European network on human biomonitoring

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The European Environment and Health Strategy, launched in June 2003 by the European Commission as the SCALE initiative (based on Science, focused on Children, aiming at raising Awareness, using Legal instruments, and including Evaluation) intends to present a new vision on how to address environment and health in an integrated way and puts health in the centre of environment policy. The strategy paid particular attention to the potential of HBM. A Technical Working Group on Biomonitoring of Children was one of the 9 working groups established under SCALE to prepare an Action Plan. They showed that within the European Union significant resources are spent and efforts are made to collect biomarker data in environmental health, but that studies are generally not using the same methodological approach, therefore limiting data comparability and accessibility within and between countries.

Objectives and general design

Based upon the Strategy, the Commission adopted in June 2004 a Communication on the Environment and Health Action Plan 2004 - 2010 in which the value of HBM as an essential tool to assess relevant exposure of the population, and the relevance and importance of coordination of HBM programmes in Europe was recognised. In Action 3 of this Action Plan, the Commission announces the development of a coherent approach to HBM in Europe in close cooperation with the Member States.

From the start, it was acknowledged that differences in threats to health, different levels of analytical capacities, differences in political and health priorities, cultural differences, and perhaps also different perceptions of ethics may render a common HBM survey carried out simultaneously in several European countries a challenge, both scientifically and politically. Therefore a step-by-step approach was chosen in which EU MS work together and exchange their capacities and expertise with a view of harmonising their way of proceeding.

The preparatory work by ESBIO (Expert team to Support BIOmonitoring in Europe) – a consortium involving researchers from 18 Member States - served to develop common protocols, strategies and scientific tools essential to ensure the collection of reliable and comparable data in all participating Member States. Tools were developed to integrate HBM results with environmental monitoring and health monitoring data.

The second step - to be launched early 2008 – foresees testing out the feasibility of a pan-European Human Biomonitoring Programme.

Expectations from Member States towards Human Biomonitoring

- **Support for existing government public health policy (promoting tobacco free society)**
- **Check efficiency of reduction measures of emission sources (do forbidden substances disappear?)**
- **Concern about increased exposure, emerging public health problem (flame retardants)**
- **Concern about exposure at levels close to those where effects can be expected/measured**
- **Support Existing Substances Regulation under REACH**
- **Produce point 0 of exposure**
- **Support for health education**
- **Assessment of respective contribution of sources**
- **Legal obligation to assess current levels in specific subpopulations**
- **Request from EU Parliament (to measure methyl mercury)**
- **Possibility for future policy actions**
- **Possible linkage to existing cohort studies and infrastructure**

The interests in background measurements are different between countries. Some countries have indicated a prerequisite of inclusion of new biomarkers and research activities. In order to cope with the diversity in interests and expectations in Member States, the current proposal:

- **builds and tests out a framework for surveillance with common approaches to recruitment of study persons, sampling, analysis, data management and communication, structured analysis of trends in levels of exposures**
- **develops new biomarkers**
- **links to policymaking.**

Two sub-populations of priority are addressed:
a) children before reaching puberty and b) women of childbearing age.
Only biomarkers of exposure which are covered by sufficient analytical experience in terms of validated analytical methods of adequate sensitivity, specificity and precision are at this moment regarded as suitable to develop and test a harmonized approach for HBM at the European level. The biomarkers for the project will be arranged in two groups representing two different scenarios: the basic one (obligatory) and an extended one (facultative). The basic scenario will cover: lead in blood, cadmium and cotinine in urine, and methylmercury in scalp hair.

It has been decided that scenario 2 will include biomarkers of exposure to: phthalates/PAHs, tin organics, brominated flame retardants (BFRs), and arsenic. Some of these biomarkers will have to be validated. The largest work package will be focused on the assessment of exposure to phthalates and PAHs. In the case of phthalates, the secondary, oxidized metabolites will serve as the biomarkers of exposure. As regards PAH exposure, two kinds of biomarkers will be measured. In the national survey, 1-hydroxypyrene and 1-,2-,3,-4-,9-hydroxyphenantrenes in urine will be determined, whereas cancer risk assessment will employ BaP-tetroles and 3-hydroxybenzo[a]pyrene in urine as well as benzo[a]pyrene DNA-adducts.

