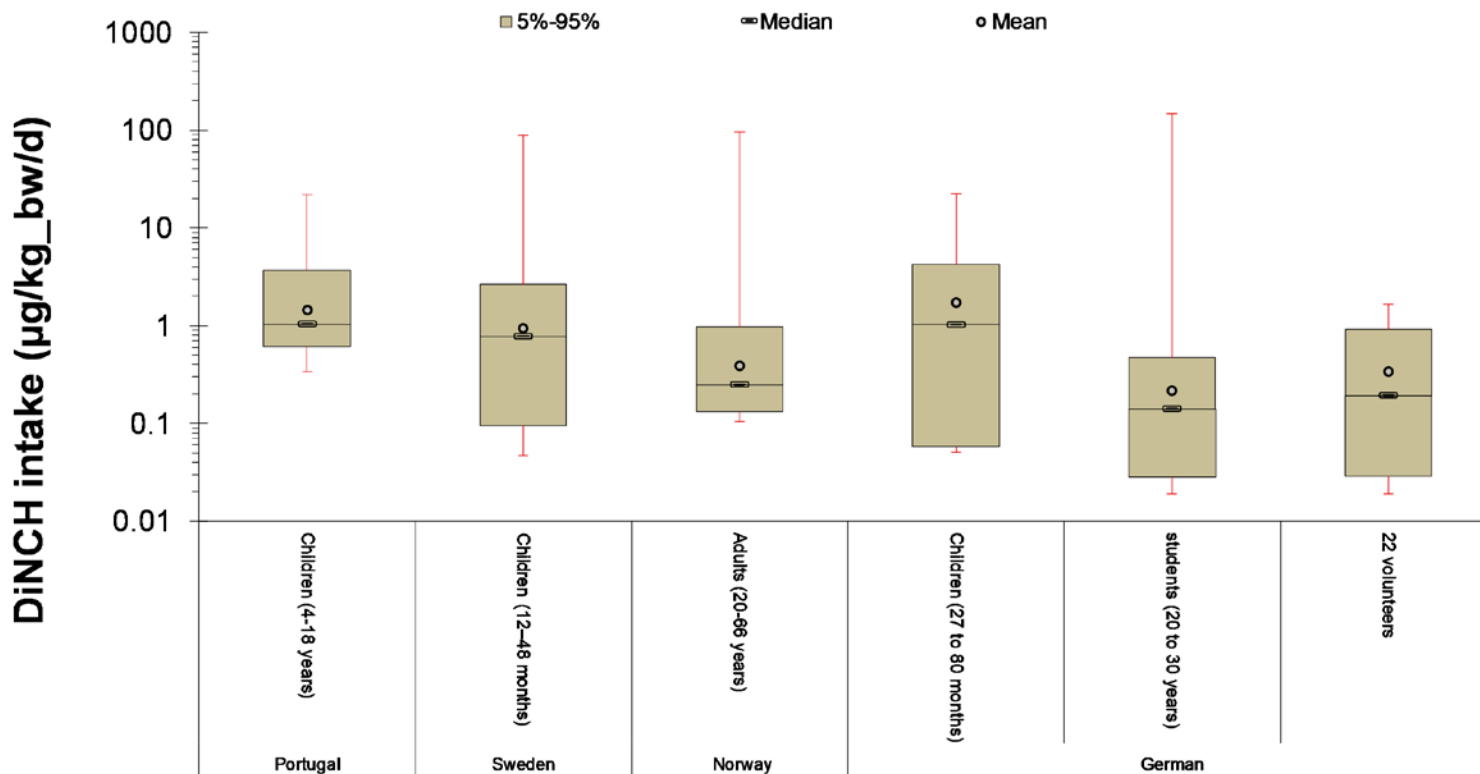
DiNP Internal Dose based on HBM data



DiNP Internal dose based on reconstructed intake from HBM data



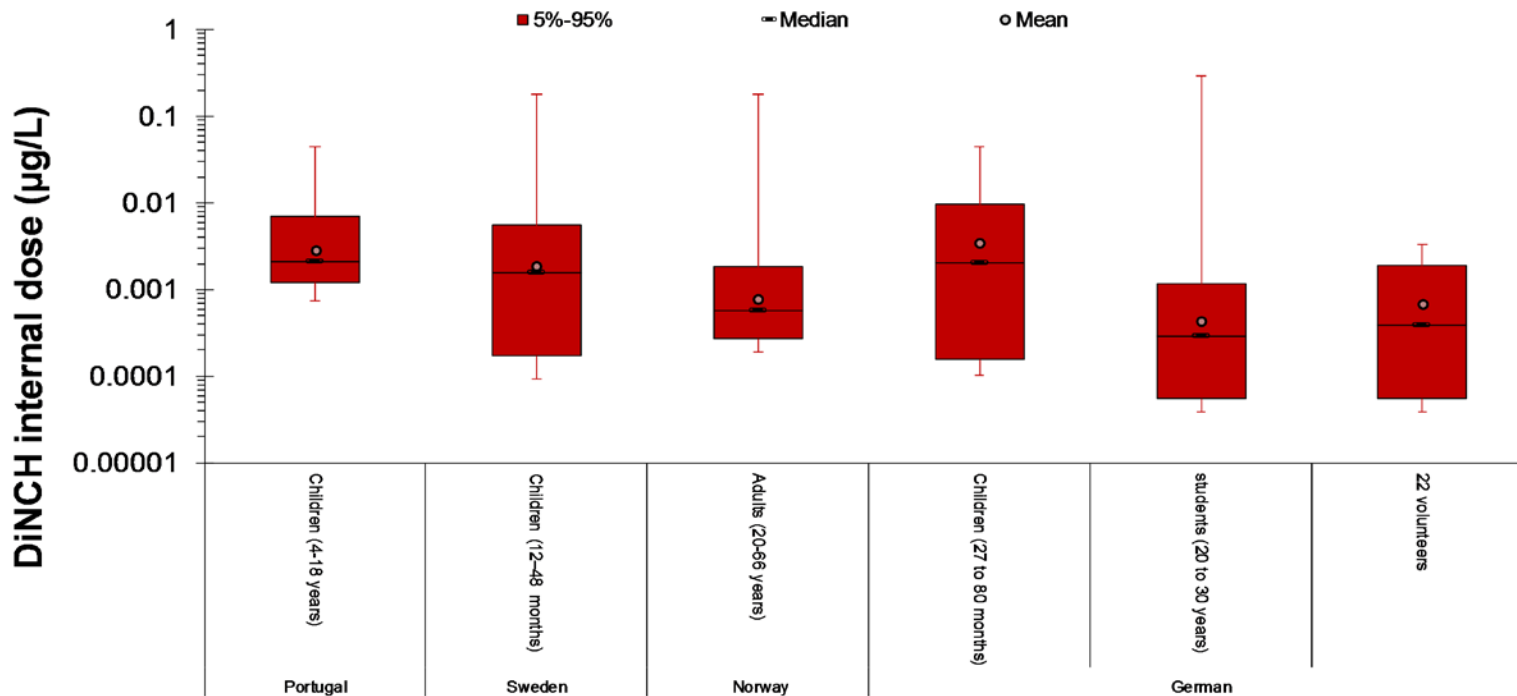
DINCH Intake based on HBM data



DiNCH Intake based on reconstructed intake from HBM data



DINCH Internal Dose based on HBM data



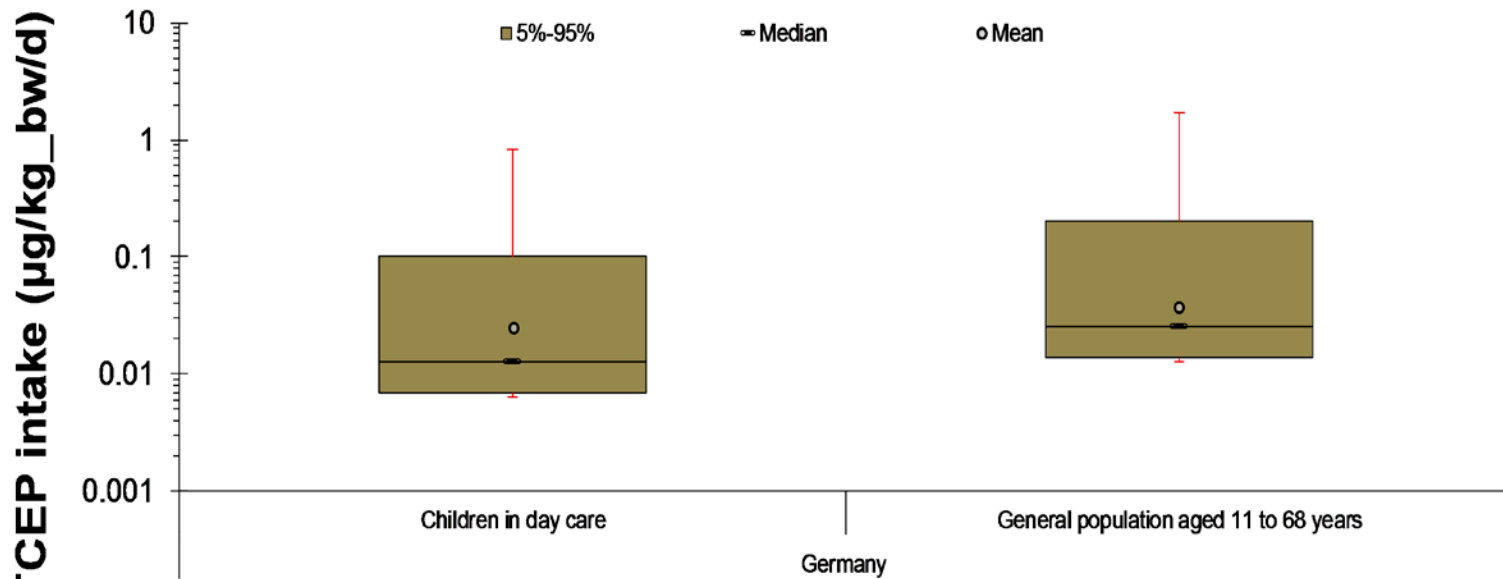
DiNCH Internal dose based on reconstructed intake from HBM data



- Organophosphate flame retardants (PFRs) are a new class of flame retardants. The health risks of PFRs have received attention recently. However, little is known about the potential toxicity of PFRs on the nervous system.
- PFRs are frequently added to consumer products including furniture, textiles, cables, building materials, paints, floor polishes and electronics for fire protection
- It was found that two types of organophosphorus flame retardants, TCEP and TCPP, caused multiple locomotor deficits in *Caenorhabditis elegans*. The behavioral alterations induced by TCEP/TCPP were characterized as Parkinsonian-like movement impairments including bradykinesia and hypokinesia.



