The Exposome and Health Impact Assessment
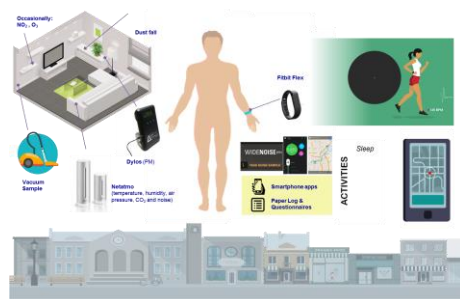
Prof. D.A. Sarigiannis, MSc, PhD

Environmental Engineering Laboratory
Department of Chemical Engineering
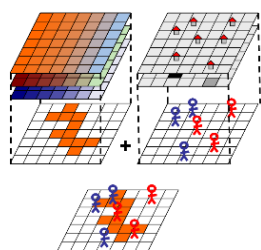Aristotle University of Thessaloniki
and
Chair of Environmental Health Engineering
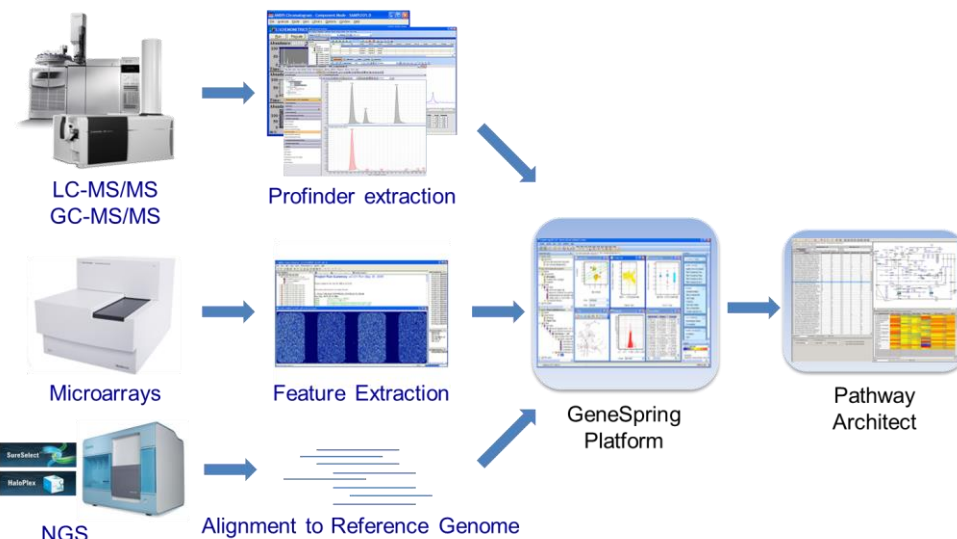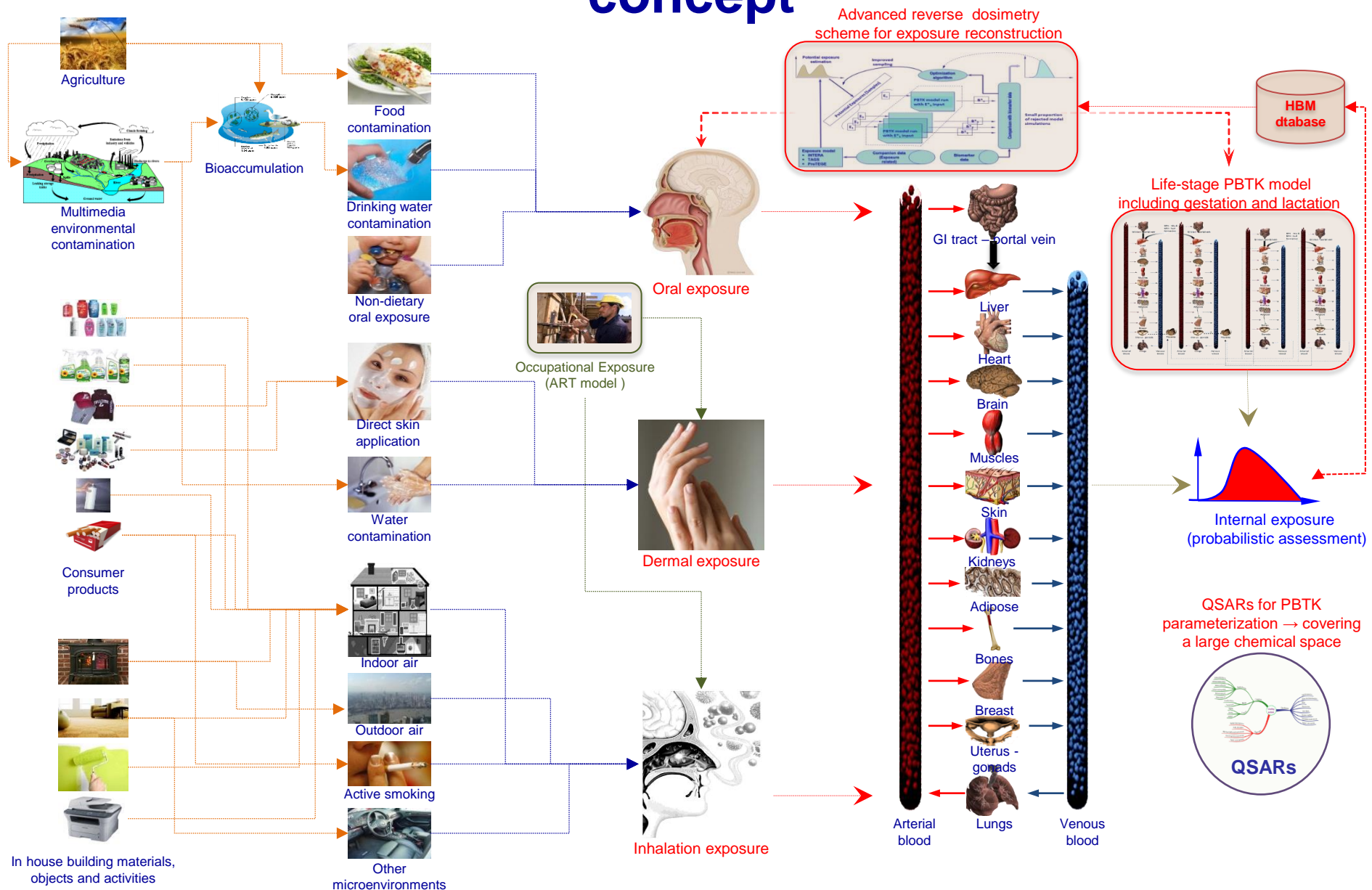Institute for Advanced Study - IUSS, Pavia, Italy