Current status of biomarkers of exposure considered priority for the HBM system in European countries

Lead

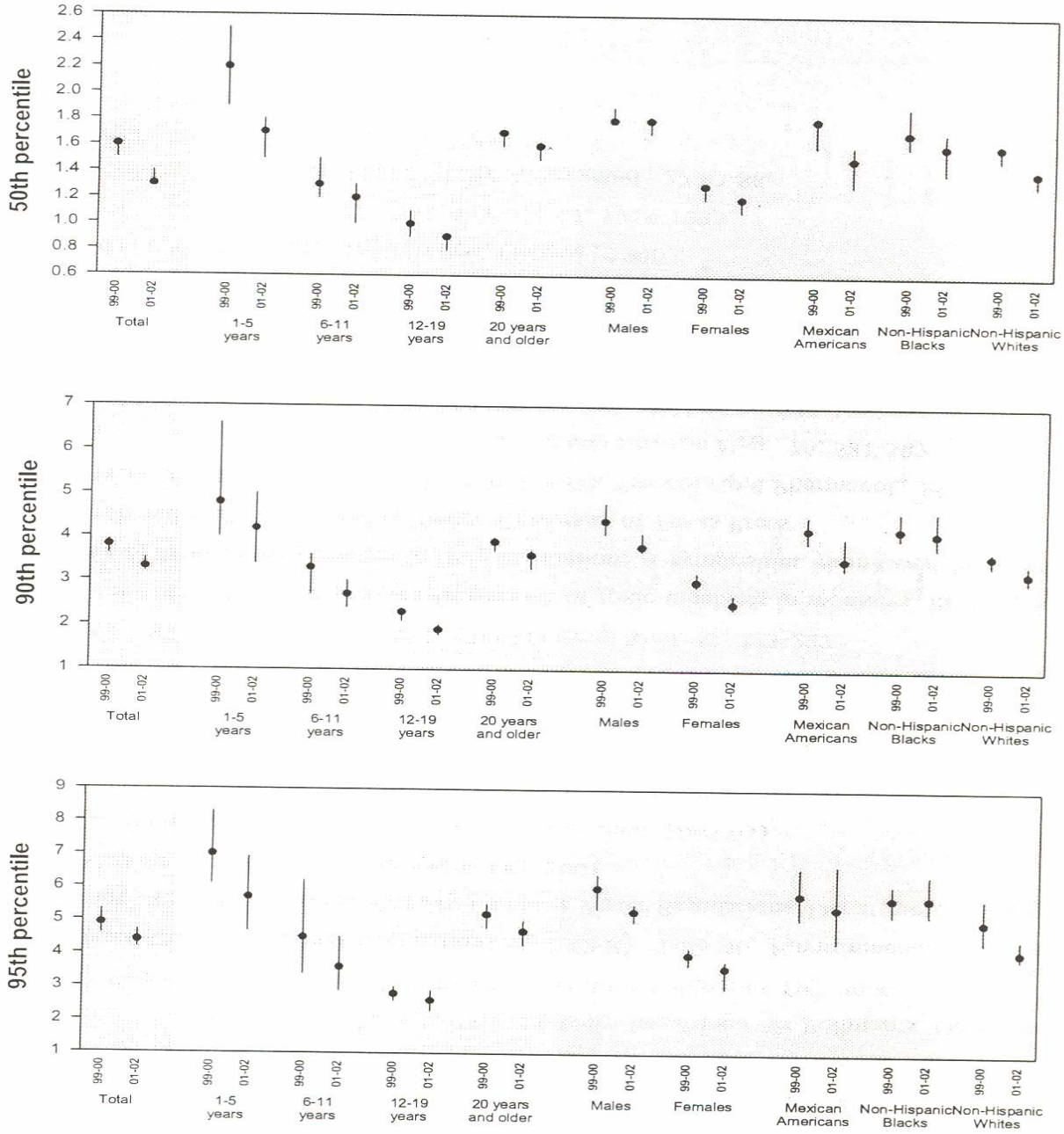
Lead is a well known neurotoxic metal. Impaired neurodevelopment in children is the most critical health effect.

Biomarkers of exposure

In environmental exposure to lead, the health effects can be related to the blood lead levels (Pb-B).
Reports on the geometric mean values in different countries revealed that in women and children Pb-B levels are within the range of 10-30 µg/ l considered as a „baseline" of minimal anthropogenic origin (Germany 16,3µg/l Kolossa-Gehring, 2007; Czech Republic 33 µg/l, Batariova et al . 2006)

Figure 6. Lead in blood

Selected percentiles with 95% confidence intervals of blood concentrations (in µg/dL) for the U.S. population aged 1 year and older, National Health and Nutrition Examination Survey, 1999-2002.



