NORDIC WORKING PAPERS

Workshop Report HBM4EU

Nordic workshop for scientists and regulatory agencies
discussing HBM4EU – The European human biomonitoring
initiative

Lisbeth E. Knudsen and Pernille Winton Hansen

<http://dx.doi.org/10.6027/NA2017-914>
NA2017:914
ISSN 2311-0562

This working paper has been published with financial support from the Nordic Council of Ministers. However, the contents of this working paper do not necessarily reflect the views, policies or recommendations of the Nordic Council of Ministers.

Workshop Report:

NORDIC WORKSHOP FOR SCIENTISTS AND REGULATORY AGENCIES DISCUSSING HBM4EU - THE EUROPEAN HUMAN BIOMONITORING INITIATIVE.

Organized by professor PhD Lisbeth E. Knudsen, Institute of Public Health, University of Copenhagen

liek@sund.ku.dk

Monday and Tuesday 20+21 March 2017 at Hotel Kong Arthur

**ARTHUR HOTELS
NØRRE SØGADE 11
DK-1370 COPENHAGEN K**

Authors: Lisbeth E. Knudsen and Pernille Winton Hansen

Section of Environmental Health, Institute of Public Health, University of Copenhagen

Table of contents

Background – the HBM4EU	4
The role of human biomonitoring in assessing and managing chemical risks	4
The initial prioritization exercise and selected substances	5
Purpose and aim of the Nordic workshop.....	7
Participants presentations.....	7
Participants.....	8
Summary of discussions on prioritization of chemicals	9
Comments on prioritization, Inputs from group discussions, Monday 20th	9
Summarized input from general discussion to further prioritisation of substances/groups of chemicals.	10
Overall conclusions from the workshop.....	12
Workshop evaluation	12
Next steps.....	12
Acknowledgements	13
References	13
Appendix I – Workshop program	14
Appendix II – Description of NORAP and NEXPO	16
Appendix III – HBM4EU partners, governing structure, substances and work packages	17
Appendix IV - The Nordic Hubs.....	20
Appendix V – List of participants.....	33
Appendix VI – Abstracts of presentations	36
Status of the HBM4EU in each country	36
Hanna Tolunen (FIN): The Finnish HBM4EU Hub	36
Britta Hedlund (S): Health related environmental monitoring in Sweden – Data for HBM4EU	37
Cathrine Thomsen (N): Biomonitoring projects and analyses work we are conducting in Norway/NIPH which might contribute to HBM4EU	38
Thorhallur Halldorsson (IS): The Icelandic Hub	38
Lisbeth E. Knudsen (DK): The Danish Hub	38
Pál Weihe (FO): Temporal tendencies of developmental exposures in Faroese birth cohorts	39
Prioritization of chemicals	40
Anna Karin Lindroos (S): Collecting biomarkers in a national dietary survey	40
Marie Louise Holmer (DK): Use of human biomonitoring data in regulation of chemicals	41
Johan Lindberg (S): Biomarker discovery/qualification for liver-toxicity.	41

Tina Kold Jensen (DK): The Odense Child Cohort	41
Nordic contributions to WP	42
Marika Berglund (S): Swedish contributions to WP8: Targeted field work surveys and alignment at EU level	42
Agneta Åkesson (S): The Central Sweden Cohorts & Biobank a National Research Infrastructure	43
Hanna Tolonen (FIN): WP11 – Linking HBM and health studies, and register data. Nordic involvement now and in future.	44
Cathrine Thomsen (N): The Norwegian Institute of Public Health’s contribution in HBM4EU	45
Anna-Maria Andersson (DK): The Capital region of Denmark participation in HBM4EU: focus on linking HBM to health studies and health effects	46
Hanne Frederiksen (DK): Non-persistent endocrine disrupting chemicals (EDCs) in Danes: Presentation of HBM-data in present and future studies.....	47
Eva Cecilie Bonefeld-Jørgensen (DK): Biomarkers of exposure and effects & Molecular Epidemiology: DK and Greenlandic birth cohorts	48
Anne Marie Vinggaard (DK): DTU’s contribution to HBM4EU	49
Ulla Birgitte Vogel (DK): NRCWE contributions and interests	49
Common Nordic interests	50
Lisbeth E. Knudsen (DK): HBM4EU and ethics.....	50
Lisbeth E. Knudsen (DK): HBM4EU and training.....	52
Anne Thoustrup Saber (DK): BIOBRAND and BIOTRACK - two ongoing biomonitoring studies of firefighters and train conductors.....	53
Marie Frederiksen (DK): Flame retardants and PCB HBM-studies from Denmark	54
Tiina Santonen (FIN): How to engage Nordic occupational health	54