TCEP Intake based on HBM data

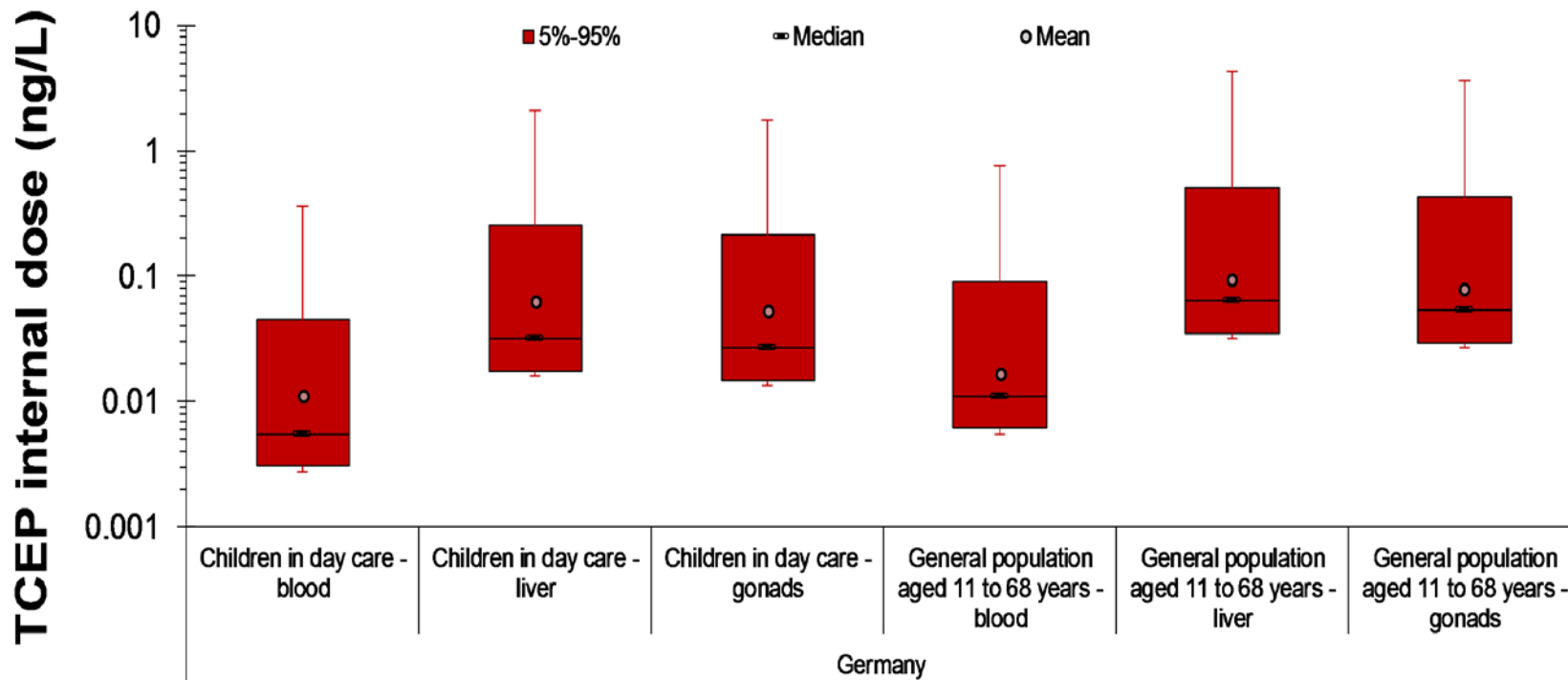


TCEP intake based on HBM data

EFSA 'provisional' TDI of 13 µg/kg_bw/d



TCEP Internal dose based on HBM data



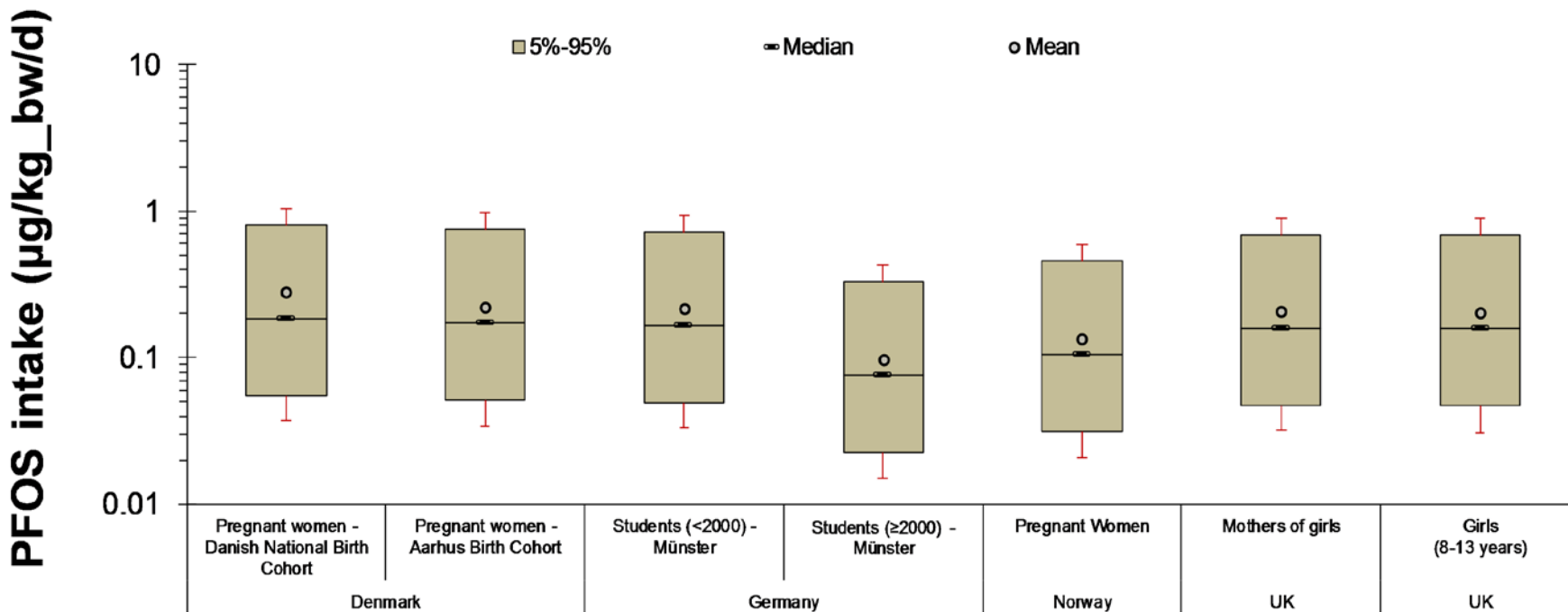
TCEP internal dose in blood, liver and gonads based on reconstructed intake from HBM data



- Perfluorinated compounds are generally hydrophobic but also lipophobic and will therefore not accumulate in fatty tissues as is usually the case with other persistent halogenated compounds.
- Prenatal exposure to PFOS did not affect learning and memory behaviors. However marginal but statistically significant deficits in the developmental patterns of choline acetyltransferase activity (an enzyme marker sensitive to thyroid hormone status) were observed in rats with a LOAEL of 1 mg/kg_bw. per day.
- Follow up of 2083 Decatur workers (Alabama) showed that workers in jobs involving high exposure to PFOS based materials had 13 times increased risk for bladder cancer mortality compared with the general population of Alabama