ENVElab — Environmental Engineering Laboratory

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External exposome

General external

Education, financial status, stress, urban–rural–industrialized environments, climate, etc

Specific external

Environmental chemicals, radiation, infectious agents, diet, lifestyle factors, occupation, etc

Internal exposome

Metabolism, sex, physical activity, age, endocrine factors, metal content, erhytrocites morphology, gut microflora, inflammation, lipid peroxidation, oxidative stress, etc

Multi - sensor techniques

Agent Based Modelling

LC-MS/MS
GC-MS/MS

Profinder extraction

Microarrays

Feature Extraction

NGS

Alignment to Reference Genome

GeneSpring Platform

Pathway Architect

Integrated exposure biology using multi-omics workflow

INTEGRA methodological concept

Agriculture

Multimedia environmental contamination

Bioaccumulation

Food contamination

Drinking water contamination

Non-dietary oral exposure

Consumer products

Direct skin application

Water contamination

Indoor air

Outdoor air

Active smoking

In house building materials, objects and activities

Other microenvironments

Oral exposure

Occupational Exposure (ART model)

Dermal exposure

Inhalation exposure

Advanced reverse dosimetry scheme for exposure reconstruction

HBM dtabase

Life-stage PBTK model including gestation and lactation

GI tract – portal vein

Liver

Heart

Brain

Muscles

Skin

Kidneys

Adipose

Bones

Breast

Uterus - gonads

Arterial blood

Lungs

Venous blood

Internal exposure (probabilistic assessment)

