

# Health Surveillance in Workers

## Role of Human Biological Monitoring

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# Analysis of biomarkers: for what purpose?

1. Detection of aggregated exposure
2. Early indicator of adaptive response
3. Response to worker's concerns
4. Worker's performance indicator
5. Testing good practice
6. Evidence in court



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# Detection of aggregated exposure

*The total of all contributions to exposure of a single substance from all sources*

- Exposures at work as well as off-work exposures
- Products used at work well as consumer products and dietary contributions
- Reflecting recent exposure as well as historic exposure
- Derived from different routes of uptake (inhalation, dermal, oral)

*Biomonitoring as 'safety net'*

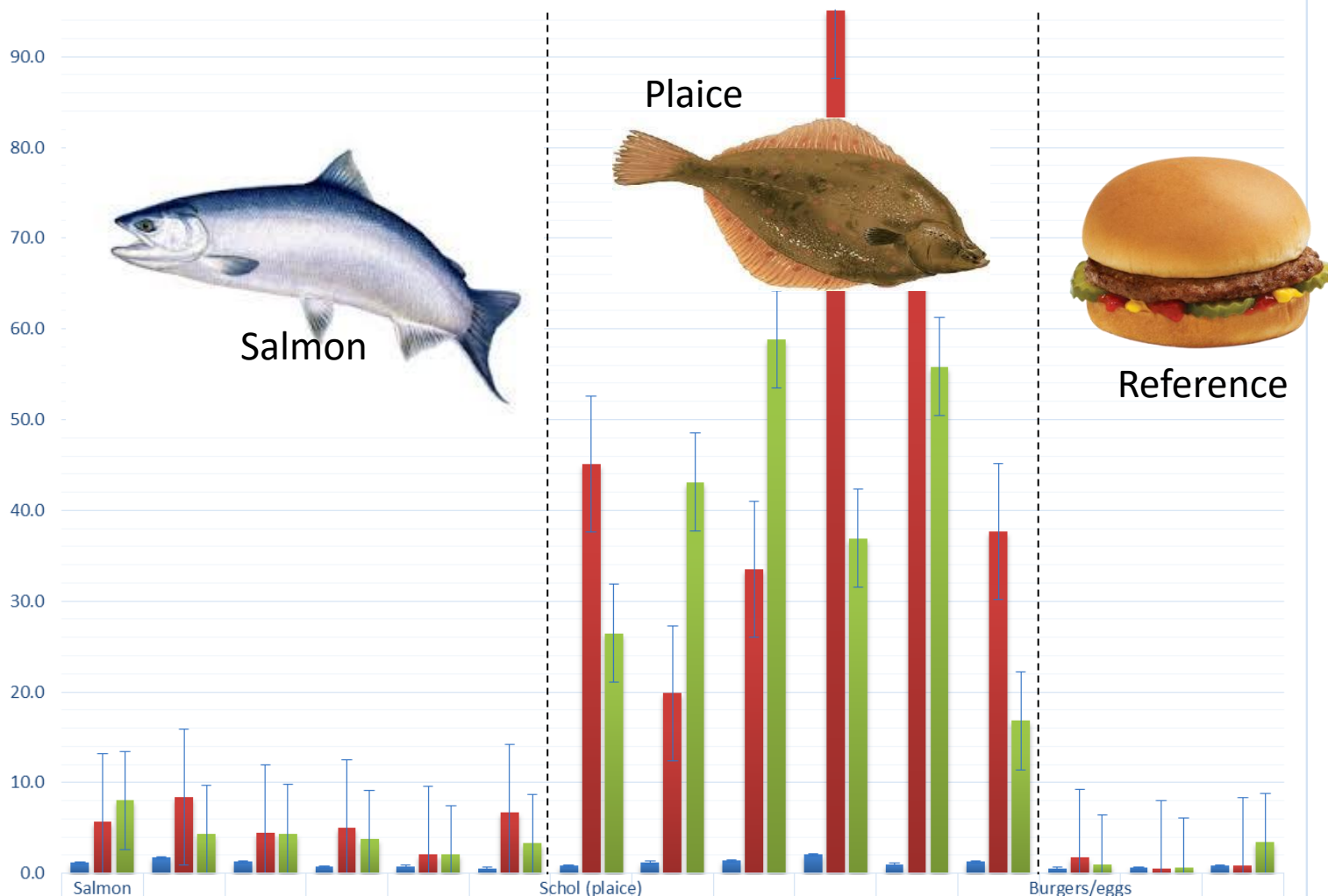
Result is often positive for ubiquitous substances

