# Biomarkers for Exposure to Polycyclic Aromatic Hydrocarbons

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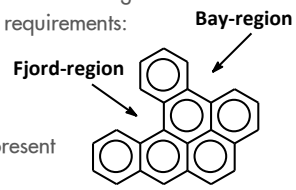
## Overview presentation

- Why Polycyclic Aromatic Hydrocarbons (PAH) ?
- Why Human Biomonitoring (HBM) ?
- Selection Criteria for Biomarkers
  - Complex mixtures
  - Types of biomarkers
  - What makes a good biomarker ?
- Biomarkers for PAH
  - Biomarkers of Exposure
  - Biomarkers of Effective Dose
- Use of HBM in Risk Assessment
- Conclusions

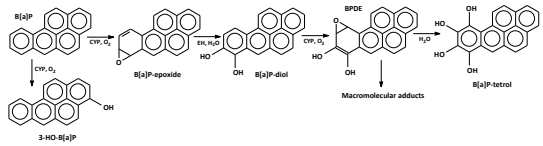
## Why PAH ?

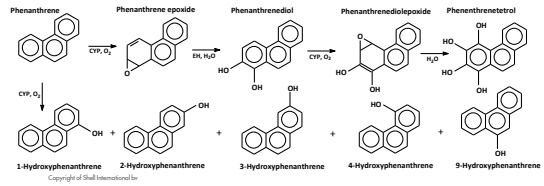
- PAH are *ubiquitous* environmental pollutants
- PAH are formed during combustion of organic matter (including fuels, tobacco, BBQ etc.)
- PAH are naturally present in coal, crude oil etc.
- Some, not all, PAH are carcinogenic
- Specific structural requirements:
  - 4-7 rings **and**
  - "Bay-region" **or**
  - "Fjord-region"
- PAH are always present as mixtures



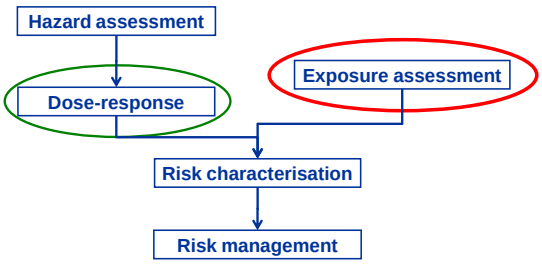
## PAH metabolism leading to genotoxicity or not






## Paradigm of Health Risk Assessment




Adapted from EC, 2003



## Why HBM ?

- Human Biomonitoring (HBM) is essentially an *exposure measurement* methodology, but may be extended beyond that in some circumstances
- It has great advantages over other exposure measurement methodologies as it integrates
  - all routes of exposure (oral, dermal, inhalation)
  - intra-individual differences (e.g. breathing volume, different working practices)
  - inter-individual differences (e.g. body weight, toxicokinetics)
- It may allow measurement close to target organs

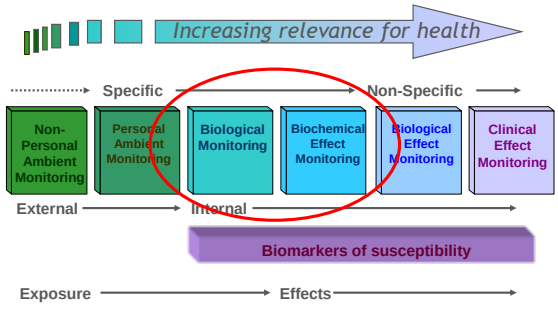
 

## Types of human biomonitoring

- **Biological monitoring**
  - biomarkers of ***exposure***, internal dose, or body burden (e.g.1-HOPyr, PbB, S-PMA)
- **Biochemical effect monitoring**
  - biomarkers of ***effective dose*** (e.g. protein-, DNA-adducts)
- **Biological effect monitoring**
  - biomarkers of ***effect*** (e.g. ChE, SCE, µAlb, *hprt*)
- **Clinical effect monitoring**
  - biomarkers of ***disease*** (e.g. Alb, AST, PSA)
- **Genotyping and Phenotyping**
  - biomarkers of ***susceptibility*** (e.g. GSTs, P450s)



## Monitoring Methods






*Ref. Boogaard, 2009*

## HBM selection criteria (for complex mixtures)

- Basically: identical to other exposure markers (air)
- Representative for the complex mixture
- Reliable, robust analytical methods available
  - Preanalytical (e.g. contamination, stability
  - Analytical (e.g. sensitivity, specificity, reproducibility, accuracy, precision)
- Ideally: toxicokinetic data available
- Related to the (most important) health effect
  - Biomarkers of Exposure
  - Biomarkers of Effective Dose

## Use of HBM in Risk Assessment

| Purpose of the study | Required knowledge | | | |
|---|---|---|---|---|
| | Analytical integrity | Toxico-kinetics | Health effects | Weight-of-evidence |
| Exposure trends | √ | | | |
| Characterisation of exposure | √ | √ | | |
| Investigation of health impact | √ | √ | √ | |
| Risk assessment /standard setting | √ | √ | √ | √ |