PFOS Intake based on HBM data

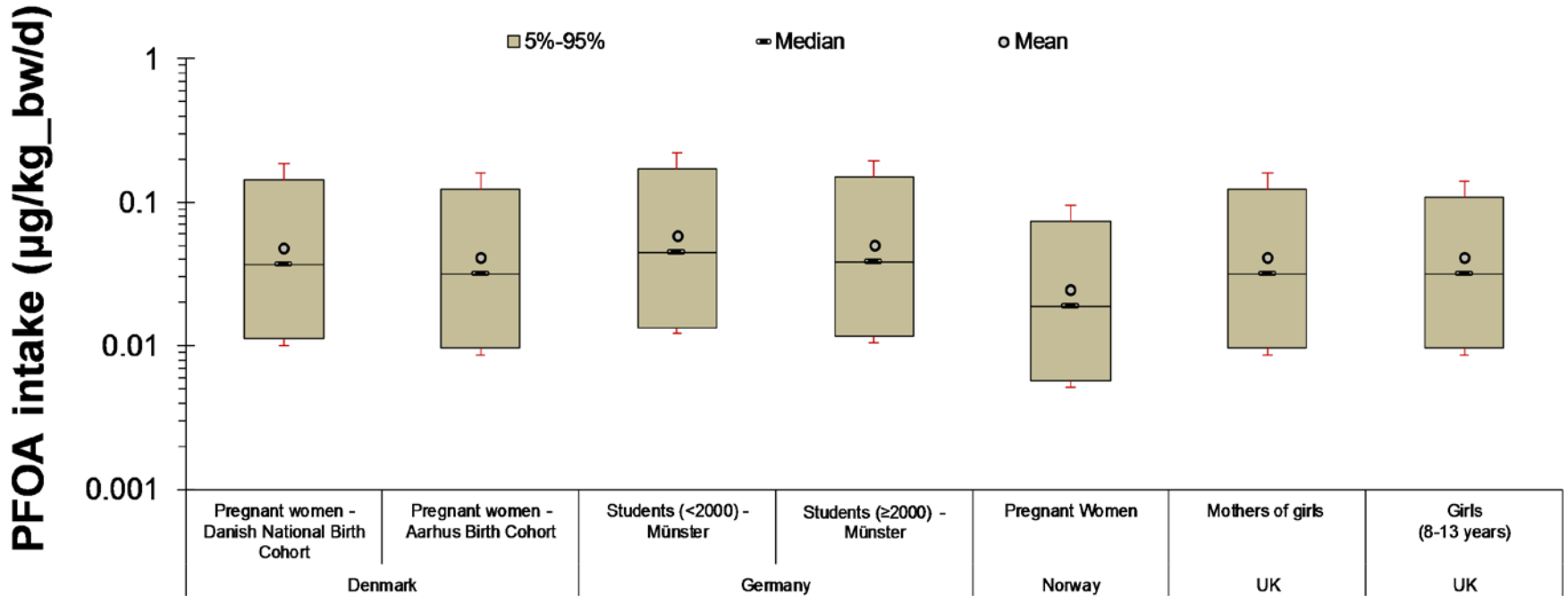


PFOS intake based on HBM data

PFOS TDI of 0.15 µg/kg_bw/d



PFOA Intake based on HBM data