Very specific strategies are required to disentangle

worker's exposures from 'background'

# Aggregate exposures: contribution of arsenic from diet

µg As/mMol creatinine



Before exposure (As/Creatinine)	0,001	0,002	0,001	0,001	0,001	0,001	0,001	0,001	0,001	0,002	0,001	0,001	0,001	0,001	0,001
After exposure (18h)	0,006	0,008	0,004	0,005	0,002	0,007	0,045	0,020	0,034	0,095	0,072	0,038	0,002	0,001	0,001
After exposure (midnight)	0,008	0,004	0,004	0,004	0,002	0,003	0,026	0,043	0,059	0,037	0,056	0,017	0,001	0,001	0,003

# Early indicator of adaptive response

According to the *meet-in-the-middle principle* (Paolo Vineis, Imperial College)

- Biomarker should reflect an 'early' non-adverse effect
- Biomarker should be a confirmed and causal risk factor of disease
- Derived from different routes of uptake (inhalation, dermal, oral)

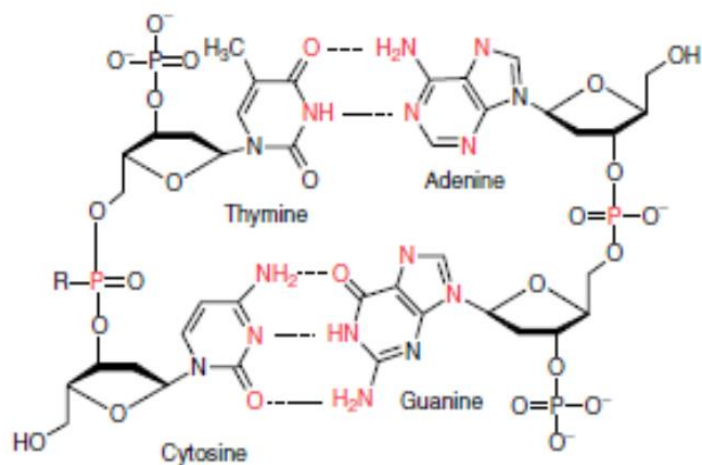
*Like a prognostic clinical biomarker?*

Value of DNA adducts and repair products?

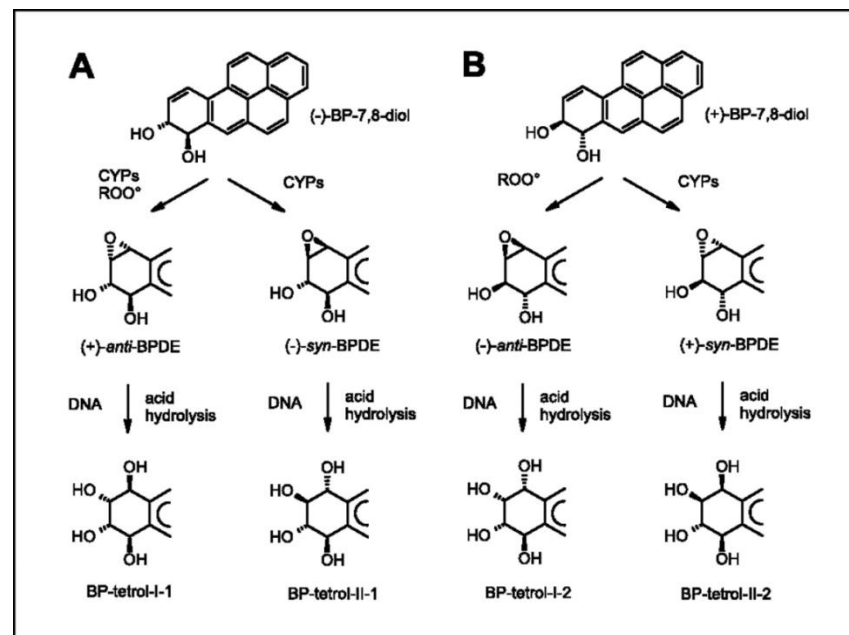
Value of urine metabolites vs. protein adducts?