*Ref: Boogaard & Money, 2008; Boogaard, 2009*

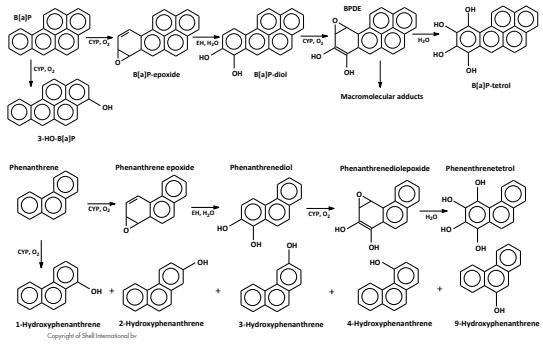
 

## Biomarkers of exposure for PAH (1)

- **3-Hydroxybenzo[a]pyrene (3HO-B[a]P):**
  - Analytical methodology highly sophisticated
  - No analytical standards available yet
  - No quality control available yet
  - Highly relevant – linked to carcinogenic PAH
  - Metabolite in detoxifying route
  - Occupational & environmental settings
- **Use of 3HO-B[a]P in Risk Assessment:**
  - Demonstrate exposure – promising but currently not suited for routine measurements

## PAH metabolism leading to genotoxicity or not

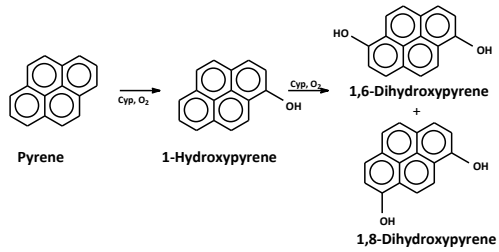


## Biomarkers of exposure for PAH (2)

- Hydroxyphenanthrenes (1, 2, 3, 4, and 9):
  - Analytical methodology sophisticated
  - No analytical standards/QC available yet
  - Not carcinogenic (no health effect…)
  - Theoretically interesting: simplest PAH with a bay-region: reflects essential metabolism
  - Allows differentiation between smokers and non-smokers
- Use of HO-Phen's in Risk Assessment:
  - Demonstrate exposure – promising but currently not suited for routine measurements




## Metabolism of pyrene





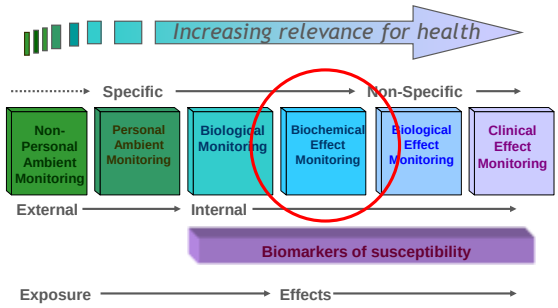

## Biomarkers of exposure for PAH (3)

- 1-Hydroxypyrene (HO-Pyr):
  - Analytical methodology available
  - Analytical standards & QC available
  - Not carcinogenic (no health effect…)
  - Highly symmetric → thermodynamic stability
  - Most abundant PAH & urinary PAH-metabolite
- Use of HO-Pyr in Risk Assessment:
  - Many studies available, both in occupational and environmental settings → reference values for (1) *specific* exposure scenario's, based on effects or links to other PAH and (2) background

→ At this moment the HBM parameter of choice




## Biochemical effect monitoring






## Biomarkers of effective dose for PAH (1)

- Protein adducts
  - Usually albumin or haemoglobin adducts (high abundancy → sensitive)
  - Longer half lives than urinary metabolites (days to months)
  - Invasive since blood is needed
  - No reference material available
  - Little toxicokinetic data available
  - No link with health effects
- Use in Risk Assessment
  - Demonstrate exposure (trends ?)




## Biomarkers of effective dose for PAH (2)

- DNA adducts
  - $^{32}$P-postlabeling: highly sensitive, low specificity
  - Mass spectroscopy: sensitive and specific, but very labour intensive and sophisticated
  - General lack of reference material
  - Invasiveness dependent on source of material
  - Little toxicokinetic data available
  - No link with health effects (!)
- Use in Risk Assessment
  - Demonstrate exposure

→ Biomarkers of effective dose markers not yet suitable for routine monitoring

## Use of HBM in Risk Assessment

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| Exposure trends | √ | | | |
| Characterisation of exposure | √ | √ | | |
| Investigation of health impact | √ | √ | √ | |
| Risk assessment /standard setting | √ | √ | √ | √ |

*Ref: Boogaard & Money, 2008; Boogaard, 2009*




## Use of HBM in Risk Assessment of PAH

- Many parameters have been investigated
- Mainly urinary biomarkers of exposure and a limited number of biomarkers of effective dose
- For most parameters there is a general lack of:
  - Analytical integrity (standards, QC and QA)
  - Toxicokinetic data
  - Links to health effects (dose-response)
- Notable exception: urinary HO-Pyr
- Although not carcinogenic itself, it can be linked to carcinogenic PAH for specific exposure scenarios
- HO-Pyr remains the method of choice




## Thank you for your attention

Questions ?