QSARs for PBTK parameterization → covering a large chemical space

QSARs

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Applying the INTEGRA methodology on bisphenol-A health risk
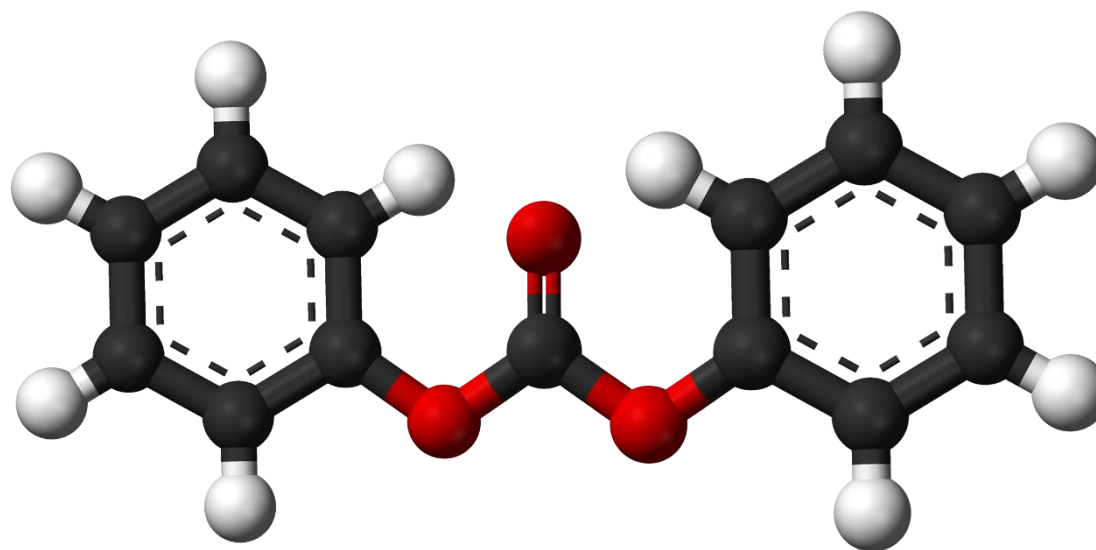
BPA – daily intake for different exposure scenarios
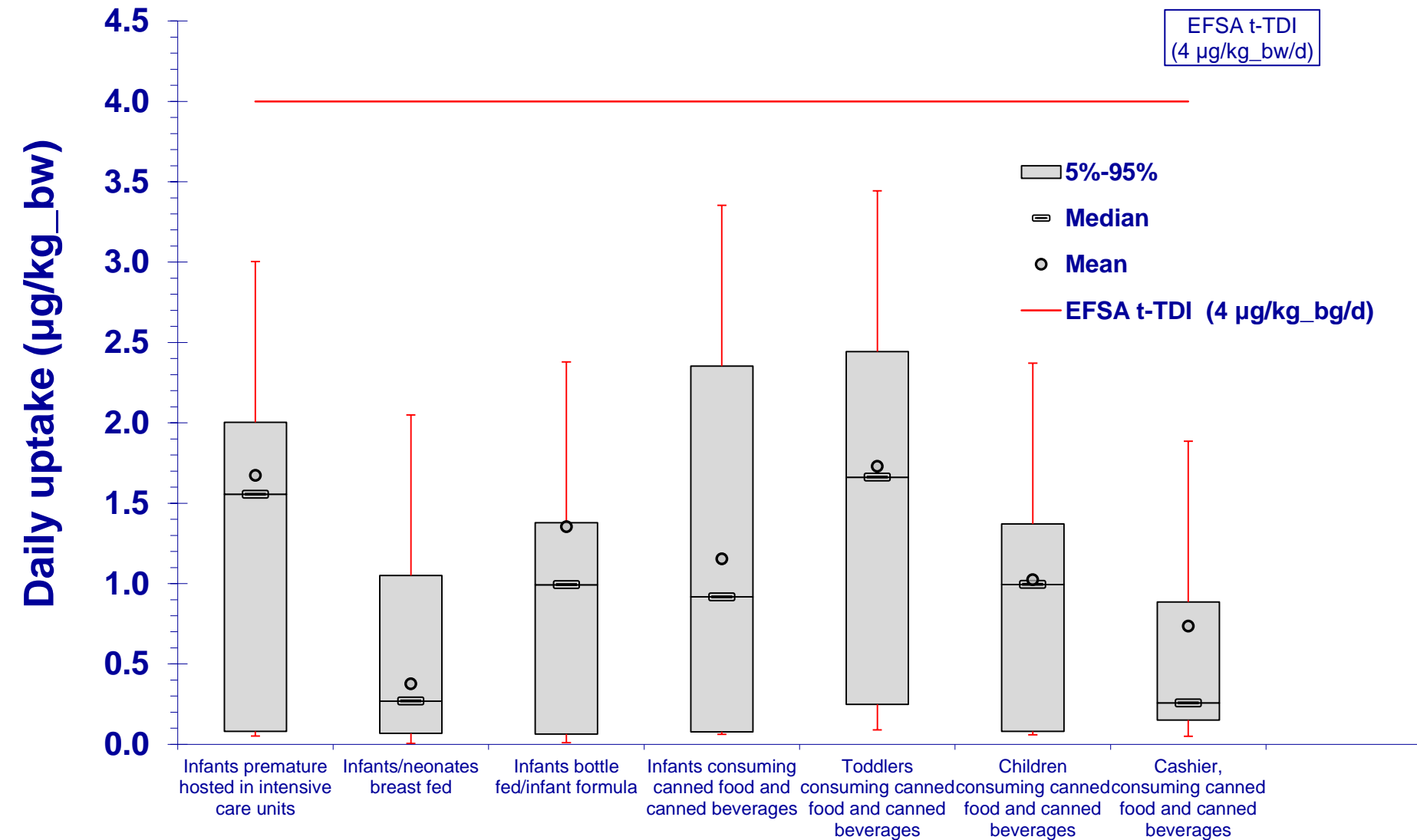
External to internal

