NEUROSOME

Exploring The Neurological Exposome

EXPOSURE MODELLING AND EXPOSURE RECONSTRUCTION FOR PHTHALATES

NEUROSOME

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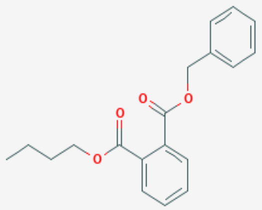
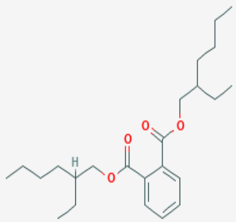
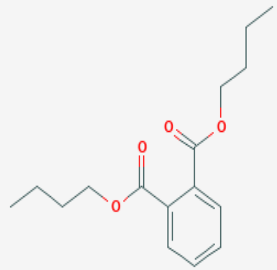


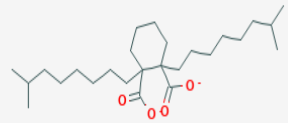
Benzyl Butyl Phthalate BBzP



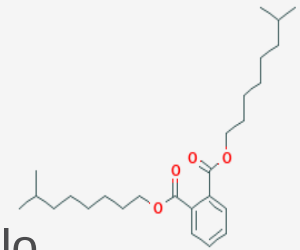
Di-ethylhexyl Phthalate DEHP



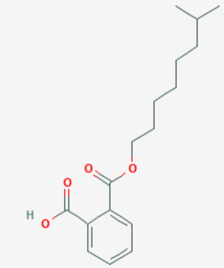
Di-n-butyl Phthalate DBP



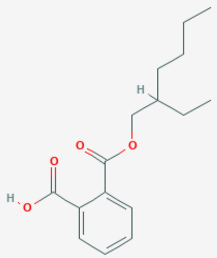
Di(isononyl)cyclohexane-1,2-dicarboxylate DINCH



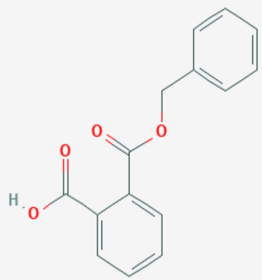
Diisononyl Phthalate DiNP



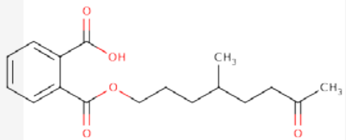
Monoisononyl Phthalate MiNP



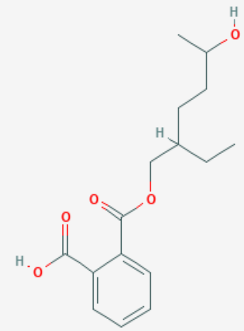
Mono-(2-ethylhexyl) Phthalate MEHP



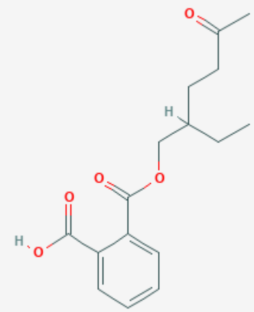
Mono-benzyl Phthalate MBzP



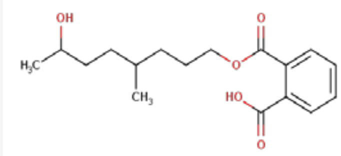
Mono-oxo-isononyl Phthalate oxo-MiNP



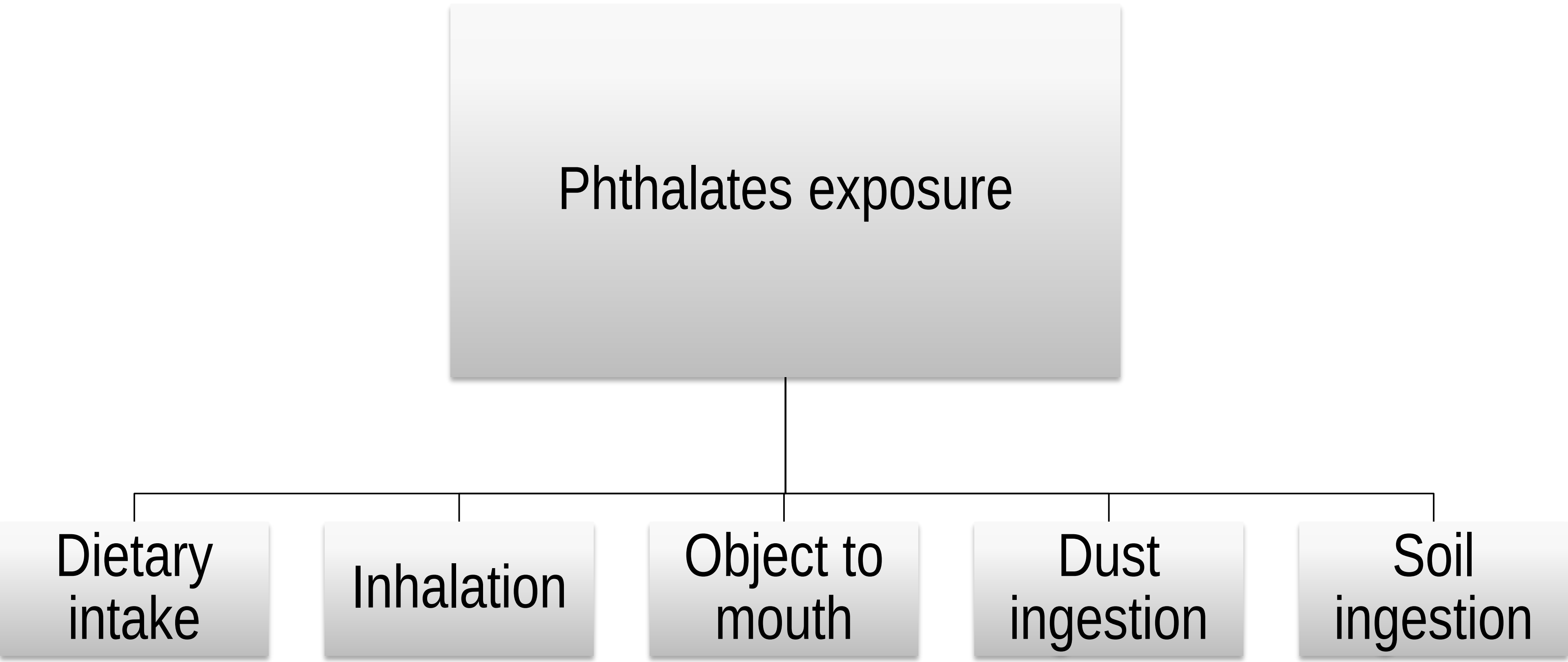
Mono(2-ethyl-5-hydroxyhexyl) Phthalate 5-OH MEHP