PFOA intake based on HBM data

PFOA TDI of 1.5 µg/kg_bw/d



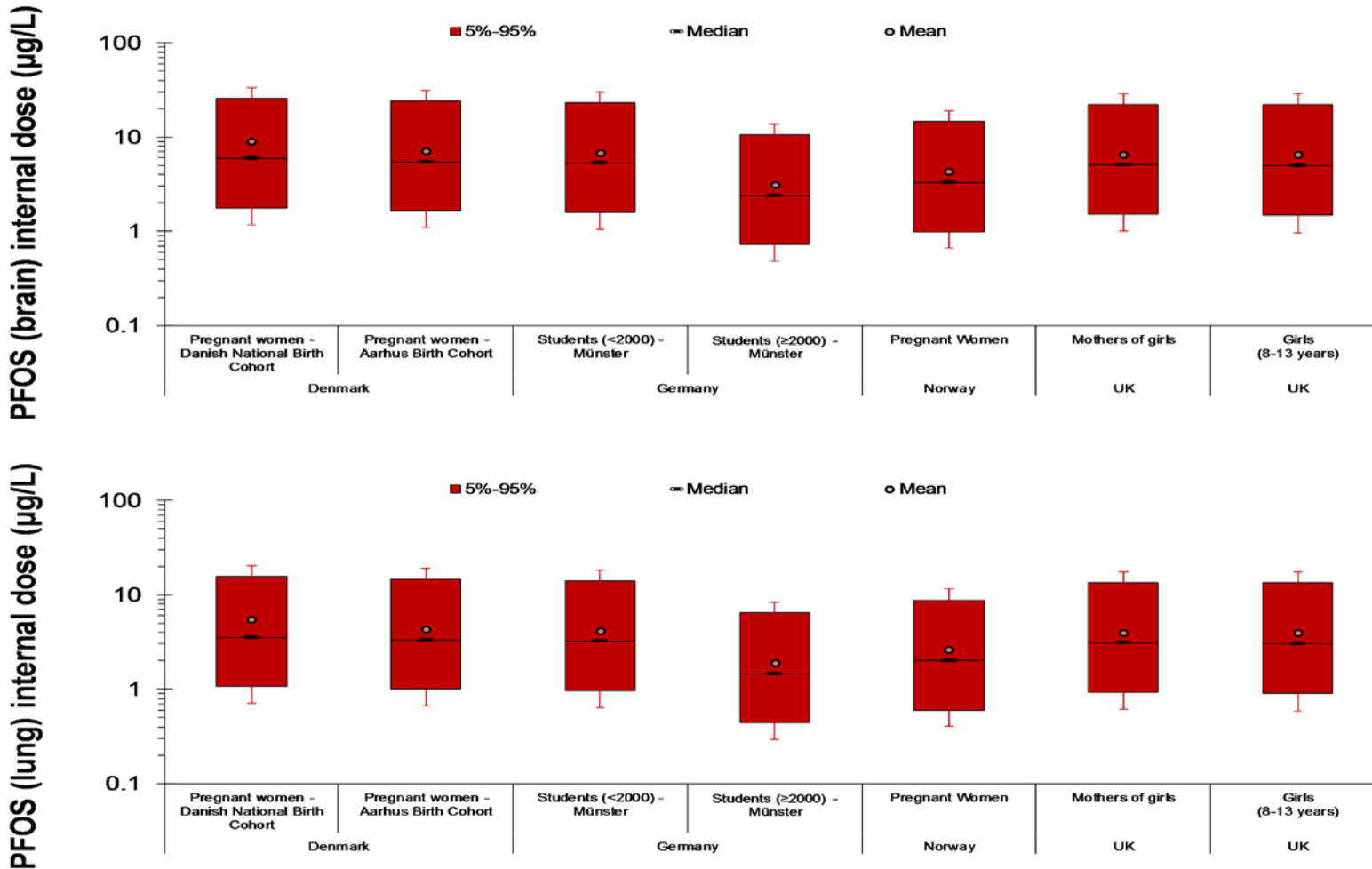
PFOS Tissue specific internal dose based on HBM data