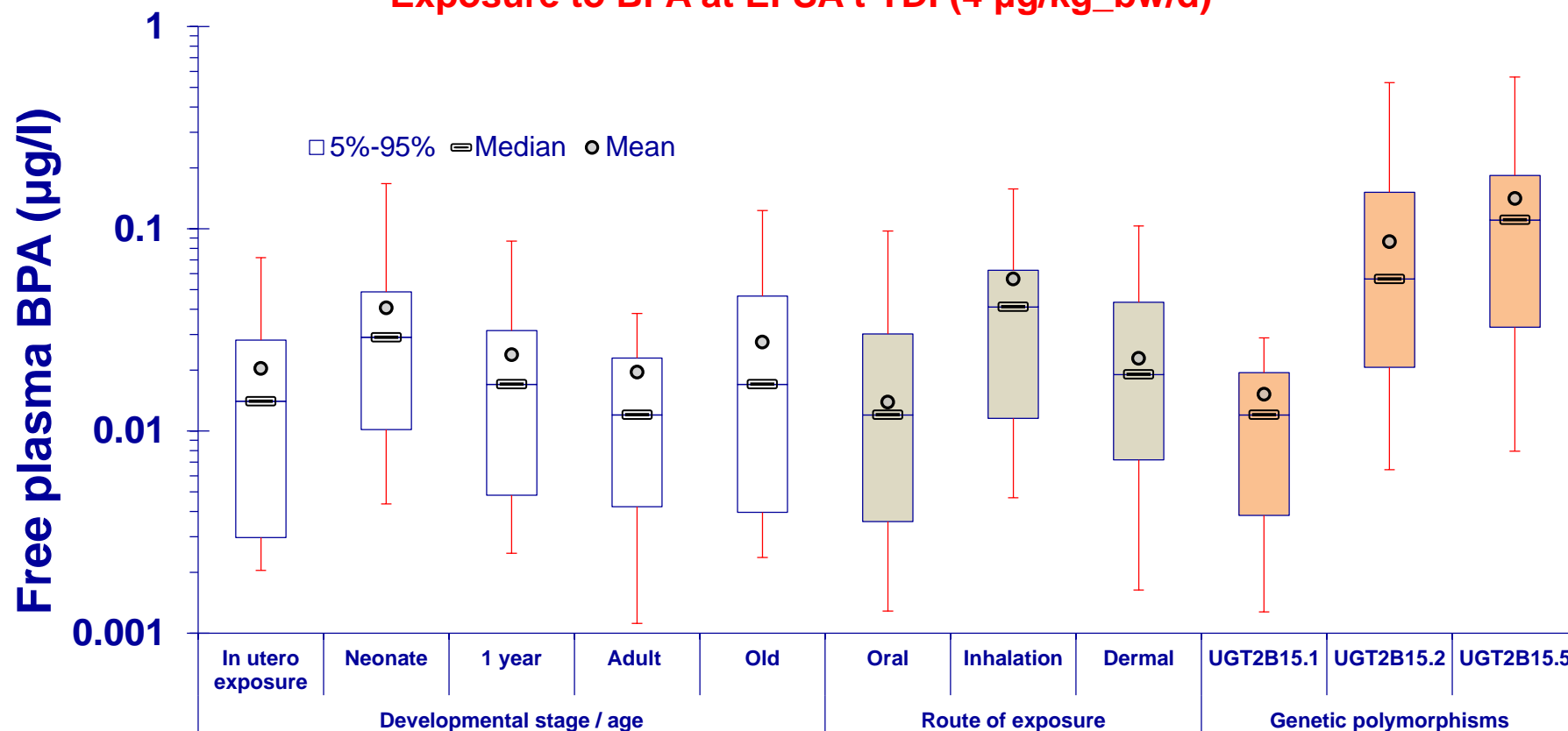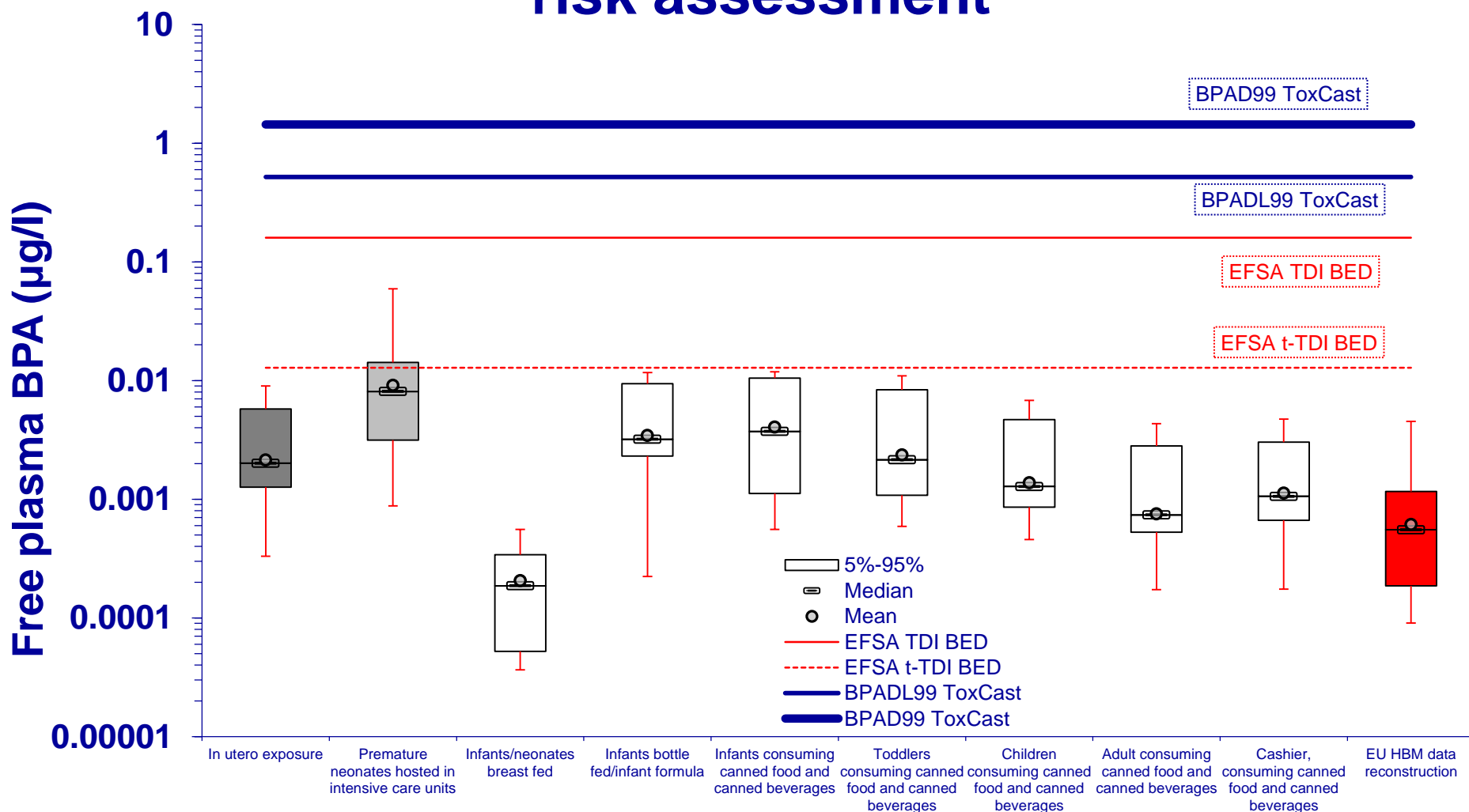## Exposure to BPA at EFSA t-TDI (4 µg/kg_bw/d)