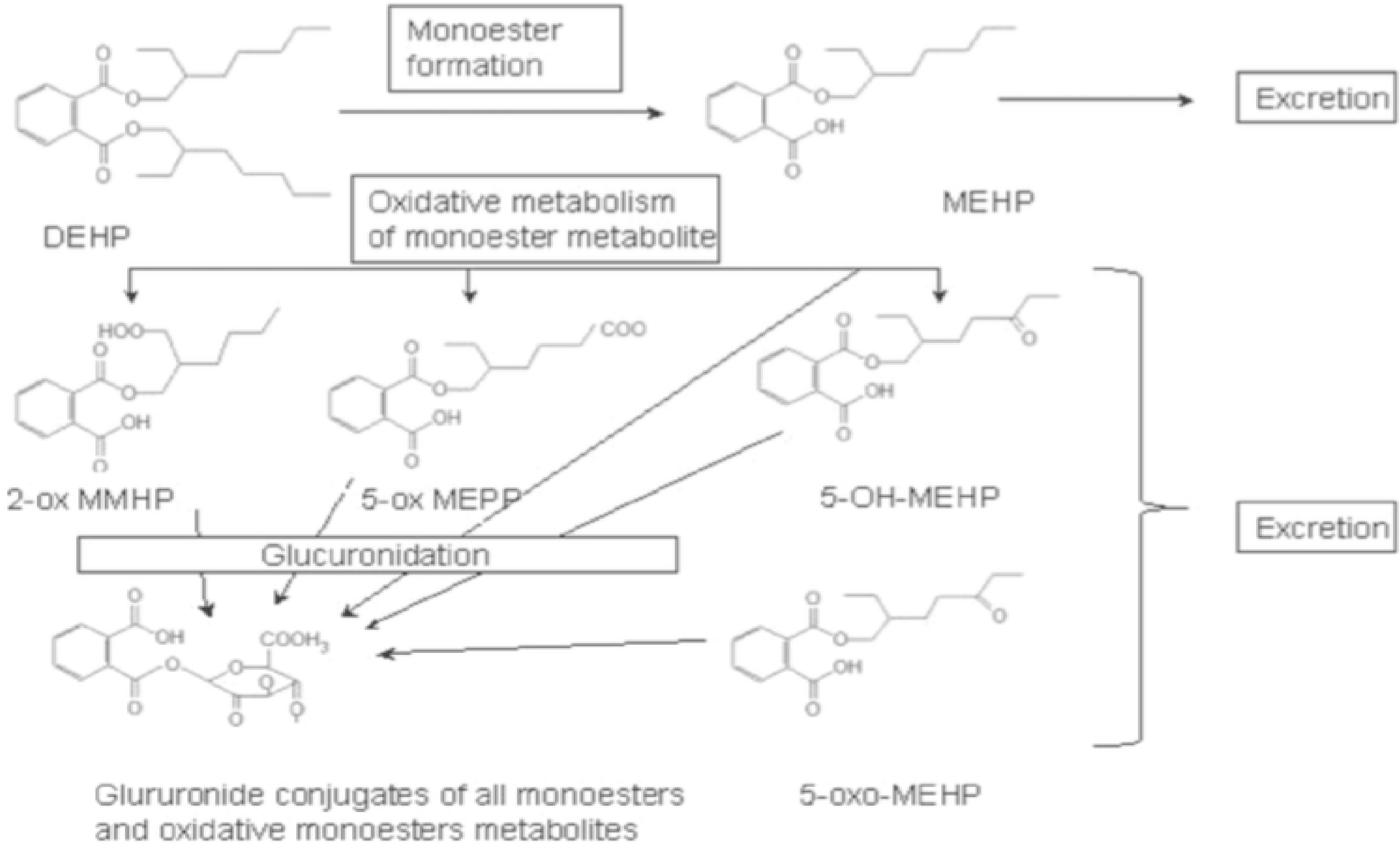


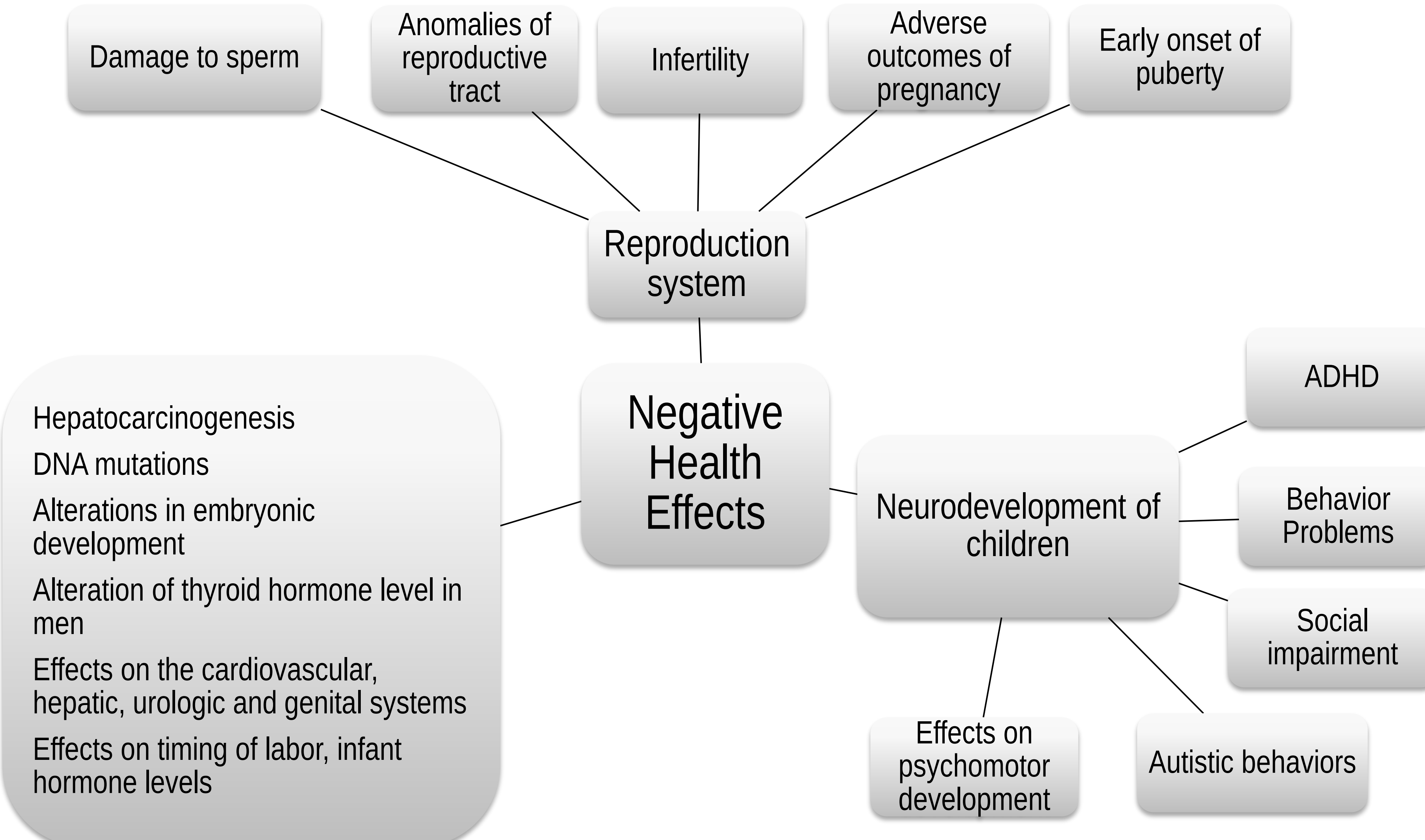
Mono(2-ethyl-5-oxohexyl) Phthalate 5oxo-MEHP



Mono(hydroxy-isononyl) Phthalate OH-MiNP


Phthalates exposure
Dietary intake
Inhalation
Object to mouth
Dust ingestion
Soil ingestion


Monoester formation
Excretion
DEHP
MEHP
Oxidative metabolism of monoester metabolite
2-ox MMHP
5-ox MEPP
5-OH-MEHP
Excretion
Glucuronidation
Glururonide conjugates of all monoesters and oxidative monoesters metabolites
5-oxo-MEHP

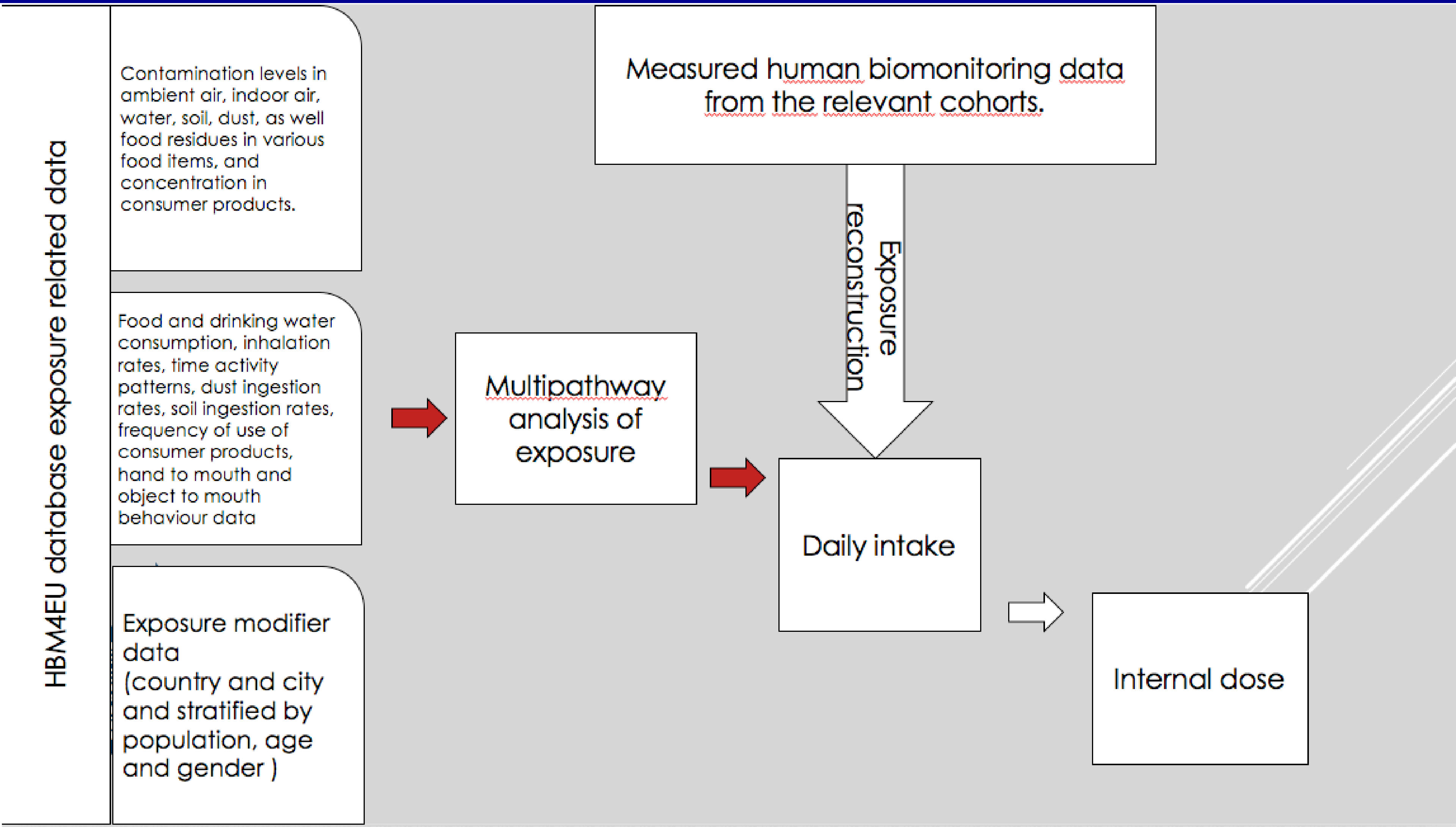

Damage to sperm
Anomalies of reproductive tract
Infertility
Adverse outcomes of pregnancy
Early onset of puberty
Reproduction system
Negative Health Effects
Hepatocarcinogenesis
DNA mutations
Alterations in embryonic development
Alteration of thyroid hormone level in men
Effects on the cardiovascular, hepatic, urologic and genital systems
Effects on timing of labor, infant hormone levels
Neurodevelopment of children
ADHD
Behavior Problems
Social impairment
Effects on psychomotor development
Autistic behaviors

Multimedia indoor air quality module (concentrations in gas, particles and dust phase starting from gaseous emissions)

Internal dose, for the assessment of phthalates and their metabolites (MEHP, 5-OH MEHP and 5oxo-MEHP) in human tissues and urine through a multi-compartmental PBPK model.

Uncertainty and variability across all stages of the assessment

Exposure assessment modeling (all possible exposure pathways and routes)


HBM4EU database exposure related data
Contamination levels in ambient air, indoor air, water, soil, dust, as well food residues in various food items, and concentration in consumer products.
Food and drinking water consumption, inhalation rates, time activity patterns, dust ingestion rates, soil ingestion rates, frequency of use of consumer products, hand to mouth and object to mouth behaviour data
Exposure modifier data (country and city and stratified by population, age and gender)
Measured human biomonitoring data from the relevant cohorts.
Exposure reconstruction
Multipathway analysis of exposure
Daily intake
Internal dose