It is important to note that since the PbB levels are log normal distributed, then even at relatively low geometric mean values, a proportion of the population will have PbB above 100 µg/l

At a geometric mean PbB level of 36 µg/l, approximately 1.5% of the population will have Pb-B above 100 µg/l, and at a geometric mean PbB level of 60 µg/l, approximately 6% of the population will have Pb-B above 100 µg/l.

In 1991 the Centers for Disease Control recommended that the Pb-B values in children should be below 100 μg/l.

The WHO Air Quality Guidelines for Europe (WHO, 2000) recommended that at least 98 % of the population exposed in the general environment should have Pb-B below 100 μg/l, and the median blood lead level should not exceed 54 μg/l.

Recent publication suggest that the effects of environmental exposure of children can occur at Pb-B levels below 100μg/l.

Children

Blood lead concentrations, even those below 100 μg/l, are inversely associated with children's IQ scores at ages 3 and 5 years, and the related declines in IQ are greater at these concentrations than at higher levels. For the sample of children whose maximal Pb-B remainded below 100 μg/l, IQ declined by 7.4 points as the lifetime average Pb-B increased from 10 to 100 μg/l (Canfield et al., 2003).

Other recent findings also suggest a possible impairment of the neuropsychological functions (Canfield et al., 2004) and lead-related deficit in colour vision (Canfield et al, 2003a) as a result of low-level lead exposure in children.

Women

During pregnancy, maternal calcium requirements increase and are maintained mostly through increased bone resorption. The latter facilitates active transfer of calcium to the fetus. Maternal lead transfer follows a pattern similar to that for calcium, without any barrier at the placental level.

This is particularly true for the last part of pregnancy and the lactation period when maternal Pb-B increases by 25-100 %.

This increase derives from the further mobilization of lead from bones. Pb-B in infants is mainly the expression of skeletal lead stores (Gulson et al., 1997; Tellez-Rojo et al., 2004).

Neurological toxicity is observed in children as a result of the ability of lead to cross the placental barrier and to cause neurological impairment in the fetus (Emory, et al. 2003; Gomaa et al., 2002)

If the main toxic event is prenatal exposure, attention should be paid to maternal lead stores and, if possible, mobilization of these stores during pregnancy should be avoided

All these findings indicate a need to reconsider the currently held notion that lead levels below 100 µg/l are acceptable from the public health perspective. In 2006 the Scientific Committee on Neurotoxicology and Psychophysiology and the Scientific Committee on the Toxicology of Metals of the ICOH (Landrigan et al., 2006) resolved that current exposure standards for lead urgently need to be reduced.

For children, the action level, which triggers community prevention efforts to reduce exposure sources, should be immediately reduced to a Pb-B concentration of 50 µg/l in nations worlwide.

Also for female industrial workers of reproductive age, the standard for Pb-B should be reduced to the lowest obtainable , preferably to 50 µg/l.

Cadmium

Critical effects

Kidney and bone are the critical target organs in chronic environmental exposure. The main critical effects include increased urinary excretion of low molecular weight proteins, as a result of proximal tubular cell damage, and also an increased risk of osteoporosis.

Sources of exposure

Food is the main source of cadmium exposure in the general population (above 90 % of total intake in non-smokers). Besides, soil and dust account for a part of local population exposure in heavily contaminated areas

