BIOMONECS

Biological Monitoring of Exposure to Carcinogenic Substances

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Outline

The idea

The project

The consortium

Achievements so far

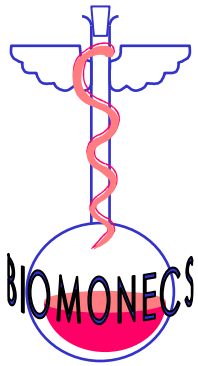
Future perspectives

How can we …

- … show the added value of biomonitoring to the European Commission (EC)?
- … convince the EC that biomonitoring is mature (in terms of infrastructure and analytical performance)?
- … show that biomonitoring can be made available to end-users on a European scale?
- … show that the service by routine labs can be self supportive in the future?

Objectives

- Knowledge transfer from universities to routine labs
- Harmonize of best practices in protocols
- Compare and improve analytical performance
- Discuss ethical implications in different countries
- Establish a consortium of service providers
- Improve the cost-benefit ratio for end-users



Consortium

Small and Medium Enterprises (SMEs)

Routine labs that have market experience with biomonitoring or with clinical or environmental analyses

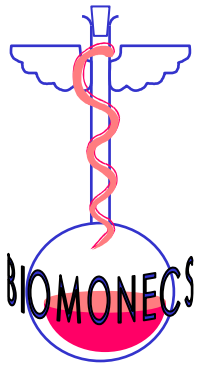
Research and Technology Development Performers (RTDs)

University labs that have a leading position in the development of new biomonitoring methods in Europe

Consortium

SME Routine Labs:
AB Biomonitoring, Cardiff (UK) – Co-ordinator of the project
Medizinisches Labor Bremen (D)
Laboratoriumsmedizin dr. Eberhard & Partners, Dortmund (D)
Labo Iliano, Destelbergen (B)
Exposure Control b.v., Wijchen (NL)

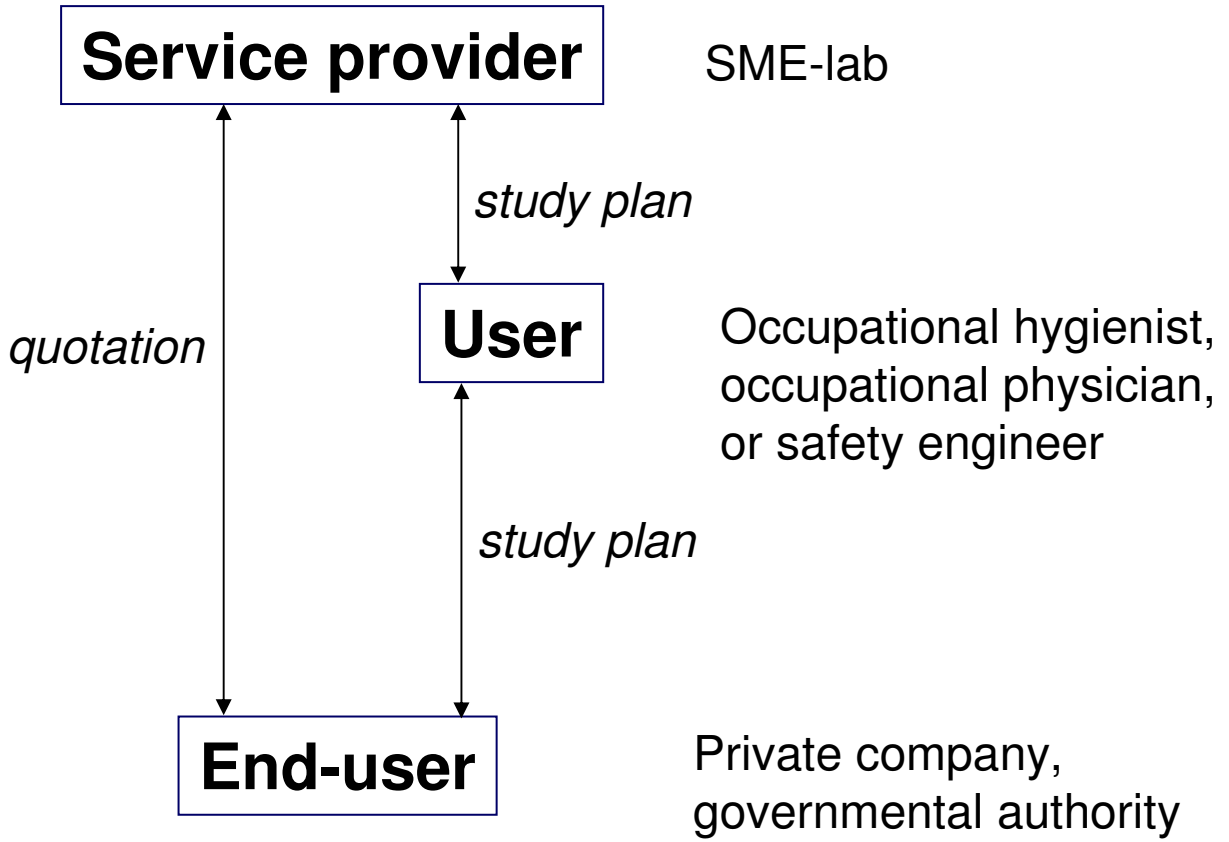
R & D University Labs:
Radboud University Nijmegen (NL) – Co-ordinator of RTD Performers
University of Duisburg-Essen (D)
University of Stockholm (S)
Frederic Alexander University of Erlangen-Nürnberg (D)
Université catholique, Brussels (B)
University of Copenhagen (DK)