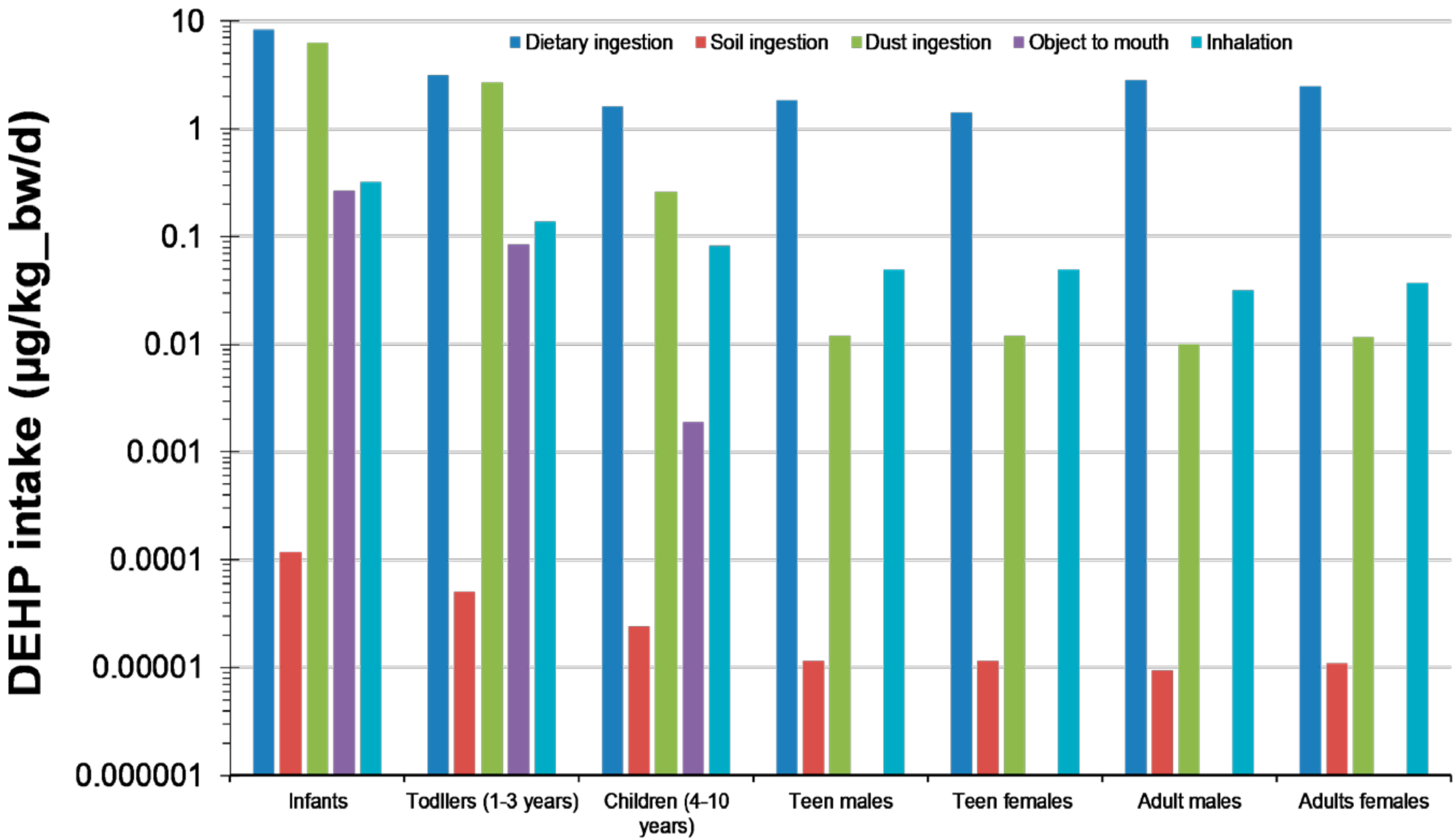


Figure 6. Daily intake of DEHP for the various age groups based on multipathway exposure

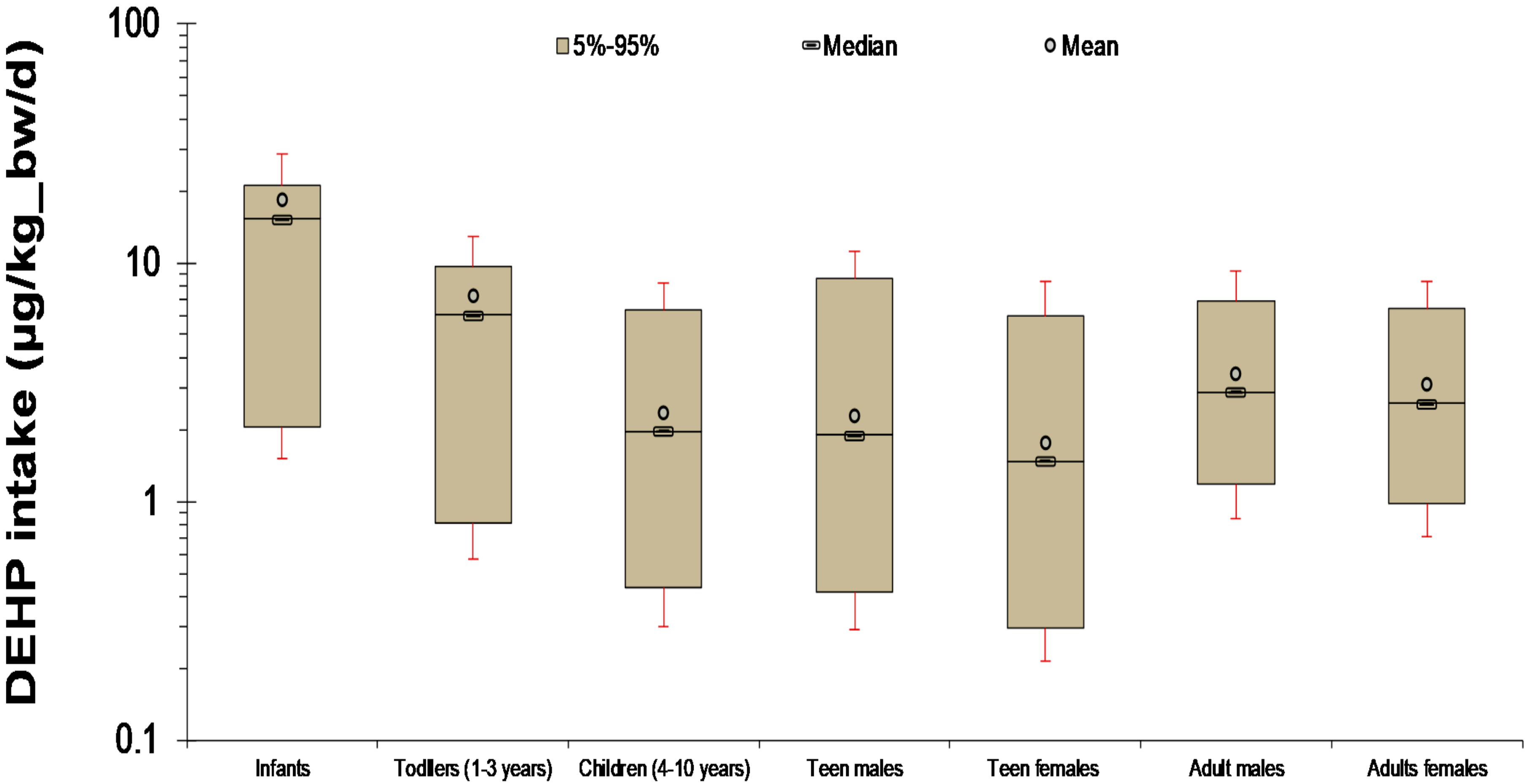


Figure 7. Aggregate intake distributions of DEHP for the various age groups

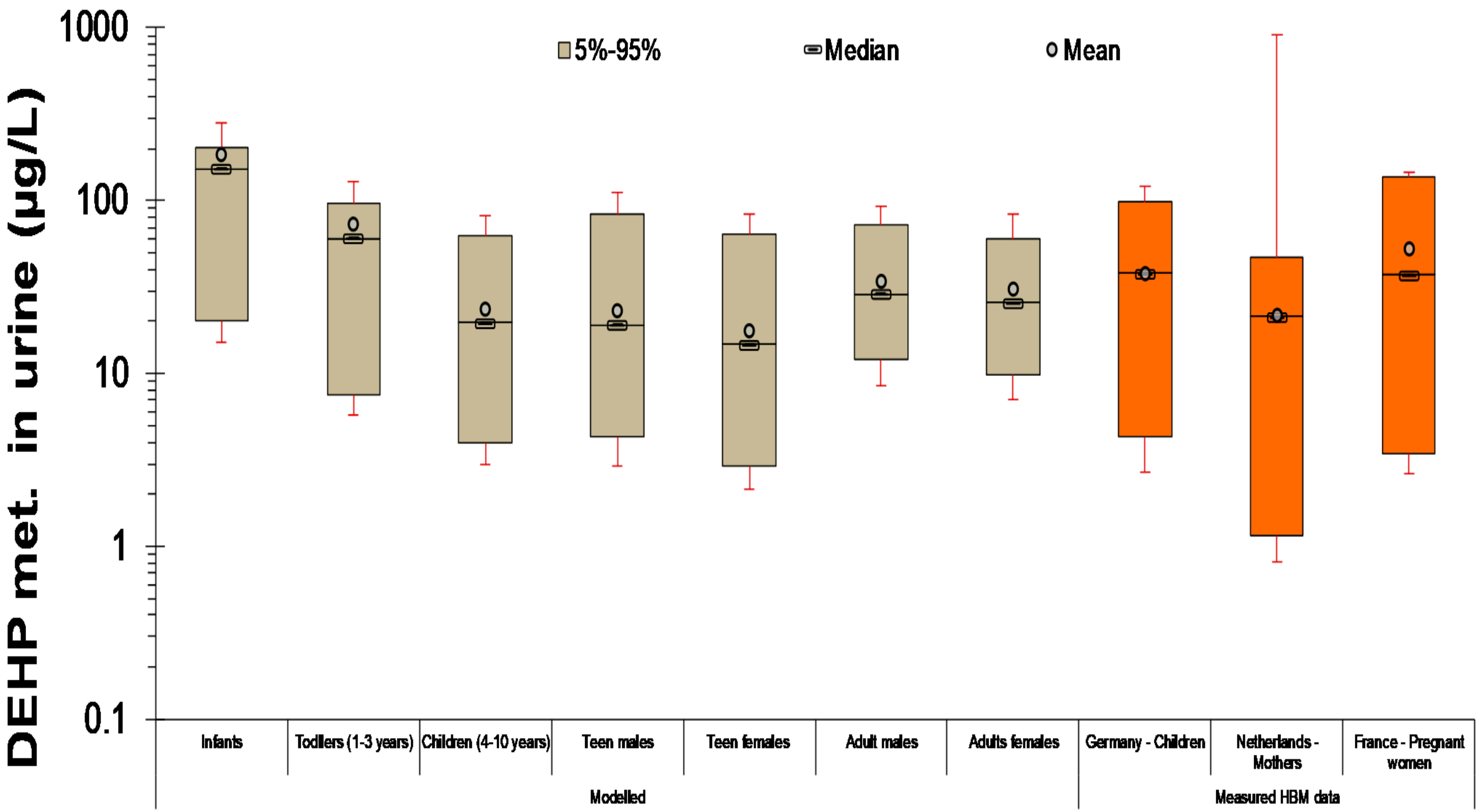


Figure 8. Expected metabolites (sum of MEHP, OH-MEHP & oxo-MEHP) in urine for the various age groups and indicative measured levels