Biomarkers of exposure

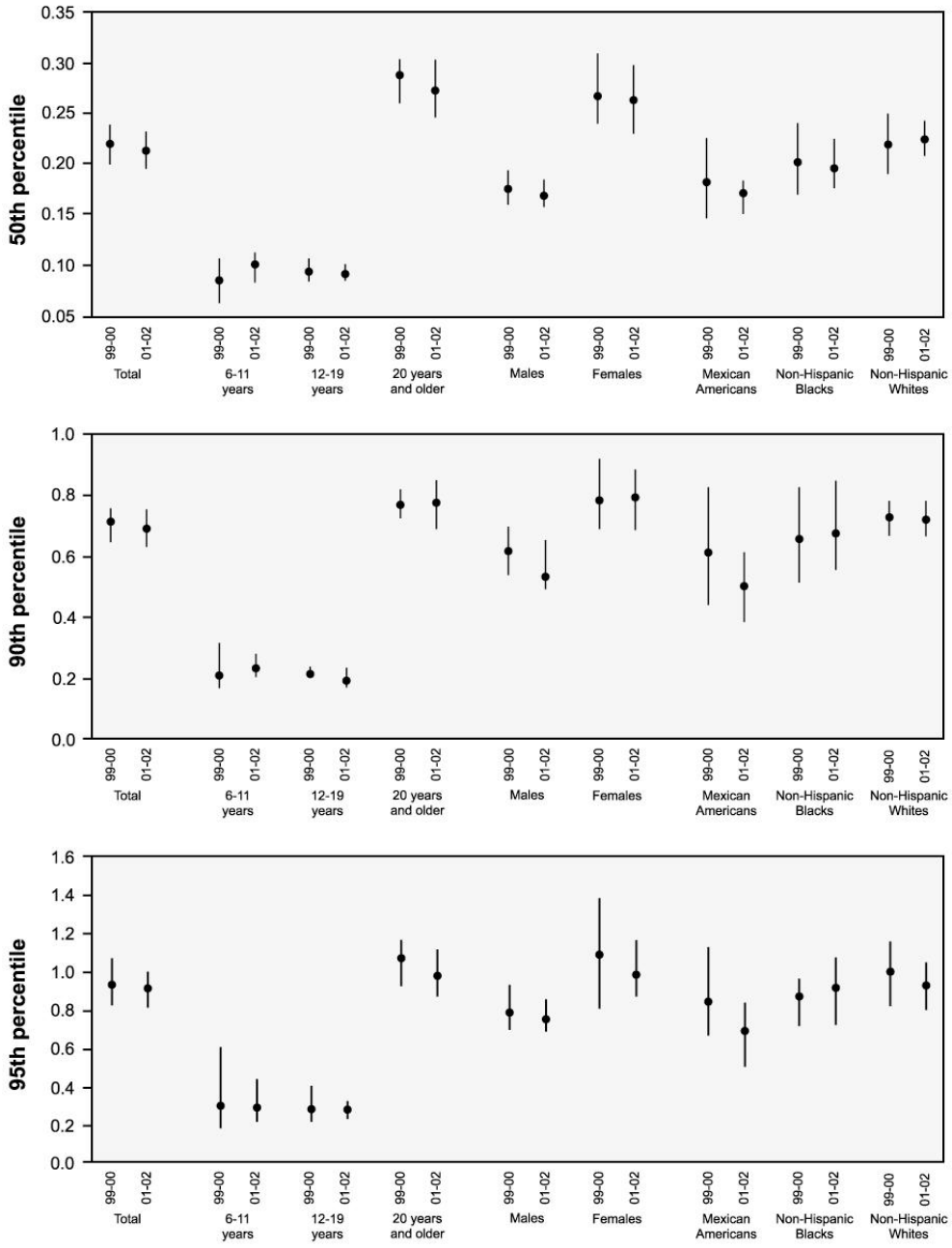
Cadmium concentration in blood (Cd-B) reflects the current exposure.
Cadmium concentration in urine (Cd -U) is mainly influenced by the body burden and it is proportional to cadmium concentration in healthy kidney.

In Germany (Backer et al., 2003), the P50 of Cd-U (n=4740, adults 18-69 years) amounted to 0.22 μg/ g creat. (0.20 in non-smokers ; 0.29 in smokers). The proposed reference value is 0.8 μg/ g creat.

In the Czech Republic (Batariova et al., 2006), the geometric mean Cd-U level amounted to 0.31 μg/ g creat. The proposed reference value (P 95) is 1.2 μg/ g creat.

Cadmium in urine (creatinine corrected)

Selected percentiles with 95% confidence intervals of urine concentrations (in μg/g of creatinine) for the U.S. population aged 6 years and older. National Health and Nutrition Examination Survey,1999-2002



Early health effects

The results of the papers published recently suggest that renal tubular damage due to cadmium exposure may develop at GM Cd-U concentrations 0.65 – 1.0ug/g creatinine, lower than previously anticipated (Jarup et al. ,2000; Akesson et al., 2005).

The available data from Europe also show that cadmium can affect calcium and phosphorous metabolism in people exposed in general environment (Staessen. et al.,1991; Alfven et al., 2000)

Trends of internal exposure

The recently published data do not show decrement of cadmium body burden in non-smokers over the last decade.