Project

- Exploratory Award in 1997
- Project structure CRAFT (investments by SMEs and full cost coverage for RTD-performers)
- Standardisation Measurement and Testing programme
- 4th FP - Key Action 4: *"Environment and Health"* in Theme *"Quality of Life and Management of Living Resources"*
- Focus on carcinogenic substances

User interface



Advisory board

Internal
Prof. Dr. Jürgen Angerer, toxicologist, University of Erlangen-Nürnberg
Dr. Lisbeth Knudsen, epidemiologist, University of Copenhagen
Prof. Dr. Harry Roels, toxicologist, Université catholique Brussels
Dr. Margareta Törnqvist, chemist, University of Stockholm

External
Dr. Peter Boogaard, toxicologist, Shell, The Hague
Dr. Jan Dankers, chemist, Analytico, Breda
Dr. Nel Roeleveld, epidemiologist, Radboud University Nijmegen
Dr. Frits van Rooy, occupational physician, Occupational Lung Centre, Groesbeek

Midterm review (appointed by EC)
Dr. Nico van Sittert, former head of toxicology unit, Shell, Amsterdam

Work program

- 10 Class I biomarkers

  Scientifically established, used in routine on a reasonable scale, methods need revision

- 13 Class II biomarkers (3 extra)

  Scientifically established, methods need to be improved for routine analysis

Class I biomarkers

Substance	Biomarker
Benzene	S-phenylmercapturic acid in urine
Benzene	t,t-Muconic acid in urine
PAH	1-Hydroxypyrene in urine
Chromium VI	Cr in erythrocytes in blood
Chromium	Cr in urine
Cyclophosphamide	Cyclophosphamide in urine
Arsenic	Organic and inorganic As in urine
Cadmium	Cadmium in urine
Nickel	Nickel in urine
Diethylhexylphthalate	Secondary metabolites[a] in urine

[a]mono(2-ethylhexyl)phthalate (MEHP), 5-carbo-MEHP, 5-hydroxy-MEHP, 6-hydroxy-MEHP, and 5-oxo-MEHP