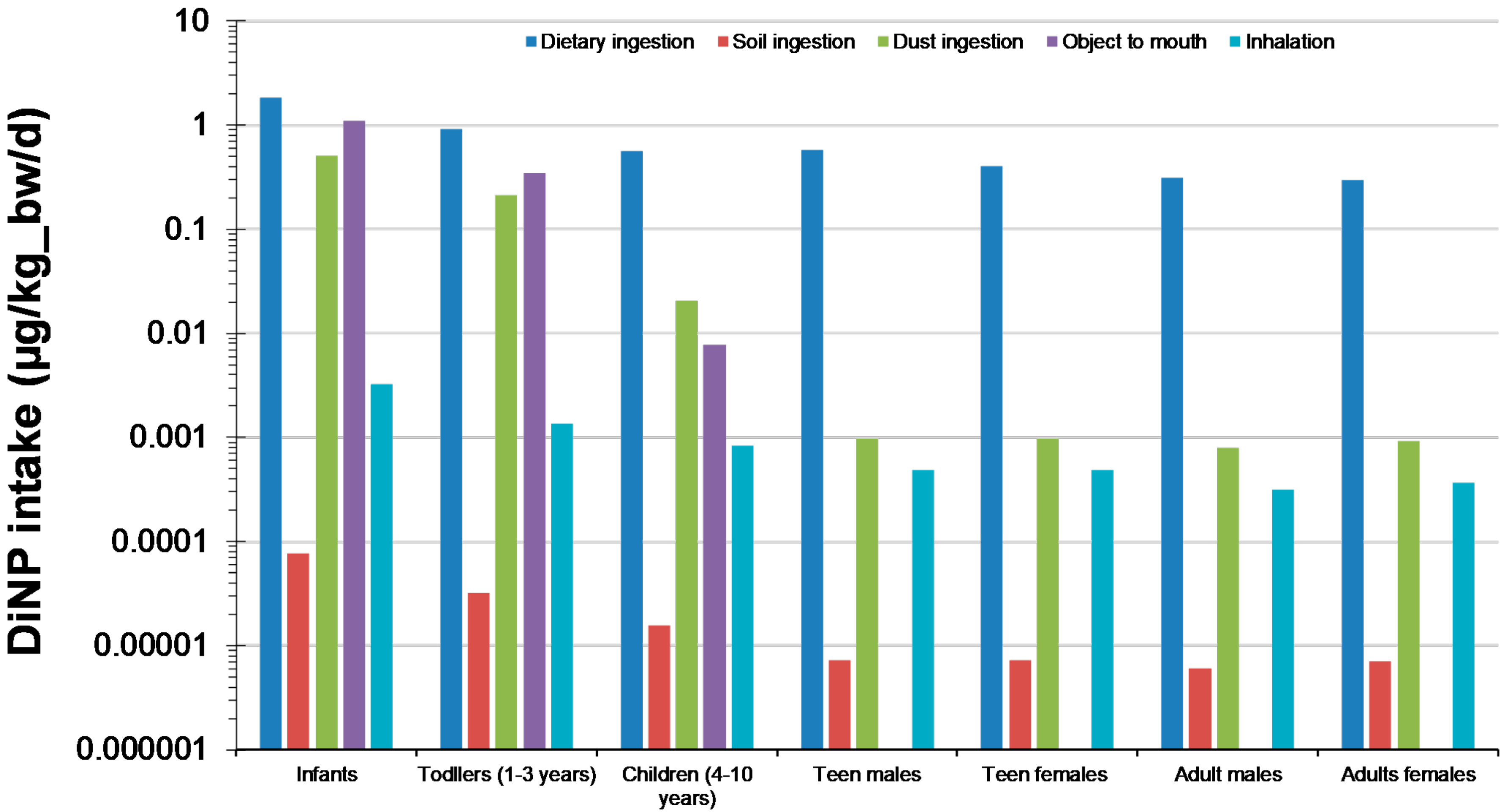


Figure 9. Daily intake of DiNP for the various age groups based on multipathway exposure

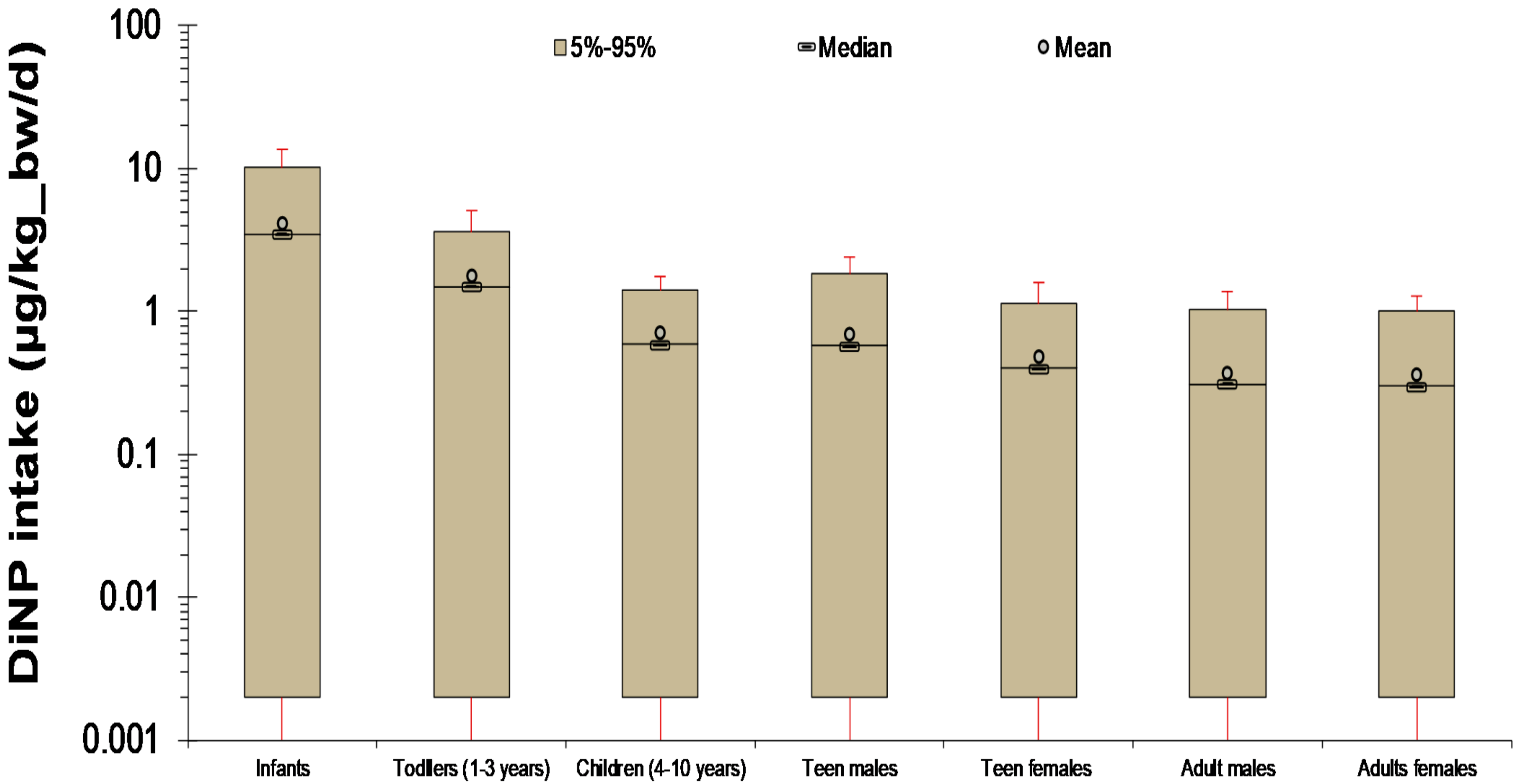


Figure 10. Aggregate intake distributions of DiNP for the various age groups

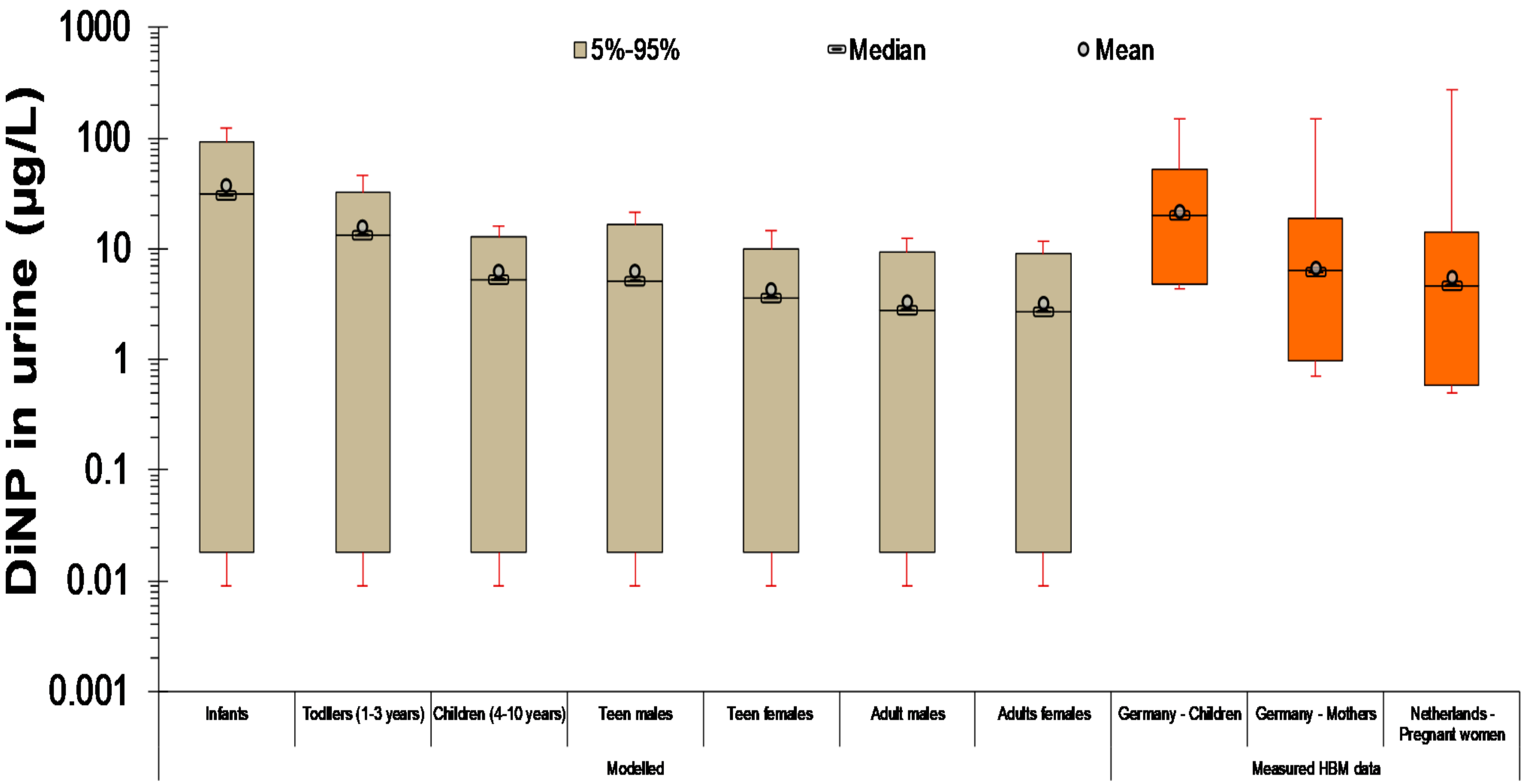


Figure 11. Expected metabolites (sum of MiNP, OH-MiNP & oxo-MiNP) in urine for different age groups and indicative measured levels