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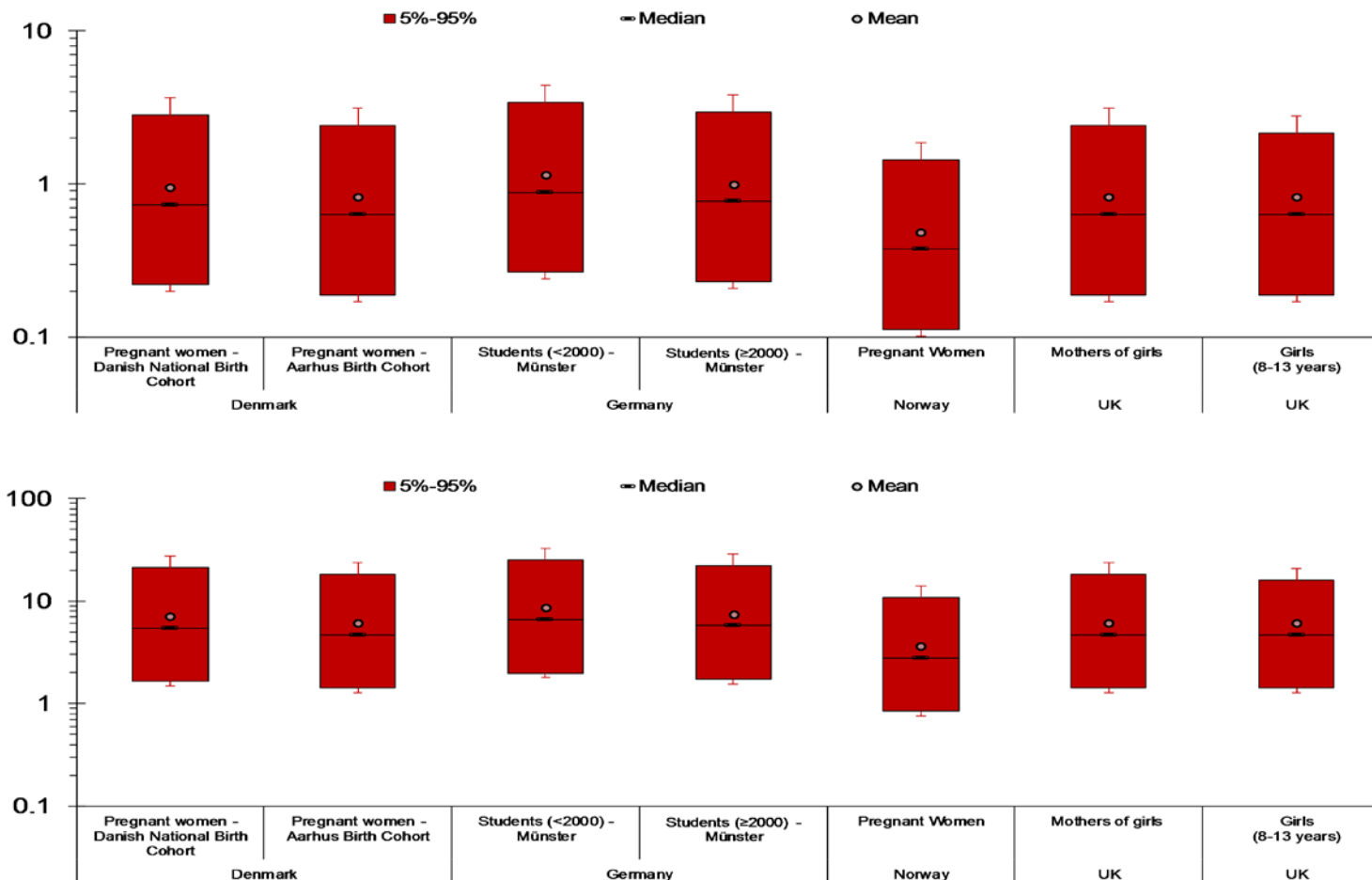
PFOS internal dose in brain and lungs based on reconstructed intake from HBM data



PFOA Tissue specific internal dose based on HBM data



PFOA (lung) internal dose (µg/L) PFOA (brain) internal dose (µg/L)



PFOA internal dose in brain and lungs based on reconstructed intake from HBM data



- Daily intake estimates for the various compounds were derived based on the exposure reconstruction results of the available aggregate HBM data
- The results show that for the majority of the compounds examined daily intake levels are below the existing regulatory thresholds.
- For BPA, mean daily intake is almost 2 orders of magnitude below the respective threshold proposed by EFSA.
- For phthalates, daily intake estimates are usually one or two orders of magnitude below the respective TDI
- Regarding TCEP, the mean daily intake estimate is below $0.1 \mu\text{g}/\text{kg_bw}/\text{d}$, which is far below the calculated 'provisional' TDI of $13 \mu\text{g}/\text{kg_bw}/\text{d}$, however, at the moment very few HBM data were available and these exposure levels are rather indicative than representative of the European countries.
- Finally, regarding the estimated intakes of PFCs, intake levels of PFOS are very close to TDI ($0.15 \mu\text{g}/\text{kg_bw}/\text{d}$ proposed by the CONTAM Panel), while the calculated levels for PFOA are one order of magnitude below the respective TDI of $1.5 \mu\text{g}/\text{kg_bw}/\text{d}$.



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THANK YOU FOR YOUR ATTENTION



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