Class II biomarkers

Substance	Biomarker
Benzene	BTX in alveolar air
Aniline	Aniline and metabolites in urine
Benzidine	Benzidine in urine
Beryllium	Beryllium in urine
Carbo- and cisplatin	Platinum in urine
o-Toluidine	o-Toluidine in urine
Acrylamide	Acrylamide Hb adducts in blood
Chloroform	Chloroform in alveolar air
Tetrachloroethylene	Tetrachloroethylene in alveolar air
Trichloroethylene	Trichloroethylene in alveolar air
Ethylene oxide	Ethylene oxide Hb adducts in blood
PAH	3-Hydroxybenzo[a]pyrene in urine
Propylene oxide	Propylene oxide Hb adducts in blood

Output

Website: www.biomonecs.com

- Free access
- Background information about the project
- Calls for pilot-project opportunities
- Downloadable documentation (not operative)
- Services

Output

<u>Generic biological monitoring protocol</u>

- Public (scientific publication)
- Compilation of best practices covering study designs, communication protocols, ethical considerations, methods of data collection
- Background documentation for end-users

Output

Biomonitoring Application Data Sheets (BADS)

- Concise documentation on carcinogenic substances for which biomarkers are available
- Based on secondary literature resources (IARC Monographs, ACGIH BEI documentation, DFG, DECOS reports, IPCS)
- Public (internet)
- Reference values

Background values

- Urine, blood, and exhaled air samples obtained from subjects from B, DE, DK, NL, S and UK (n = 64)
- Characterization of low non-occupational exposures
- Assessment of analytical performance by analysis of repeatability in a series of duplicate analyses against IUPAC criteria