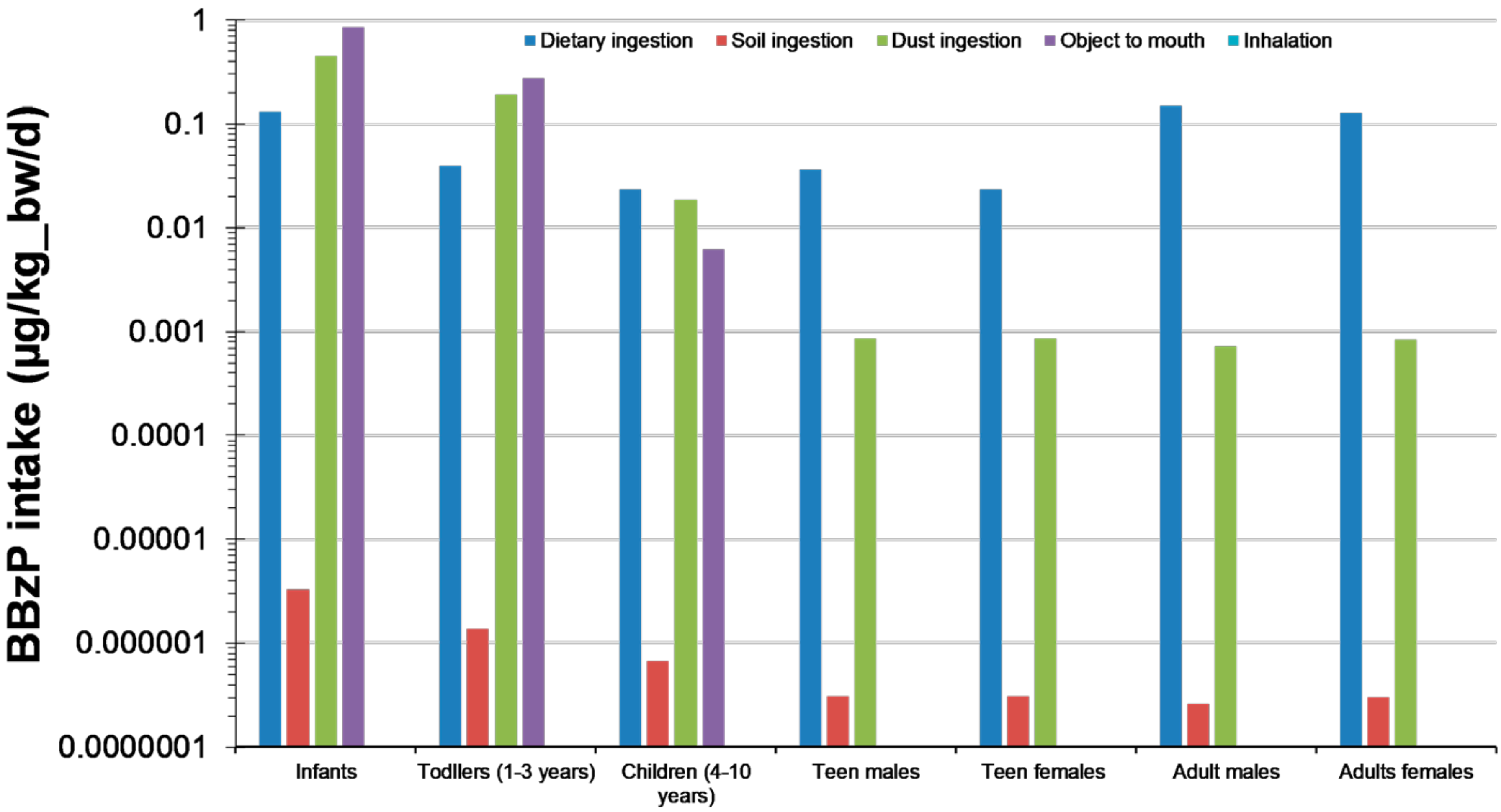


Figure 12. Daily intake of BBzP for the various age groups based on multipathway exposure