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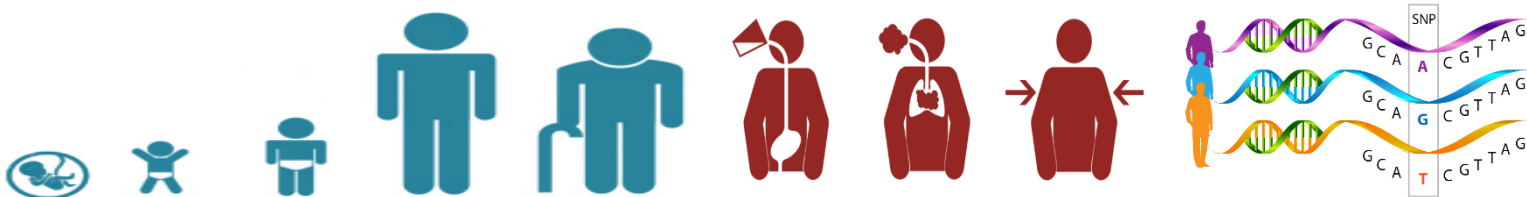
Internal dosimetry allows biologically plausible risk assessment

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Applying the INTEGRA methodology on PAHs
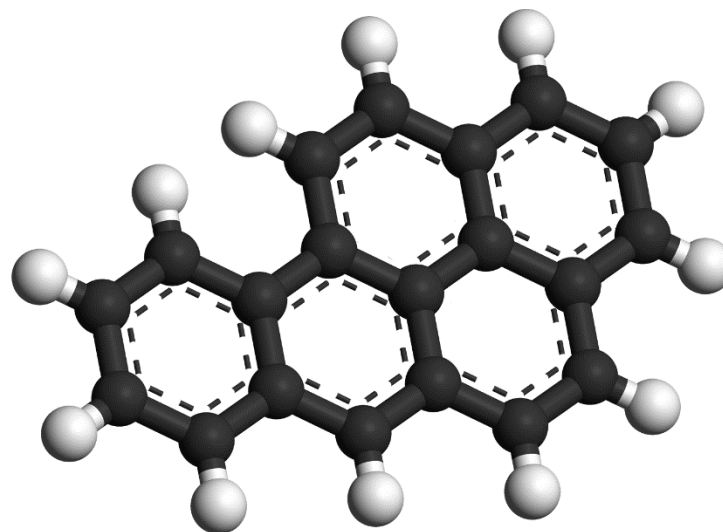
External and internal exposure to B[a]P