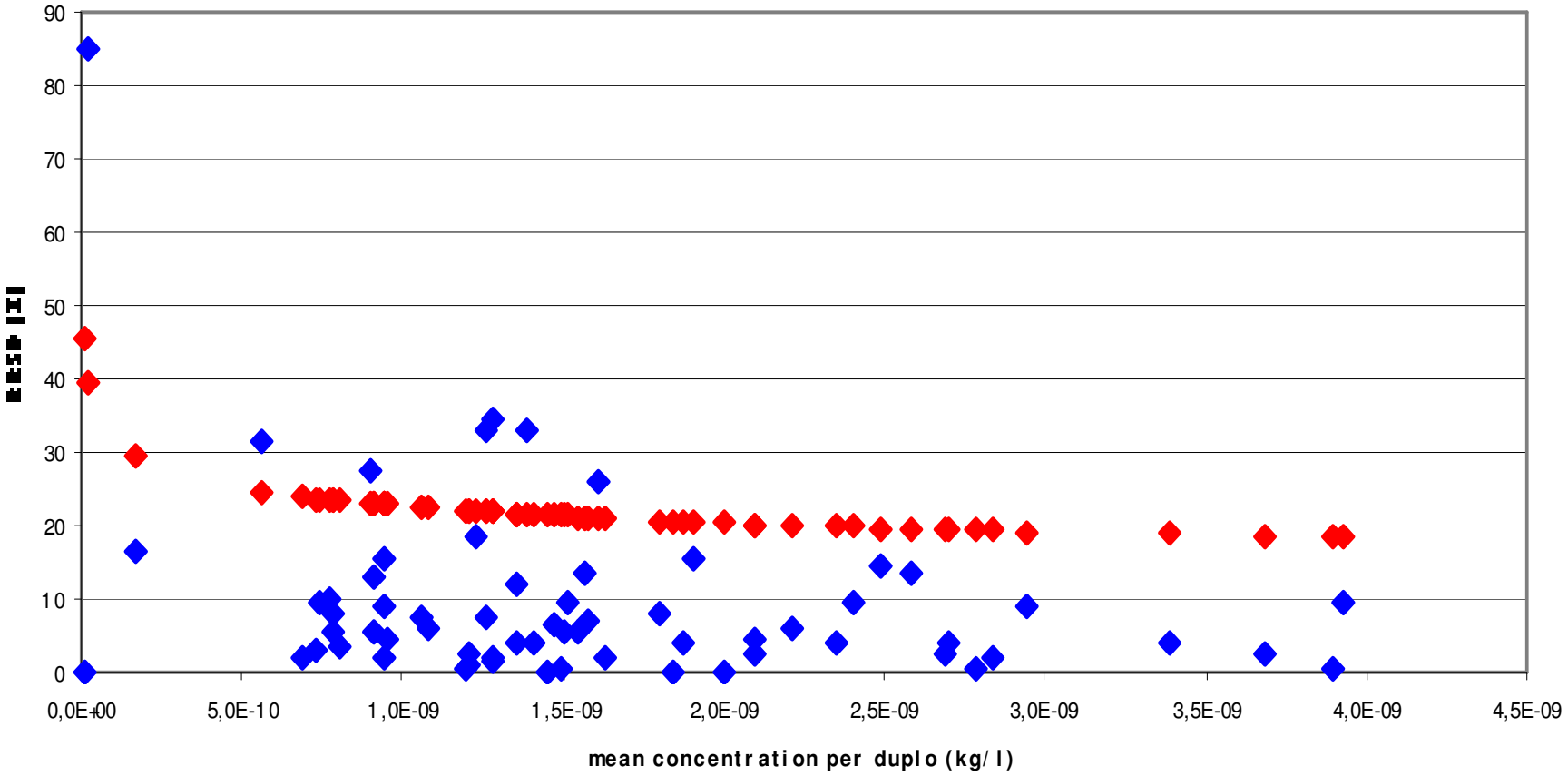
Background values

Biomarker	Median	Range	0.95 perc.
S-phenyl mercapturic acid (nmol/mol creatinine)	1.2	<0.02-4.5	3.1
1-Hydroxypyrene (nmol/mol creatinine)	0.07	0.02-0.31	0.19
Cadmium in urine (µg/g)	0.14	<0.02-1.46	0.74
Chromium in urine (µg/g)	<0.10	<0.05-13.2	0.42
Cyclophosphamide (µg/g)	nd	nd	nd
Total arsenic (µg/g)[a]	9.4	3.4-54.2	23.0
Nickel (µg/g)	0.15	<0.01-4.13	3.3