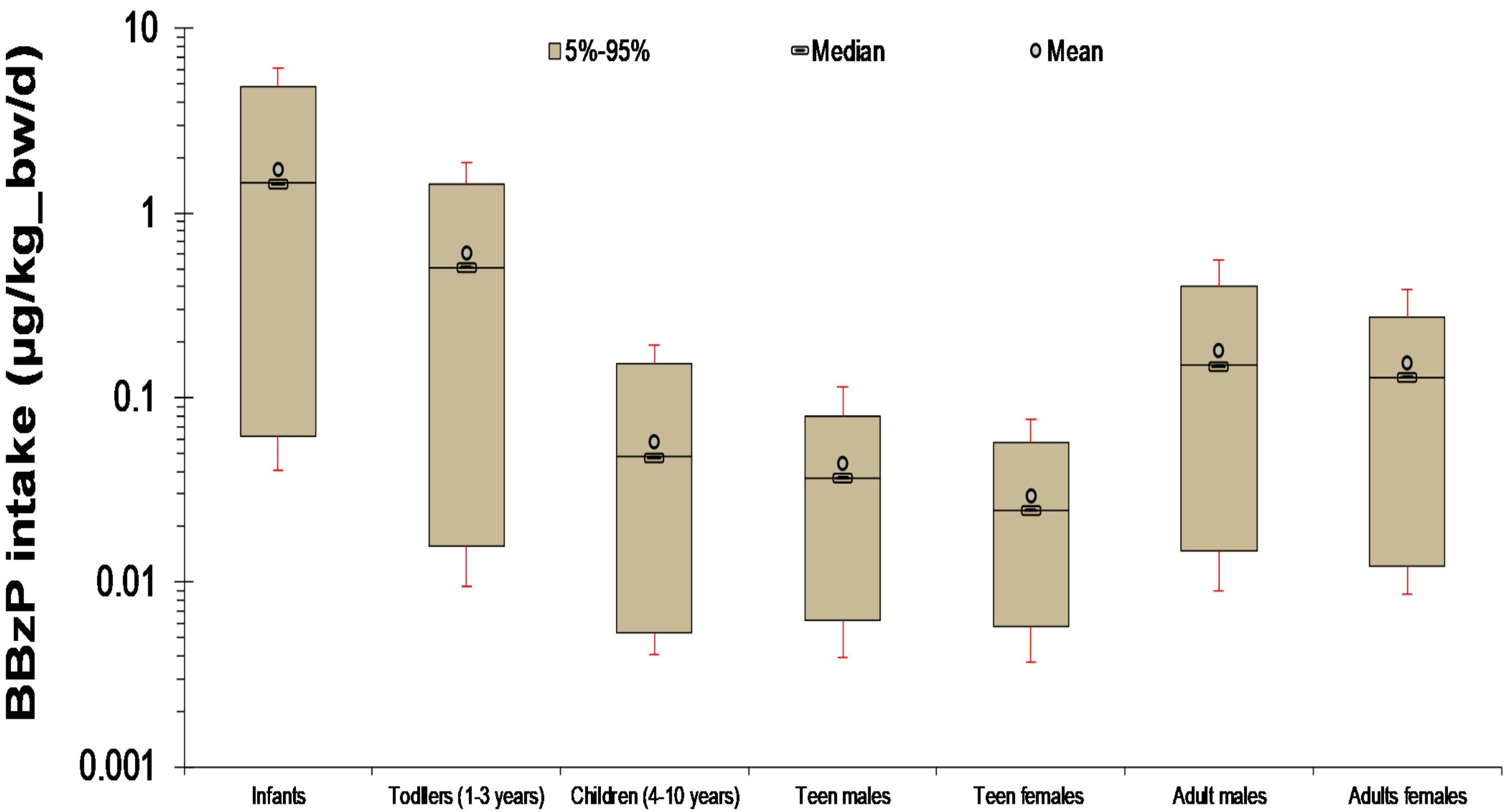


Figure 13. Aggregate intake distributions of BBzP for the different age groups

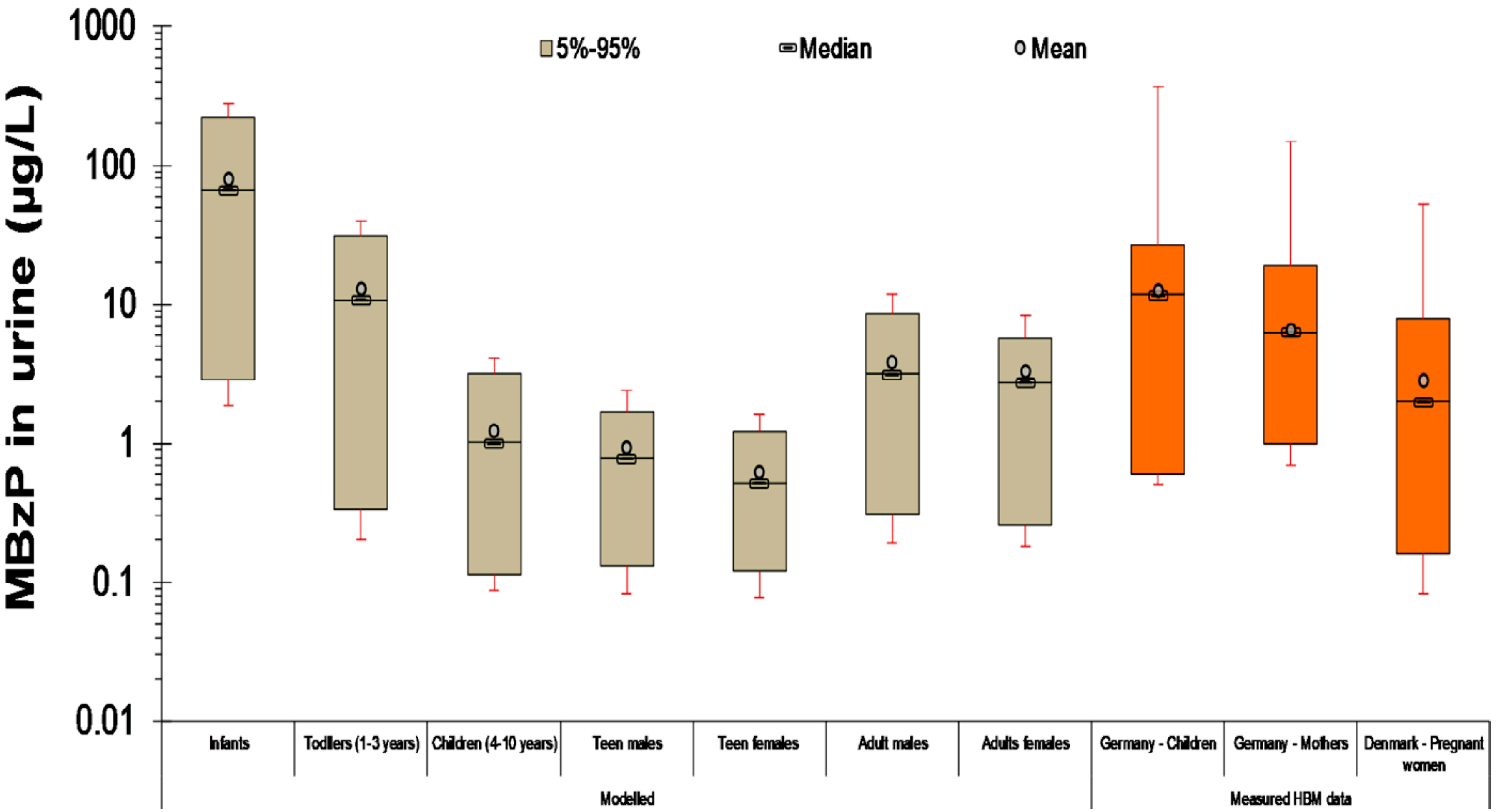
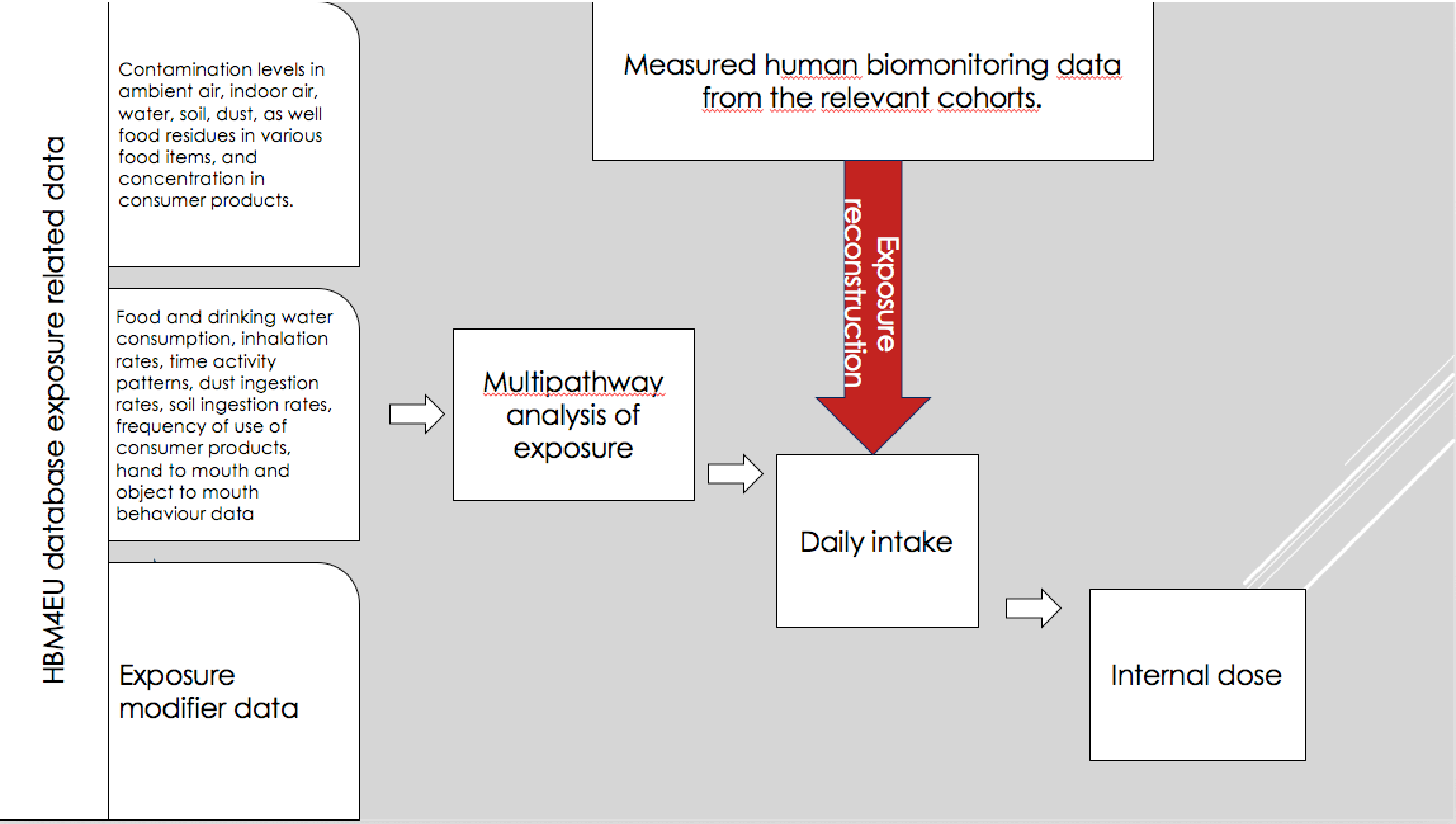


Figure 14. Expected metabolite (MBzP) in urine for the various age groups and indicative measured levels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Exposure reconstruction
Daily intake
Internal dose