How should these outcomes be presented to the worker?

# DNA-adduct and repair products



Benzo[a]pyrene adducts



Benzo[a]pyrene repair products

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# Response to worker's concerns

Treating the individual outcome as a reflection of uptake to satisfy:

- Uncertainty concerning complex procedures or involvement in spill
- May satisfy questions related to personal behaviour/hygiene issues
- What is the *real* worker's incentive? (Fear?)

*Biomonitoring to satisfy concerns?*

A low value or non-detect may be reassuring

A high value may lead to questions difficult to answer.

What value to be used as biological guidance value?

What is the health relevance?

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# Human Biomonitoring for emergency responders *with potential contact to hazardous substances*

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In 2015, altogether 241 analyses were carried out in 70 samples of 61 **firefighters collected after ten emergency operations**. In most cases, specific biomarkers were analyzed, or 1-hydroxypyrene (1-OHP) as an exposure marker for pyrolysis products. Exposure was very low in general while **excursions of the internal action values** were observed only in a few cases. The **standardized program** tackles critical aspects of HBM for emergency responders after chemical incidents. It **enables the optimization of procedures** and contributes to the preparedness in case of large incidents [...]. Furthermore, HBM provides information on the **efficacy of the protection equipment** of the emergency responders, and allows for a differentiation between exposed and non-exposed persons.





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# Worker's performance indicator

Commissioned by the employer e.g.

- Alcohol and drugs testing in demanding tasks
- As part of an ALARA strategy
- Keep a registry of exposure to CMR substance:



*Biomonitoring as in a 'doping test'*

What is worker's participation arrangement?

Are individual results kept confidential from employer?

How about ethics issues e.g. voluntary participation?

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# Personal hygiene in a lead transformer factory



*Invite the management to participate*

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# Testing of good practices

Field test to evaluate the efficacy of an intervention

- Gloves to reduce skin absorption (reduce or enhance exposure)
- Respiratory protection (technical specs vs. field performance)
- Personal hygiene issues

*Biomonitoring as tool for evaluation*

How does a protective technology perform in practice?

Is the extra effort of wearing PPE worthwhile?

# Skin protection in dermatology nurses

Comparison of excretion of 1-hydroxypyrene (1-OHP, total and increase from baseline). Based on collection of urine during 24 h after application of CTO.



Subgroup	1-Hydroxypyrene in urine (1-OHP)	2004		2007	
		Median	Range	Median	Range
Paired observations (N = 6)	Total (nmol)	1.6	0.84-5.0	0.69*	0.45-3.4
	Increase (μmol/mol creat)	0.05	-0.01-0.18	0.03	0.01-0.17
Unpaired observations (N = 10 –12)	Total (nmol)	1.5	0.74-5.0	0.64*	0.15-2.8
	Increase (μmol/mol creat)	0.04	-0.09-0.18	0.02	-0.01-0.05

\*  $p < 0.05$  Scheepers et al. *Scand J Work Environ Health* 2009; **35**:212-221

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# Evidence in court

The forensic toxicologist uses biomarker as evidence

- Employer would like to demonstrate 'low exposures' in retrospect
- (Ex)-worker with diagnosed disease would like to demonstrate (excess?) exposure

*Biomonitoring as an 'insurance' for the employer?*

What is the value of biomarkers in jurisdiction?

What is the weight of evidence of a positive finding in a medical file or (...) in an employer's register?

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# Collection of biological tissues following a chemical incident

## New blood tests for train disaster locals

Mon 03/06/2013 - 13:41 MB

Between 1,200 and 1,500 people that live near to the site of last month's Wetteren (East Flanders) rail disaster are to be given **new blood and urine tests**. According to the **judicial authorities** this is necessary for damages claims to be made. The original samples that were taken have a limited storage life. The new samples will be treated to allow them to be kept for longer.

**FLANDERS**  
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# Statements

1. Do employers and workers have the same interest? If not, how can they be aligned or combined?
2. Biomarkers reflecting uptake and bioactivation are more valuable than biomarkers reflecting detoxification and elimination
3. Biomarkers from the 'omics' era are the 'holy grail' in preventive medicine.



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*Mission: stimulate good use of human biological monitoring, explore new areas of application and share knowledge and experience.*

*What you can find*

On this website you will find information for professional users of HBM. We also hope to inform other potentially new users.