The time trends for cadmium, mercury and lead were evaluated in Sweden. The concentrations in erythrocytes (Ery) were determined in a subsample of the population- based MONICA surveys in 1990, 1994, and 1999 in a total of 600 men and women aged 25-74 years. Annual decreases of 5 – 6 % were seen for Ery-Pb and EryHg levels. For Cd , the decline in Ery-Cd was seen only among smokers, indicating that Cd exposure from tobacco smoke has decreased while other environmental sources of Cd have not changed significantly (Wennberg *et al*., 2006).

The margin of safety between the present dietary daily intake of cadmium and the level of intake which can bring about health effects is very narrow. For highly exposed subpopulations, this margin may even be non-existing. Population groups at risk include the elderly, diabetics and smokers. Women may be at an increased risk because they absorb more cadmium than men due to the lower iron stores.

Therefore, monitoring of cadmium levels in urine is highly recommended.

Methylmercury

The effects of methylmercury on the adult differ both quantitatively and qualitatively from the effects observed after prenatal or, possibly, postnatal exposure. The critical organ is the nervous system and the critical effects include developmental neurologic abnormalities in human infants, and paraesthesia in adults. Prenatal exposure was reported to cause psychomotor retardation in infants.

The benchmark dose, based on a combination of all childhood neurologic endpoints (onset of walking and talking, neurologic scores, mental symptoms, and seizures) was calculated by the U.S. EPA (IRIS, 1995).

A benchmark level of 11 μg/g in maternal hair has been established, equivalent to maternal blood level of 44 μg/l or daily intake of 1.1 μg/kg/day.

Benchmark dose calculations have also been performed for methylmercury-associated delays on evoked potential latencies in two cohorts of children from the Faroe Islands and from Madeira (Murata et al., 2002). The obtained BMDL 5 % of approximately 10 μg/g maternal hair was similar to that calculated for other neurological variables (Budtz-Jorgensen et al., 2002) in the Faroese children and in the New Zealand population (Crump et al.,1998).

The US National Academy of Sciences Committee on the Toxicological Effects of Methylmercury, applying an uncertainity factor of 10, arrived at the value of about 1 µg/g mercury in maternal hair. A daily intake of 0.1µg/kg/day, the USEPA current RfD, would result in such level (Bellinger, 2000)

Biological indicators of exposure

About 90% of mercury found in red blood cells was in the form of MeHg. THg in plasma was associated with both IHg and MeHg. **THg in hair reflects MeHg exposure at all exposure levels, and not IHg exposure.** The small fraction of IHg in hair is most probably emanating from demethylated MeHg. THg in urine reflected IHg exposure.

THg in RBC and hair are suitable proxies for MeHg exposure. THg in urine is a suitable proxy for IHg exposure.(Berglund et al., 2005)

The present background level of Hg-H associated with no or low fish consumption or low fish methyl mercury concentration amount to 0.25 µg/g in Germany (Drasch et al., 1997), 0.8 µg/g in Denmark (Grandjean et al., 1992), 0.28 µg/g in the north of Sweden (Oskarsson et al., 1996), 0.06 mg/kg in non-fish eating people in Sweden (Lindberg et al. ,2004)

Much higher Hg-H levels result from the consumption of large amounts of fish or sea mammals. In the Faroe Islands, the mean Hg-H levels ranged from 1.6 µg/g (1 fish meal per week) to 5.2 µg/g (4 fish meals per week) (Grandjean et al., 1992). In fishermen from Madeira (Portugal) and their families, levels of 38.9 µg/g were found in men and 10.4 µg/g in women (Renzoni, 1998). Bjornberg et al. (2005) investigated Swedish women with high fish consumption. The average total fish consumption was approximately 4 times/week. T-Hg in hair (median 0.70 mg/kg, range 0.08-6.6 µg/g) was associated with MeHg in blood).

These results show that not only on the islands such as Faroe Islands or Madeira but also in the continental Europe, high fish consumption can result in hair mercury levels several times higher than the 1 µg/g recommended by the US Academy of Sciences.

Environmental tobacco smoke (ETS)

Passive smoking is defined as the non-smokers inhalation of tobacco smoke produced by active smoking of others.