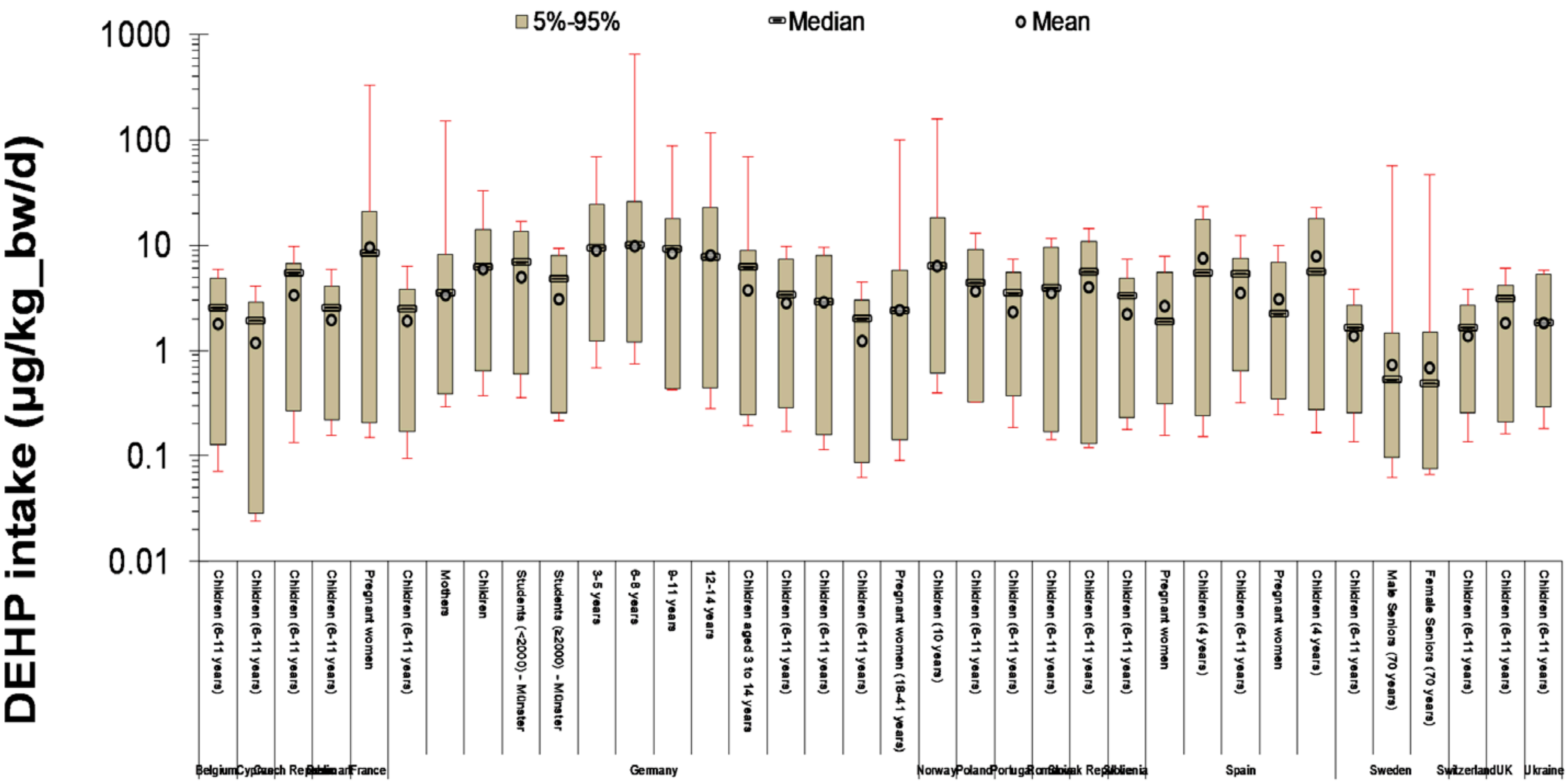

Figure 21. DEHP intake estimates based on HBM data

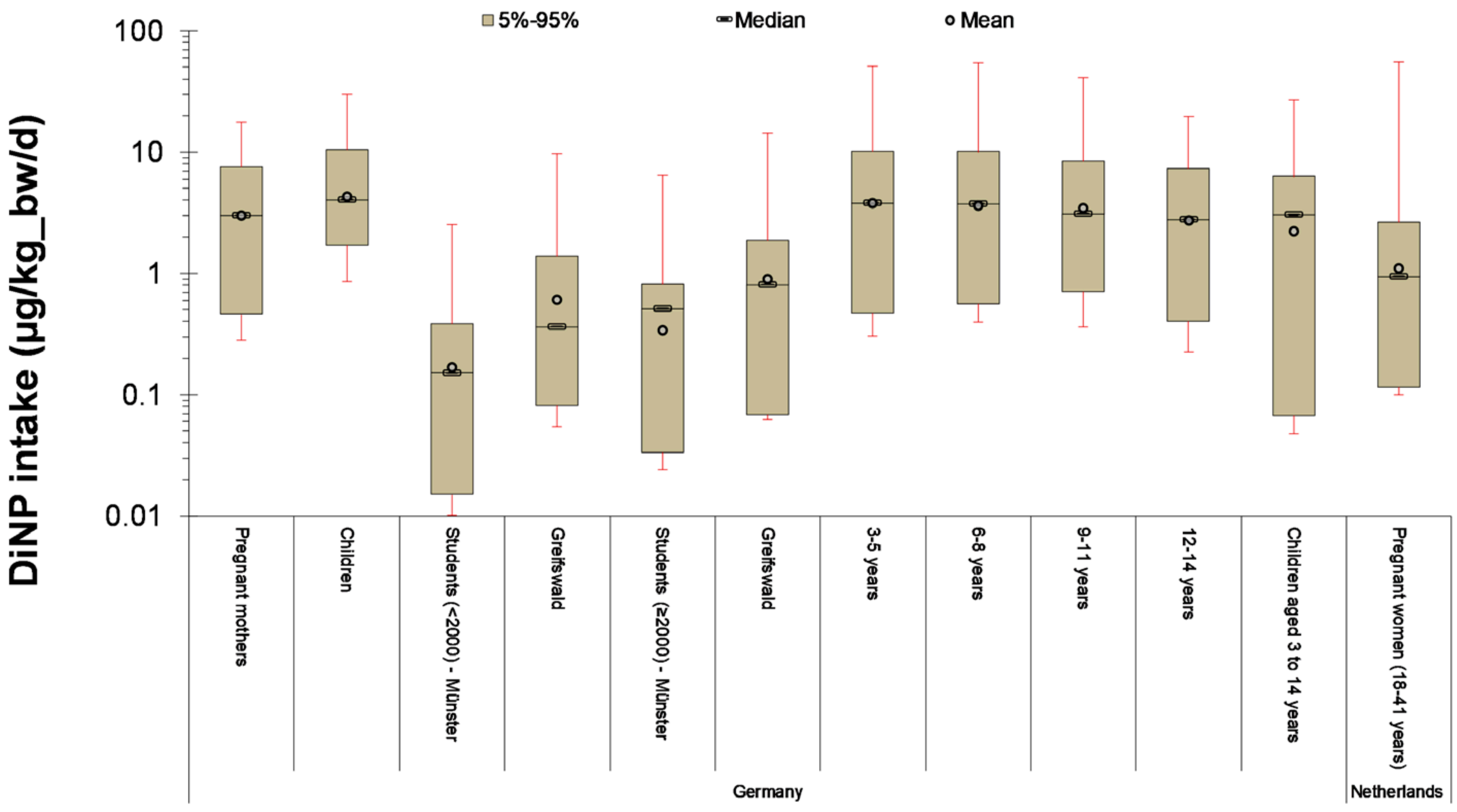

Figure 22. DiNP intake estimates based on HBM data

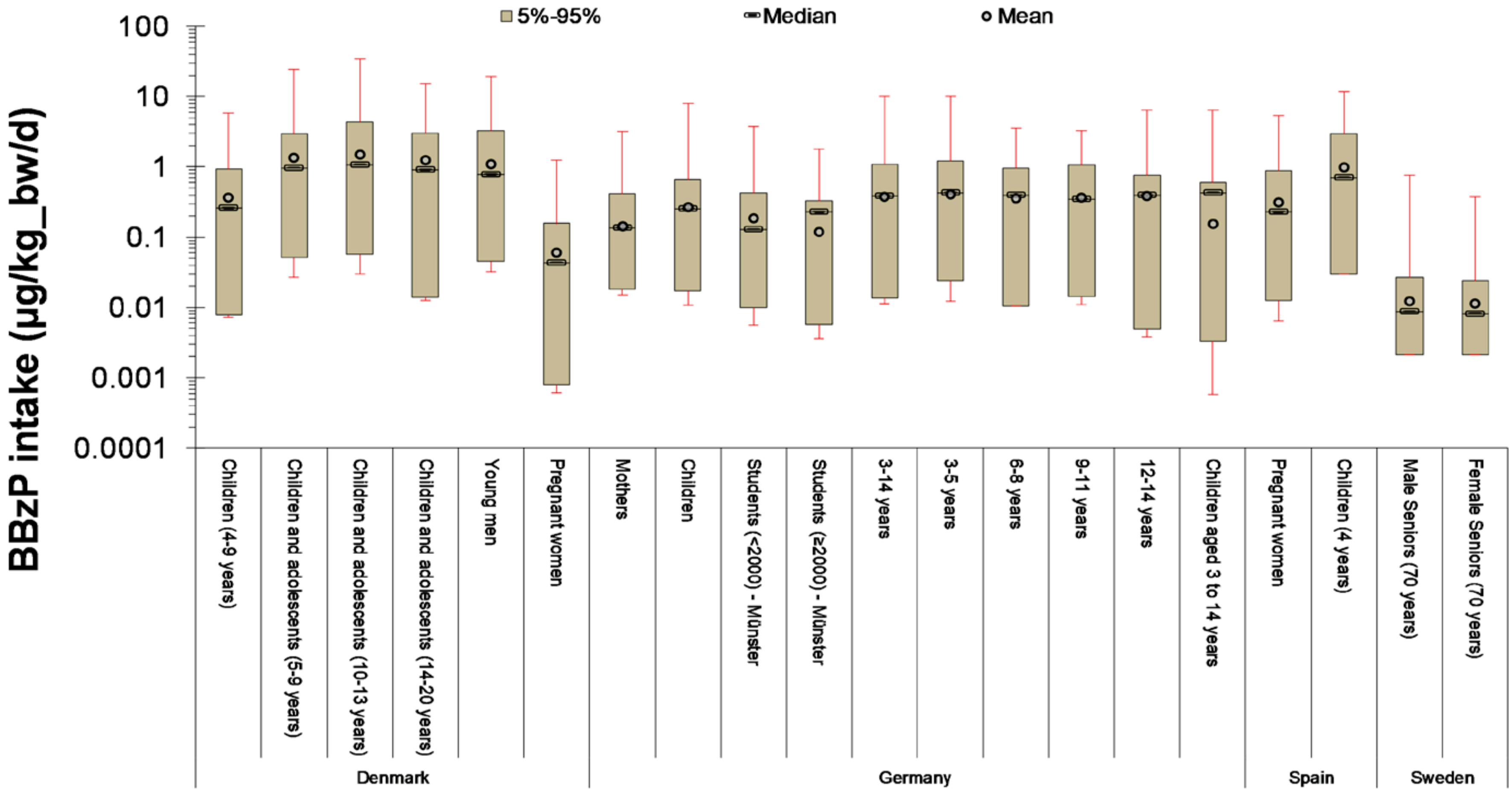

Figure 23. BBzP intake estimates based on HBM data

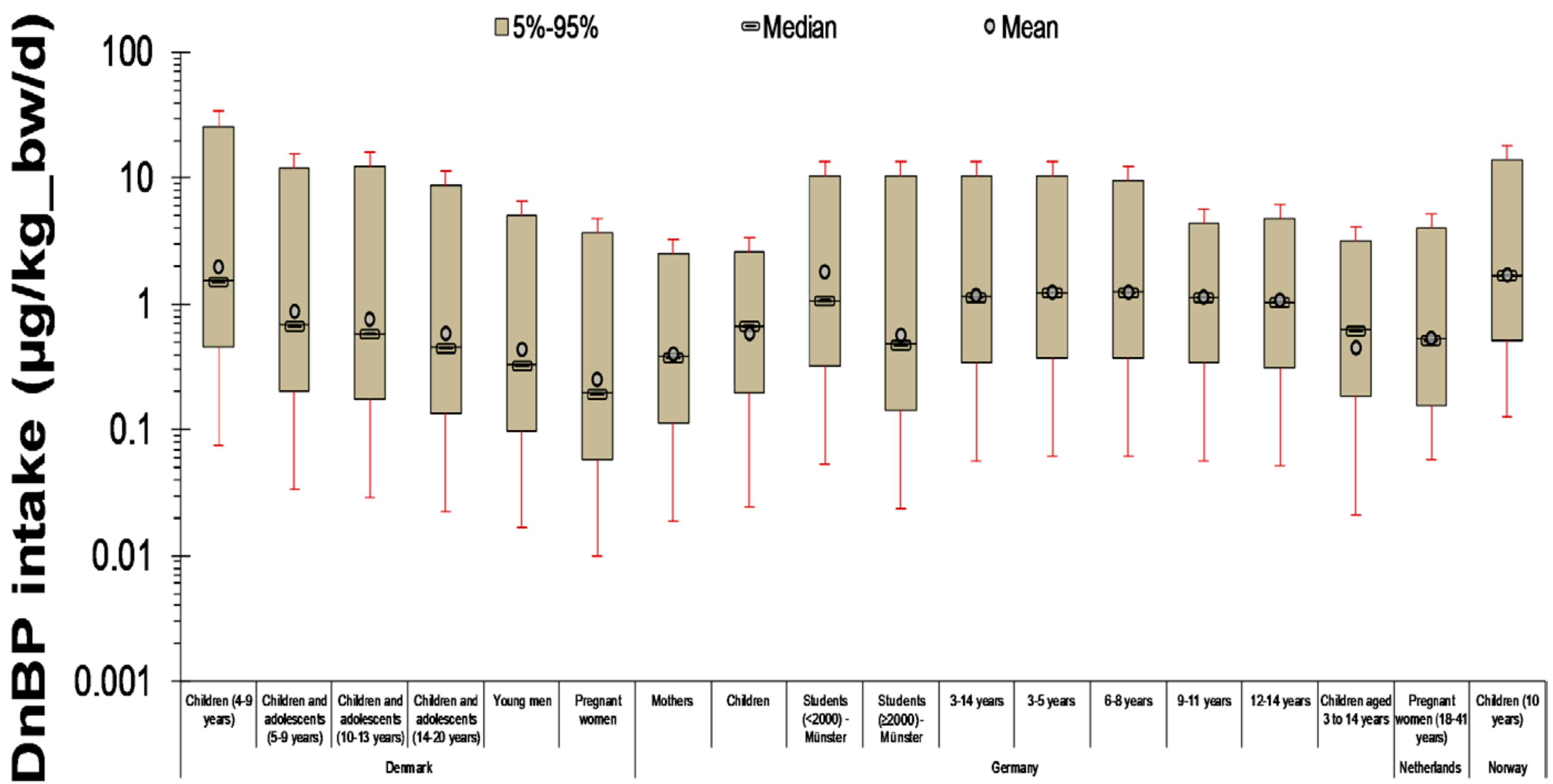

Figure 24. DnBP intake estimates based on HBM data

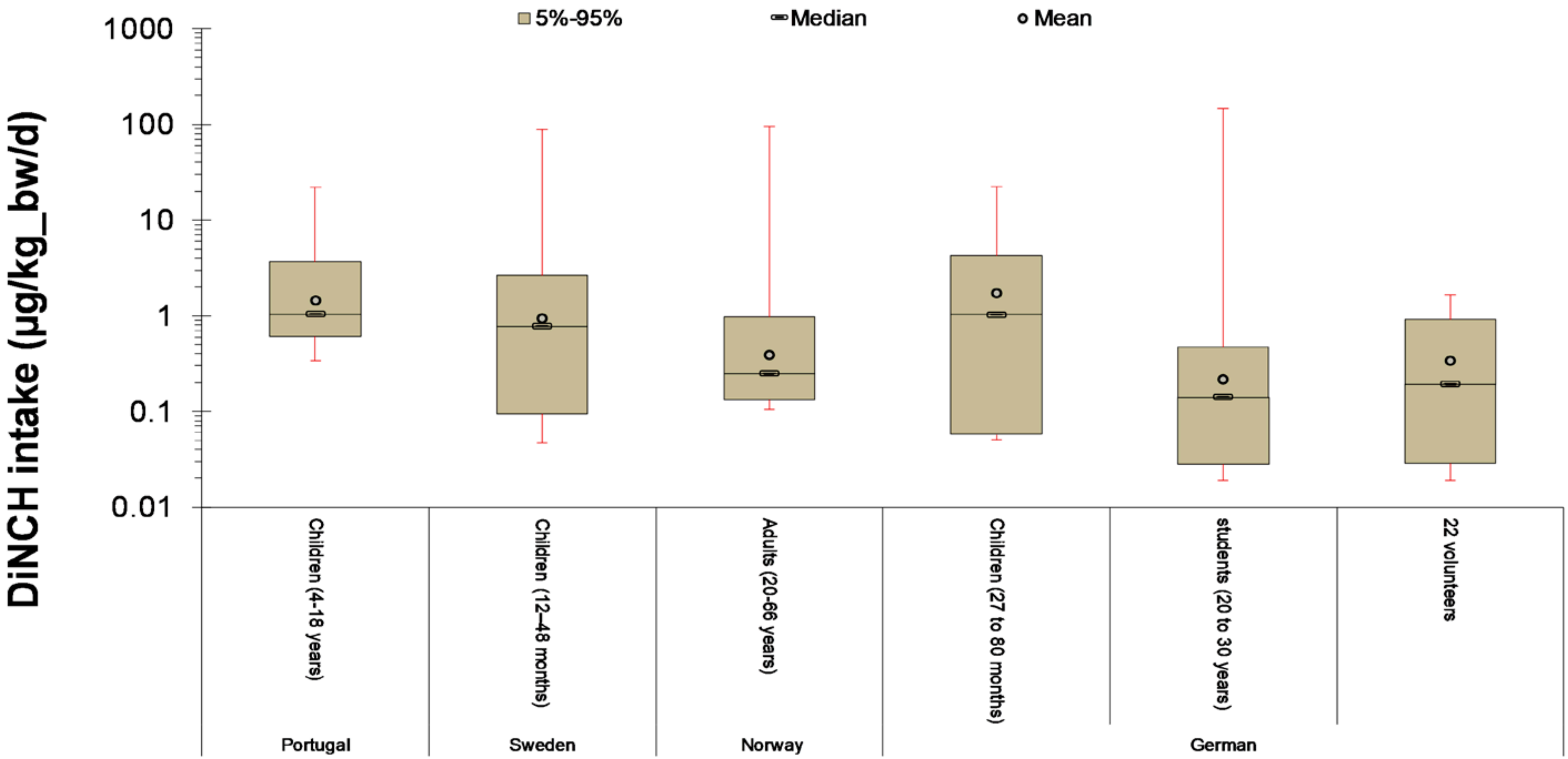

Figure 25. DiNCH intake estimates based on HBM data

THANK YOU FOR YOUR ATTENTION

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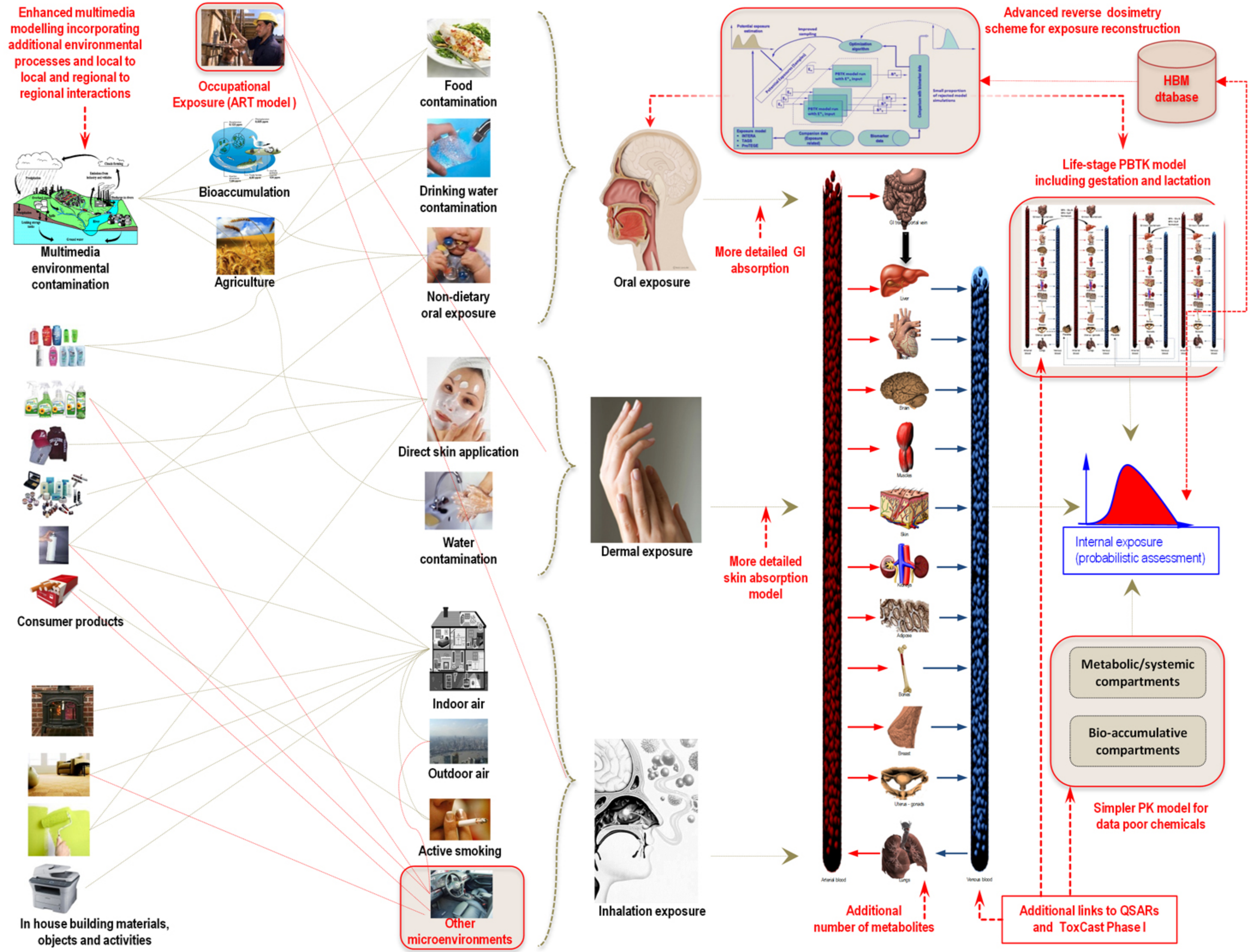
Enhanced multimedia modelling incorporating additional environmental processes and local to local and regional to regional interactions
Occupational Exposure (ART model)
Bioaccumulation
Agriculture
Multimedia environmental contamination
Food contamination
Drinking water contamination
Non-dietary oral exposure
Direct skin application
Water contamination
Consumer products
Indoor air
Outdoor air
Active smoking
Other microenvironments
In house building materials, objects and activities
Oral exposure
Dermal exposure
Inhalation exposure
More detailed GI absorption
More detailed skin absorption model
Advanced reverse dosimetry scheme for exposure reconstruction
HBM dtabase
Life-stage PBTK model including gestation and lactation
Internal exposure (probabilistic assessment)
Metabolic/systemic compartments
Bio-accumulative compartments
Simpler PK model for data poor chemicals
Additional number of metabolites
Additional links to QSARs and ToxCast Phase I

Integra

The program offers a number of generally applicable models ranging from **multimedia environmental model** to indoor air quality model and from exposure models for the **different exposure routes** (inhalation, oral and dermal) to a **generic PBPK model to evaluate internal doses** in target tissues and a **database containing several types of data** ranging from human physiological parameters to emission data from consumer products, from human biomonitoring (HBM) data to physical/chemical properties and from indoor and outdoor concentration levels to building characteristics. Data are stored along with their geographical information in order to allow users to build realistic exposure scenarios to represent typical exposure conditions for specific countries and/or cities in Europe. Together, the database and models provide the tools to assess exposure for a wide range of scenarios, whereby only additional information on exposure determinants.