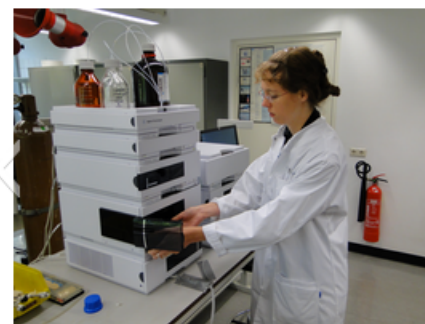
*Who we are*

This website is hosted by individuals with a track record in HBM in academic research.

# Downloads

- [Guideline for biological monitoring after a chemical incident](#) (in Dutch)
- [HBM Biomarkers list](#) (pdf)
- Master class Human Biological Monitoring:
  - Part 1
  - Part 2
  - Part 3
- [Biological Monitoring in Public Health](#) (pdf)
- [Biomarkers of Exposure to Carcinogens](#) (pdf)
- Biomonitoring application datasheets (BADs) pdf files:
  - [Acrolein](#)
  - [Acrylonitrile](#)
  - [Arsenic](#)
  - [Benzene](#)
  - [Cadmium](#)
  - [Chromium](#)
  - [Cyanides](#)
  - [Dioxin \(TCDD\)](#)
  - [Ethylene oxide](#)
  - [Fluorides](#)
  - [Hydrogen sulfilde](#)
  - [Methyl bromide](#)
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  - [Toluene](#)
  - [Xylenes](#)

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# Biomonitoring application datasheets (BADS)

- Acrolein
- Acrylonitrile
- Arsenic
- Benzene
- Cadmium
- Chromium
- Cyanides
- Dioxin (TCDD)
- Ethylene oxide
- Fluorides
- Hydrogen sulfide
- Methyl bromide
- Polycyclic Aromatic Hydrocarbons (PAH)
- Styrene
- Toluene
- Xylenes



## HBM Biological Application Data Sheet

**ACROLEIN**Update: May 2010**Identity**

Name (parent)	Acrolein
UN number	1092
CAS number	107-02-8
Intervention value (AGW in mg/m <sup>3</sup> )	1
Structure	C <sub>3</sub> H <sub>4</sub> O

**Occurrence**

Chemical state (at 20°C)	Liquid
Physical appearances	Colorless or yellowish liquid, with a acrid, pungent odor.
Industrial products	Acrolein is used in the preparation of polyester resin, polyurethane, propylene glycol, acrylic acid, acrylonitrile, and glycerol. Acrolein is formed during the incomplete combustion of organic materials, tobacco smoke and the burning of fat containing foods.

**Physicochemical properties**

Molecular weight	56.1
Vapor pressure (mbar at 20°C)	293

## Biological monitoring

Biomarkers	3-hydroxypropylmercapturic acid (3-HPMA) in urine
Molecular weight	221.3
Involved enzymatic metabolism	Glutathione- S-transferase
Biological material	Urine
Type of sample	Spot urine, 24-hour urine
Sampling strategy	< 24 h
Excretion pattern	Half-life of acrolein in urine 20 minutes [8]
Materials	Not reported
Transportation	Not reported
Storage	-20°C [9]
Stability	Not reported
Measurement principle	LC-APCI-MS/MS-SRM [10] HPLC-MS/MS [9, 11, 12] LC-MS-MS [13]
Aliquot for 1 analysis	1 mL [11] 0.2 mL [10] 2 mL [9]
Pretreatment	Solid phase extraction
Limit of quantification	LOD: 5 µg / L (HPLC-MS/MS) [9] LOD: 6 µg/ L (HPLC-MS/MS) [12] LOQ: 50 µg/ L urine (HPLC-MS/MS) [11] LLOQ (lower limit of quantification): 35 µg / L (LC-MS/MS) [13] Estimated LOQ: 0.9 µg/L (LC-APCI-MS/MS-SRM) [10]
Recommended adjustments	Creatinine
Preferred units for expression of	nmol / g of creatinine

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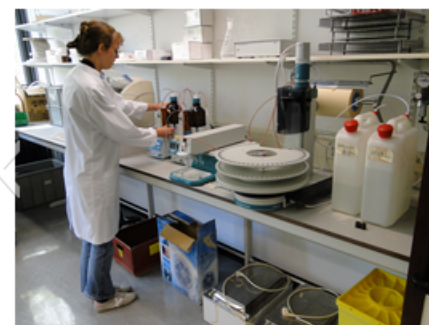
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# 215 biomarkers for 160 substances