Exposure to airborne emissions
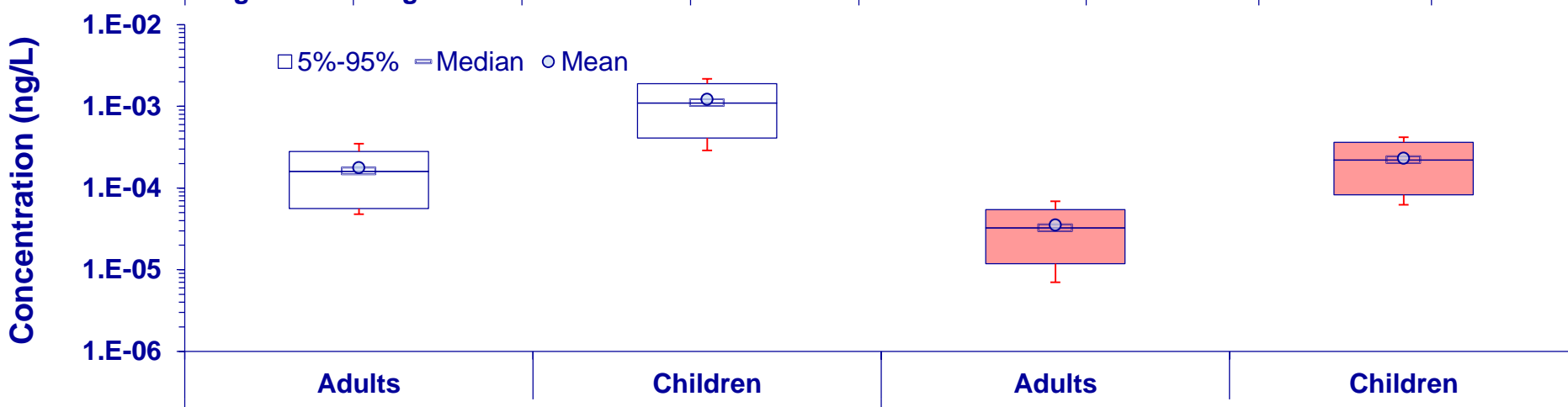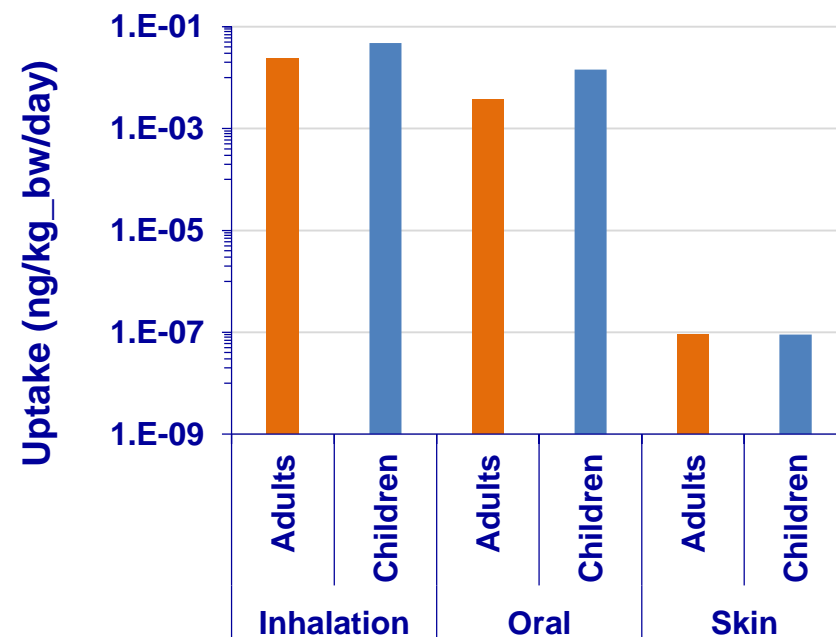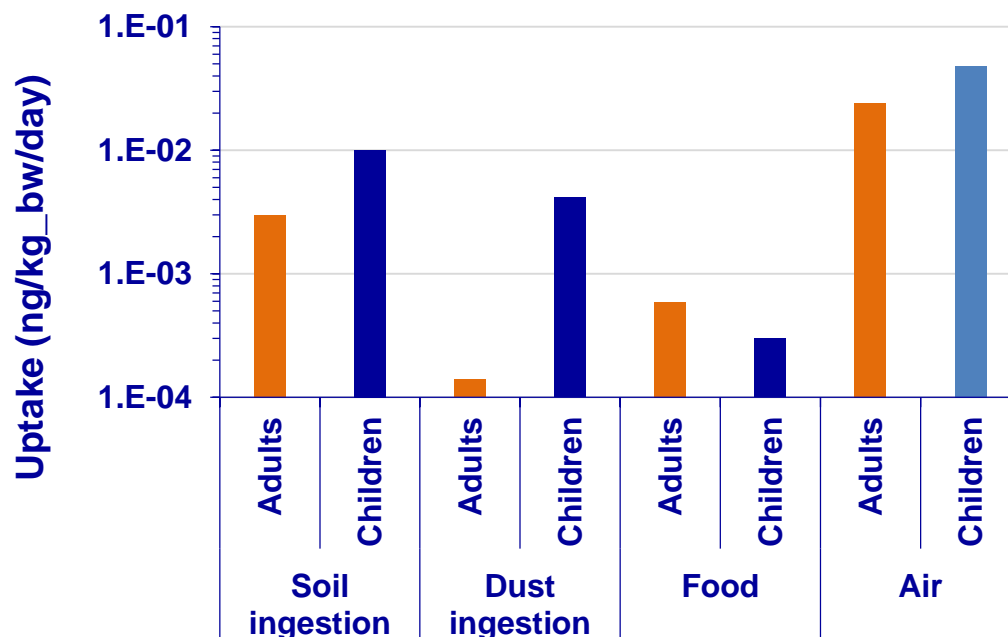
External and internal exposure to B[a]P