Integra

An exposure assessment in INTEGRA is a tiered process, starting with the basic information on **physical/chemical properties** of chemicals, products and the exposed population. Subsequently, **suitable models are selected per exposure route**, according to the product usage scenario. INTEGRA offers a number of well described exposure and uptake models to estimate inhalation, dermal and oral exposure to compounds. Three different levels of exposure assessment are implemented in the platform, starting from the occupational one (i.e. Tier 0), to the comprehensive environmental one (i.e. Tier 1) to a reverse dosimetry to determine the external exposure consistent with HBM data input data. INETGRA offers a number of well described multimedia and exposure and uptake models to estimate inhalation, dermal and oral exposure to chemicals. Furthermore, the software also accepts stochastic distributions as input to a wide range of exposure parameters assessed via Monte Carlo methods (probabilistic exposure assessment).

Integra

The modelling environment comprises several components, as follows:

1. Multimedia environmental modelling module to estimate the concentration of chemicals in different environmental matrixes (i.e. air, water, soil and food) taking into consideration the exchange between the different environmental media.
2. Emissions-concentrations module, linking sources to indoor concentrations, taking into account the physicochemical processes in indoor settings: dispersion, ventilation, gasparticle-dust partitioning, etc.
3. Exposure module including several models for the dermal, inhalation and oral routes, taking into account time-microenvironment-activity patterns and inhalation rates based on activity, gender and body weight.
4. Internal dosimetry module, which computes aggregate exposure by absorption factors for each route, links temporal patterns to internal dose through a generic Physiology Based ToxicoKinetic (PBTK) model. It estimates the internal doses of contaminants and their metabolites at the target tissue.
5. An exposure reconstruction module to assess backward the exposure which is responsible for the human biomarker values measured.
6. Uncertainty and variability of exposure and risk determinants are assessed along the full chain assessment through hierarchical modelling using Markov Chain Monte Carlo.