ETS is a complex mixture of thousands of compounds in particulate and vapor phase, and cannot be measured directly as a whole. Instead, markers such as nicotine are used to quantify environmental exposure. Inhalation of tobacco smoke is the main source of nicotine exposure for the general population. Cigarettes contain about 1.5 % nicotine by weight.

Biological indicators of exposure

Up to 92 % of the nicotine delivered in smoke is absorbed from the lungs into the blood stream.
Cotinine is a metabolite of nicotine and is currently regarded as the best biomarker in active smokers and in nonsmokers exposed to environmental tobacco smoke. Measuring cotinine is preferred over measuring nicotine because cotinine persists longer in the body. Nicotine has a half-life in blood plasma of several hours. For cotinine, the half-life in blood plasma is about 16 hours (CDC, 2005).

Cotinine can be measured in serum, urine, saliva, and hair.

Concentrations of cotinine in urine are higher than in other biological media.

The average cotinine levels:

- **non-smokers <4.0 – 27.9 μg/l**
- **passive smokers 11.4 – 46.0 μg/l**
- **smokers 1080 – 3050 μg/l**

At the same level of ETS exposure, young children have nearly two times higher urinary cotinine levels than adults (Willers et al., 1995).

Non-smoking children exposed to parental tobacco smoke at home showed in average higher cotinine concentration than non-exposed:GM 8.1 μg/l vs. 2.7 μg/l Maternal smoking showed a stronger effect than paternal smoking (Thaqi et al., 2005).

Tobacco smoke is the most important preventable cause of premature mordbidity and mortality. ETS has been classified by IARC as class I carcinogen.

Based on the combined evidence from several studies , WHO has estimated that some 9 -13 % of all cancer cases can be attributed to ETS in a nonsmoking population (50 % exposed to ETS. In infants, the proportion of lower respiratory illness attributed to ETS exposure can be estimated at 15-26% , assuming that 35% of the mothers smoke at home. Those estimates, when applied to the European population , will result in approximately 3 000-4 500 cancer cases per year among adults, and between 300 000 and 550 000 episodes of lower respiratory illness per year in infants.

- **ETS has been shown to increase the risks for a variety of health effects in non-smokers exxposed at typical environmental levels.**
- **Children need specifically protection from ETS at home. There is no evidence for a safe exposure level.**
- **Cotinine is a major metabolite of nicotine and its levels in urine can be used to track exposure to ETS among non-smokers**

Three biomarkers (Pb-B, Cd-U and MeHg-H) have health-based guidance values and risk associations for adverse health outcomes.

Cotinine levels in urine can be used to track exposure to ETS among non-smokers.

Methods of determination, reference materials and external quality assurance system are available for all four presented parameters.

Development and validation of biomarkers

Development and validation of biomarkers are another key elements of the HBM Pilot Project.

Most chemical substances which are the focus of discussion on environmental health worldwide can be measured with HBM (e.g. the CDC program). However, there is a need for a larger number of validated biomarkers that would allow for an accurate risk assessment and clear risk communication.

The validation efforts aim at harmonizing analysis and data interpretation of particular „ high focus” substances in at least five Member States. The substances in question include: phthalates and PAHs, organotin compounds, inorganic arsenic, brominated flame retardants (BFR)).

In addition, the use of saliva as a matrix in HBM will be assessed.

Subproject 1.

- **Harmonization, implementation, validation and capacity building of methods for determining phthalate and PAH metabolites in urine.**
- **Selection of representative groups of the Member States to determine preliminary background levels in the general population.**

Subproject 2.

- **Development and validation of new parameters for PAH exposure**

(BaP tetrols in urine, 3-HO-BaP in urine, BaP-DNA adducts in blood) using methods of instrumental analysis.

Subproject 3

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We do hope that in spite of the complexity of the problem, the implementation of HBM on the European scale will start as soon as the next year.

Thank you for your attention.

The implementation of HBM will be carried out in two steps.

At first, it will be necessary to test the feasibility of the approach through a European-wide Pilot Study covering 24 EU Member States. The study will consist in measuring four well validated biomarkers in vulnerable sub-populations.

The activities of the Pilot Study will also include the development and validation of other biomarkers of exposure and effect. The focus is on substances and methods as selected by MS authorities and institutions at several meetings of the EU Consultative forum.