Exposure to smoked fish

Scenario of "smoked fish"

- Concentration in fish is estimated by the multimedia model at 10^{-7} μg/kg

- Smoked fish analysis / B[a]P levels in smoked fish range from 0.08 to 4.1 μg/kg (median of 1μg/kg and consumption of 110 grams of fish)

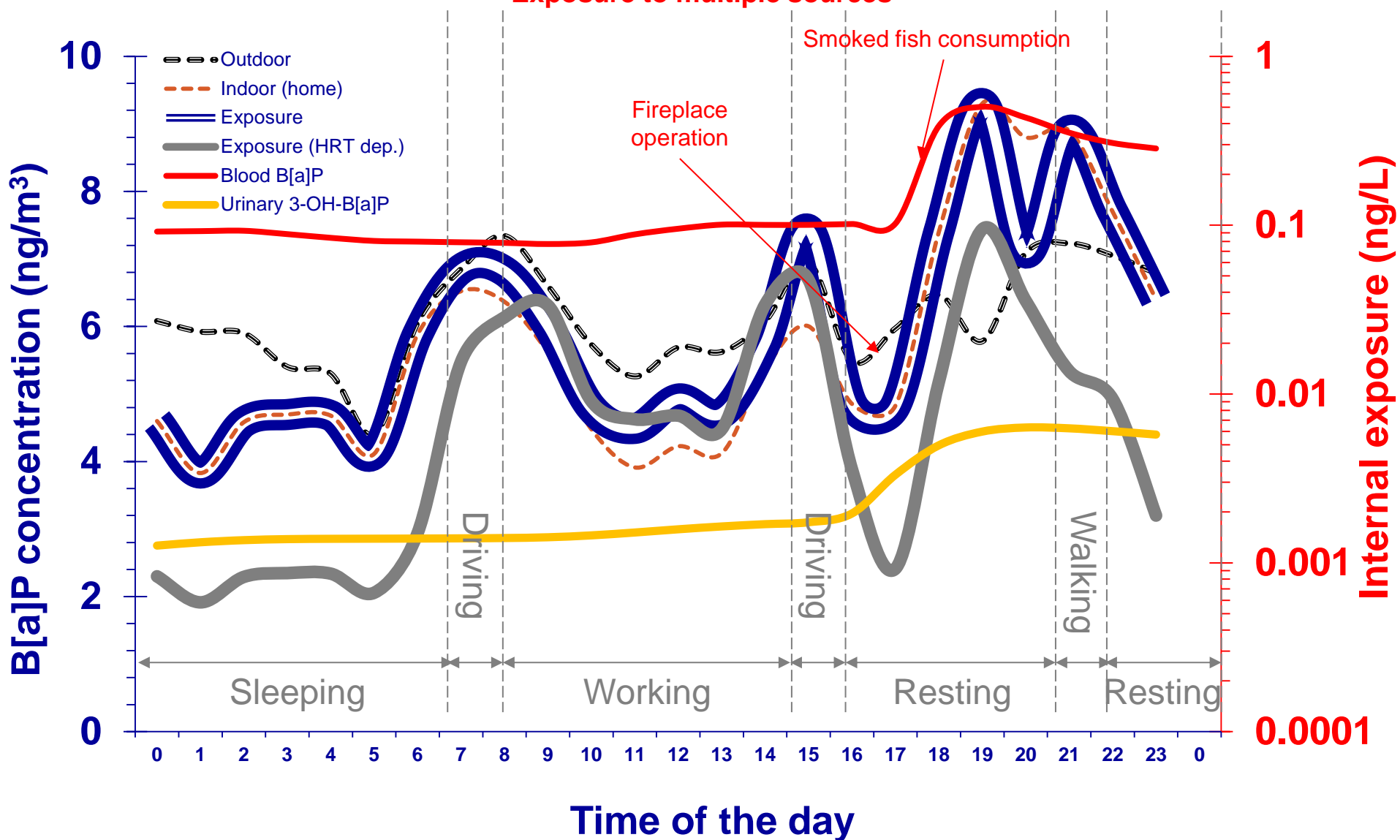- Intake due to smoked fish consumption dominates among other pathways
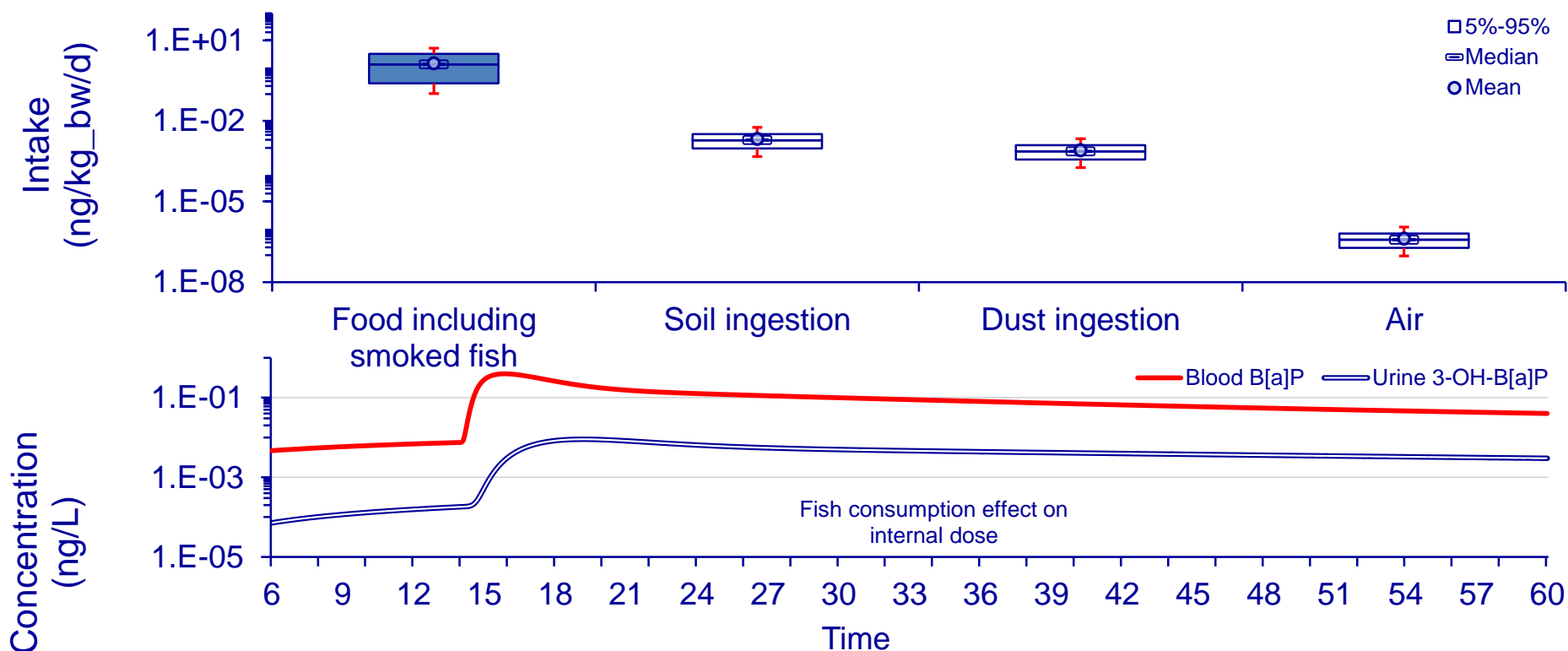
External and internal exposure to B[a]P