HBM List of biomarker (update December 2013).pdf - Adobe Acrobat Reader DC

Bestand Bewerken Beeld Venster Help

Start Gereedschappen Document 2 / 11



## LIST OF BIOMARKERS FOR HUMAN BIOMONITORING STUDIES FOLLOWING CHEMICAL INCIDENTS (VERSION 1.3 - DEC 2013)

This table is based on Boogaard P.J. (2009) Biomonitoring of the Workplace and Environment. In: Ballantyne B. Marrs T. Syversen T (eds) General and Applied Toxicology. 3rd edition. John Wiley and Sons. Chisester. UK. p. 2759-2789 (permission for reuse granted)

No	Substance	CAS no.	Biomarker	Medium	Materials sample collection	Sample pretreatment	Storage/transport	Detection method	LOQ (provide units)	Elimination half life in humans (h)
0010-1	Acetone	67-64-1	Acetone	urine	URM		CT	GC-MS	0.6 mg/L	
0020-1	Acetylcholinesterase inhibitors (organophosphates, carbamates)	-	Acetylcholinesterase	erythrocytes	EDT		CT/AT	Colorimetric	10 hU/L	32d
0030-1	Acrylamide	79-06-1	N-(Carbonamidethyl) valine from HB adduct	blood	EDT	RHB	FT	GC-MS/MS	4 pmol/g Globin	60 d
0030-2			Acrylamide mercapturic acid	urine	URM		AT	LC-MS/MS	1 µg/L	
0040-1	Acrylonitrile	107-13-1	N-Cyanoethylvaline from HB adduct	blood	EDT	RHB	FT	GC-MS/MS	0.2 ng/g Globin	60 d
0040-2			Cyanoethylmercapturic acid 1-cyano-2-hydroxyethylmercapturic acid	urine	URM		FT	LC-MS/MS	1 µg/L	8 h [8]
0050-1	Aluminium (Al) and its inorganic compounds	7429-90-5	Aluminium	urine	URM		AT	ICP-MS	0.03 µg/L	~8h
0050-2				serum	EDT	PL	AT	AAS	0.5 µg/L	
0060-1	4-Aminobiphenyl	92-67-1	4-Aminobiphenyl from HB adducts	blood	EDT	RER	CT	GC-MS	3 ng/L	60 d
0060-2			4-aminobiphenyl	urine	URM		FT	GC-MS	1.5 ng/L	~ 9 h
0070-1	Aniline	62-53-3	Aniline	urine	URM		AT	GC-MS	1.0 µg/L	3 h (BEI)
0070-2			p-Aminophenol	urine	URM		FT	GC-MS/MS	5 µg/L	
0070-3			Aniline Hb adducts	blood	EDT	RER	CT	GC-MS	3 ng/L	60 d
0080-1	Antimony (Sb)	7440-36-0	Antimony	urine	URM		AT	ICP-MS	0.1 µg/L	24 h (BAT)
0090-1	Arsenic (As), elemental and soluble inorganic compounds	7440-38-2	As (inorganic and methylated metabolites)	urine	URM		AT	LC-ICP-MS	0.001 µg/L	2 d (BAT)
0090-2				blood	EDT		CT	AAS	2 µg/L	
0100-1	Arsenic trioxide (As <sub>2</sub> O <sub>3</sub> )	1327-53-3	Arsenic	urine	URM		AT	LC-ICP-MS	1 ng/L	2 d (BAT)
0100-2				blood	EDT		CT	AAS	2 µg/L	
0110-1	Benzene	71-43-2	S-Phenylmercapturic acid	urine	URM		CT	LC-MS/MS	0.5 µg/L	9 h (BEI)
0110-2				urine	URM		FT	LC-MS/MS	10 µg/L	

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Links to websites of authorities that providing guidance values:



Finnish Institute for Occupational Health (FIOH), Helsinki, Finland (direct access to guidance values)



Scientific Committee on Occupational Exposure Limits (SCOEL), Brussels, Belgium (direct access to guidance values)



American Conference of Governmental Industrial Hygienists, Cincinnati, OH, USA (no direct link to guidance values)



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