Phthalates and PAH

Phthalates are among the most abundant environmental contaminants worldwide. Phthalate diesters are the most commonly used plasticisers, primarily to make polyvinyl chloride soft and flexible. In soft PVC, they can make up 40 % of the polymer. Currently, over 1 million tons of phthalates are produced annually in Western Europe alone. As the phthalates are not chemically bound to the polymer, they leach, migrate or gas out of the plastic articles into the environment.

The EU has classified three phthalates: di-(2-ethylhexyl) phthalate (DEHP), di-n-butylphthalate (DnBP) and benzylbutyl phthalate (BBP), as toxic to reproduction.

Biomarkers of exposure

HBM has been proven to be an excellent tool for human phthalate exposure assessment in several studies, mainly from Germany and the USA. Biomonitoring data show that the general population is ubiquitously exposed to phthalates.

Until some years ago, only the primary phthalate metabolites were determined in blood and urine. They were, however, susceptible for contamination. In the meantime, the parameter spectrum has been increasing, implementing the secondary, oxidized metabolites which are not prone to contamination and have longer half-lives than the simple monoesters.

Table 1: Phthalate biomarkers used for survey

Phthalate		metabolite (U)	
DnBP	*Di-n-butyl phthalate*	MnBP	*mono-n-butyl phthalate*
DiBP	*Di-iso-butyl phthalate*	MiBP	*mono-iso-butyl phthalate*
BBzP	*Butylbenzyl phthalate*	MBzP	*monobenzyl phthalate*
DEHP	*di(2-ethylhexyl) phthalate*	MEHP	*mono-(2-ethyl-hexyl) phthalate*
		5OH-MEHP	*mono(2-ethyl-5-hydroxyhexyl) phthalate*
		5oxo-MEHP	*mono(2-ethyl-5-oxohexyl) phthalate*
		5cx-MEPP	*mono(2-ethyl-5-carboxypentyl) phthalate*
DiNP	*di-iso-nonyl phthalate*	OH-MiNP	*mono-iso-nonyl phthalates with one hydroxy group*
		Oxo-MiNP	*mono-iso-nonyl phthalates with one keto group*
		cx-MiOP	*mono-iso-octyl phthalates with one carboxy group*

Table 3: New phthalate biomarkers for a better estimation of risk

Phthalate		metabolite (U)		oxidation
DnBP	*Di-n-butyl phthalate*	3OH-MnBP	*Mono-3-hydroxy-n-butyl phthalate*	ω-1
		4OH-MnBP	*Mono-4-hydroxy-n-butyl phthalate*	ω
		3-cx-MnPP	*Mono-3-carboxy-n-propyl phthalate*	ω
DiBP	*Di-iso-butyl phthalate*	3OH-MiBP	*Mono-iso-hydroxy butyl phthalate*	ω-1
		4OH-MiBP	*Mono-4-hydroxy-iso-butyl phthalate*	ω
		3-cx-MiPP	*Mono-3-carboxy-iso-propyl phthalate*	ω
DEHP	*di(2-ethylhexyl) phthalate*	3cx-MEPP	*mono(2-ethyl-3-carboxypropyl) phthalate*	β
		4cx-MEBP	*mono(2-ethyl-4-carboxybutyl) phthalate*	α
		M-1OH-EHP	*mono-2-(1-oxoethylhexyl) phthalate*	ω-n
		M-1oxo-EHP	*mono-2-(1-oxoethylhexyl) phthalate*	ω-n
DiNP	*di-iso-nonyl phthalate*	cx-MiHpP	*mono-iso-heptyl phthalates with one carboxy group*	α
		cx-MiHP	*mono-iso-hexyl phthalates with one carboxy group*	β
DiDP	*di-iso-decyl phthalate*	OH-MiDP	*mono-iso-decyl phthalates with one hydroxy group*	ω-n
		oxo-MiNP	*mono-iso-decyl phthalates with one keto group*	ω-n
		cx-MiNP	*mono-iso-nonyl phthalates with one carboxy group*	ω-n
		cx-MiOP	*mono-iso-octyl phthalates with one carboxy group*	α
		cx-MiHpP	*mono-iso-heptyl phthalates with one carboxy group*	β

PAHs are an important environmental-health problem of worldwide concern. A number of studies have been conducted to estimate the internal PAH exposure. Most of them used the urinary metabolite 1-hydroxypyrene (1HP) as a biomarker of pyrene.

Monohydroxylated phenantrenes (OH-Phen), metabolites of phenantrene, are also used as suitable biomarkers for PAH-exposure.