Exposure to multiple sources

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Limitations and Strengths

- Need for large parameter space for proper parameterization

- Demanding data for validation

- Need for training for proper use

- Integrated exposure and health impact assessment

- Refined exposure assessment that allows consideration of complex co-exposure scenarios

- Explicit treatment of variability and uncertainty

- Socio-economic status, age, gender clusters

- Exposome-based health impact assessment

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Conclusions

- INTEGRA has been selected as the external-internal comprehensive exposure assessment modelling tool from CEFIC-LRI and can be found at: http://cefic-lri.org/lri_toolbox/integra/

- INTEGRA allows the successful assimilation of multiple type of environmental, exposure and HBM data, giving them both scientific and regulatory context – exposure reconstruction holds a key role in this aspect

- The generalization of INTEGRA PBTK model (facilitated by advanced QSARs for toxicokinetics parameterization) ensures the use of a harmonized model covering a large chemical space

- INTEGRA results in reduced uncertainties for exposure assessment, allowing precise assessment of the contribution of different sources, leading thus to targeted interventions
    - *This further facilitates targeted (precise) prevention, one of the exposome key objectives*

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Conclusions

- The ability of INTEGRA to translate biomonitoring data into actual exposure data for risk assessment use has been widely recognized:

  – INTEGRA will be the tool used by ECHA for the evaluation of PAHs biomonitored data collected in HBM4EU

  – INTEGRA will be the tool for HBM data assimilation and exposure reconstruction used in HBM4EU regarding hundreds of chemicals (POPs, industrial chemicals currently in use and emerging substances)

  – CONCAWE is already testing multiple exposure PAHs scenarios with INTEGRA

  – INTEGRA will be used by EFSA for the assessment of BPA exposure

Thank you for your kind attention

www.enve-lab.eu

A connectivity perspective to environmental health