nd, not detected; [a]total of inorganic and organic As

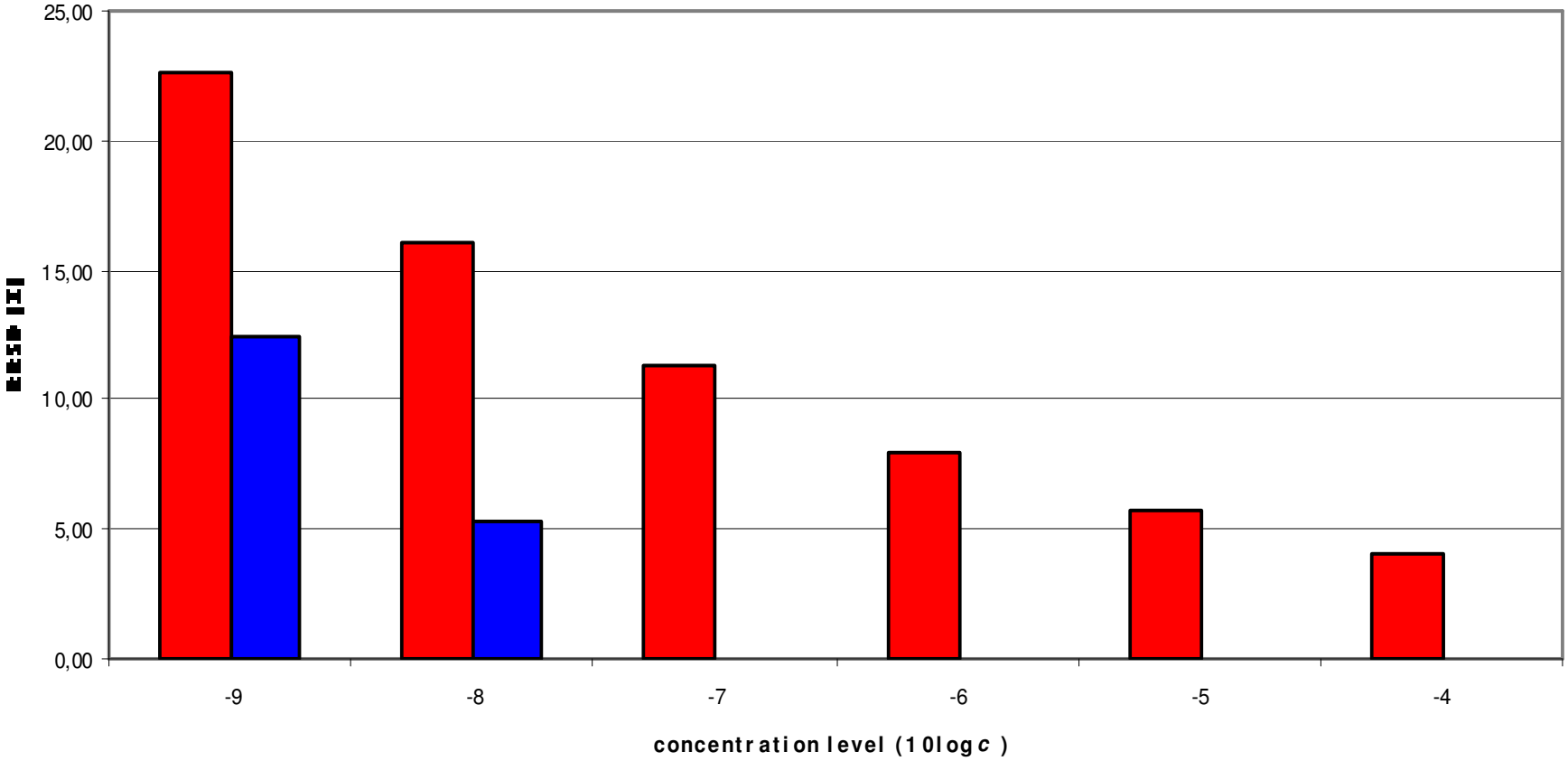
Analytical performance

Reproducibility relative standard deviation in relation to concentration



Analytical performance

Reproducibility relative standard deviation in relation to concentration level



Pilot studies

Completed

Arsenic in semiconductor industry
Benzene in oil refinery
Benzene on off-shore drilling platform
BTX in car paint industry
Cadmium in former copper smelter
Chromium in galvanization industry
Chromium in pigment industry
Chromium in welding
Cis-platinum in hospital pharmacy
Cyclophosphamide in hospital
DEHP in rubber industry
Ethylene oxide in pharmaceutical industry
PAH in hospital dermatology clinic
PER in galvanization industry
Propylene oxide in pharmaceutical industry

In progress/preparation

Beryllium in hard metal industry
Chromium in aerospace industry
Chloroform in swimming pool
Ethylene oxide in hospital sterilization
Nickel in aerospace industry

Where are we now?

- So far, it was not possible to find pilot study opportunities for all biomarkers
- Interest from users and end-users was not equally distributed across EU member states
- Evaluation of lab performance is not entirely completed but so far results are good
- Some practical problems occurred during pilot studies but most of them could be solved

Acknowledgements

Dr. C. van der Heijden
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Dr. H.-W. Schiwara
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Further reading …

M. Jakubowski & M. Trzcinka-Ochocka (2005)
Biological monitoring of exposure: trends and key developments
Journal of Occupational Health 47:22-48

P.T.J. Scheepers & G.A.H. Heussen (2005)
New and improved biomarkers ready to be used in health-oriented exposure and susceptibility assessments: report of the 6th International Symposium on Biological Monitoring in Occupational and Environmental Health
Biomarkers 10:80-94