Recently, the Human Biomonitoring Commission of the German Federal Environmental Agency published a reference value (background burden of the non-smoking general population) of 0.5 µg hydroxypyrene per litre urine.

Table 2: PAH biomarkers used for national survey

Substance	Biomarker
Pyrene	1-Hydroxypyrene
Phenanthrene	1-, 2-, 3-, 4-, 9-Hydroxyphenanthrenes

Table 4: Research on PAH-biomarkers for a better assessment of risk

Substance	biomarker
benzo[a]pyrene	*marker of exposure (urine)* "Phenanthrene-tetroles" Tetrahydroxy-tetrahydro-benzo[a]pyrene; "BaP-tetroles" 3-Hydroxybenzo[a]pyrene
benzo[a]pyrene	*DNA-Adducts (blood)* DNA-adducts (ELISA) r-7, t-8-dihydroxy-t-9,10-oxy-7,8,9,10-tetrahydrobenzo[a]pyrene; "anti-B[a]PDE" (instrumental analysis)

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Brominated flame retardants (BFR) - HBM of PBDEs

Flame retardants have a wide range of applications in today's consumer products, textiles, electronic etc. Polybrominated diphenyl ethers (PBDEs) are one of the main groups of BFR. They have primarily been produced in three technical formulations, PentaBDE, OctaBDE and DecaBDE, each of which is a mixture of individual PBDE-congeners.

Due to the large production volume, lack of regulations, and their persistence, PBDEs are now ubiquitous environmental pollutants. They have been identified in various environmental media, as well as in human tissues.

PBDEs levels are increasing in the environment and biota at an exponential rate. In Swedish human milk, PBDE concentrations have increased from 1972 to 1997 with redoubling every 5 years, but samples from 1998 and later showed decreasing levels.

The performed intake estimations showed that the single largest food group contributing to the PBDE intake was fish. A significant contribution came from farmed salmonid fish.

In experimental studies, PBDEs have had low acute toxicity but in repeated exposure they could produce thyroid hormon disruption, developmental neurotoxicity, and some changes in fetal development

Human samples such as serum/plasma, human milk, and adipose tissue have been used for biomarker studies to assess the extent of human exposure to PBDEs.

An American study on breast milk gives evidence for much higher levels (ca. 200 ng/g fat) than in Sweden (3 – 4 ng/g fat) or South China (1.5 – 17 ng/g fat).

The following PBDE-congeners are considered to be most important for human biomonitoring purposes: BDE-47, 99,100,153, and 209.

Perfluorooctanoic acid/Perfluorooctane sulfonate (PFOA/PFOS)

PFOA/PFOS are important representatives of the group of perfluorinated surfactants used in a wide variety of industrial processes and products.
Studies revealed an extreme persistence in the environment, and their tendency to bioaccumulation and biomagnification.
Organic fluorine has been found in the serum of all human populations studied. PFOA was the principal organic fluorine compound in human serum bacause it has a long biological half-life.

PFOA produces marked hepatic effects including hepatomegaly, focal hepatic necrosis, hypolipidemia, and alteration of hepatic lipid metabolism in a number of animal species.

Little is known about the toxic potential of PFOA in humans.

Organotins have a wide use as a biocides, surface wood preservatives, stabilizers of PVC and other plastics. Several organotin compounds are in common use: mono-, di- , and tributyltin (MBT, DBT and TBT), mono- and dioctyltin (MOT,DOT) and triphenyltins (TPT). Toxicity data indicate that human exposures to these compound may impair the immune, nervous and reproductive systems.

Inorganic arsenic is a known human carcinogen. Investigation of the arsenate/arsenite/MMA,DMA will be carried out by assessing the levels of these arsenic compounds in urine. The use of saliva as an alternative non-invasive matrix will also be studied.

Saliva as a matrix for HBM

Saliva is a promising non-invasive matrix for human biomonitoring. The saliva content of chemicals, chemical residues or metabolites can be used as an indicator of exposure.

Non-invasive matrixes have an obvious advantage in large-scale biomonitoring programs because the samples are easy to collect, process and store, plus the ethical obstacles are greatly reduced.

However, the use of saliva in environmental analysis is still in its infancy and the predictive value needs to be established.

The project gives an opportunity to compare the levels of contaminants in saliva with those in other matrixes like blood, urine and hair in the same individuals.

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