Background – the HBM4EU

The role of human biomonitoring in assessing and managing chemical risks¹

The use of chemicals in a broad range of products, including medicinal and veterinary products, as well as in agriculture and pest control, provides benefits to society. At the same time, human and environmental exposure to hazardous chemicals represents a cost in terms of impacts on human health and reduced environmental quality. Recognizing this, the European Union's 7th Environmental Action Programme sets the goal of assessing and minimizing risks to the environment and health associated with the use of hazardous substances by 2020.

A major hurdle to the reliable risk assessment and management of chemicals is the lack of harmonized information at European level concerning the exposure of citizens, including workers, to chemicals and their interplay with other concurrent environmental exposures and impact on health. Individuals are exposed to a complex mixture of chemicals in their daily lives through the environment, products, food and drinking water and at work. For many chemicals, the health impacts over a lifetime associated with exposure remain unknown. In addition, understanding of the health impacts of exposure to mixtures of chemicals is limited.

Human biomonitoring allows estimation of exposure to chemicals by measuring the substances themselves, their metabolites or markers of subsequent health effects in body fluids or tissues. Information on human exposure can then be linked to data on sources and epidemiological surveys, in order to inform research on the exposure-response relationships in humans.

With the aim of addressing knowledge gaps and promoting innovative approaches, the European Commission launched a call for a European Human Biomonitoring Initiative, under Horizon 2020's Societal Challenge on health, demographic change and wellbeing. The objective is to create a European joint program for monitoring and scientific assessment of human exposures to chemicals and potential health impacts in Europe, building on previous activities undertaken at EU and national levels.

The consortium formed after successful application is led by the German Environment Agency (UBA) and brings together leading European expertise on HBM from 22 EU Member States, as well as Norway, Iceland, Israel and Switzerland in the project HBM4EU. Key objectives include:

- Harmonizing procedures for human biomonitoring across the 26 participating countries, to provide policy makers with comparable data on human internal exposure to chemicals and mixtures of chemicals at EU level
- Linking data on internal exposure to chemicals to aggregate external exposure and identifying exposure pathways and upstream sources
- Generating scientific evidence on the causal links between human exposure to chemicals and health outcomes
- Adapting chemical risk assessment methodologies to use human biomonitoring data and account for the contribution of multiple external exposure pathways to the total chemical body burden
- Feeding information on exposure pathways into the design of targeted policy measures to reduce exposure

---

¹ From: <http://www.eea.europa.eu/themes/human/human-biomonitoring>

In order to achieve these objectives, the consortium plans to harmonize human biomonitoring initiatives in 26 countries, by drawing on existing expertise and building new capacities. National Hubs are established in each country to coordinate activities, creating a robust Human Biomonitoring Platform at pan-European level.

This initiative contributes directly to the improvement of health and well-being for all citizens, by investigating how exposure to chemicals affects the health of different groups, such as children, pregnant women, fetuses and workers. Research will investigate how factors such as behavior, lifestyle and socio-economic status influence internal exposure to chemicals across the EU population. This knowledge will be fed directly into policy making to reduce chemical exposure and protect human health.

HBM4EU will run for five years, from 2017 to 2021, with the long-term objective of establishing a sustained programme. In developing priorities for HBM4EU under the first annual work plan, the consortium conducted a prioritisation exercise to identify those substances to be the focus of activities. Additional rounds of prioritisation will be carried out during the project lifespan in order to respond dynamically to policy needs.

The first year will be largely dedicated to collecting and collating existing HBM data for the nine prioritised substance groups, making data available, as appropriate, via the Information Platform for Chemical Monitoring, and determining which current policy questions can be answered using existing data. This will allow us to evaluate the extent to which a solid database of comparable HBM data from across the EU can be subject to systematic analysis, so providing answers to key policy questions.

The initial prioritization exercise and selected substances²

In developing priorities for the first annual work plan, the consortium implemented an exercise to prioritise substances for action, taking into account both national and EU level policy needs for knowledge on chemical exposure and health outcomes.

As a first step, substances for which knowledge is needed to support current EU policy making were identified through close dialogue with an EU Policy Board. Input from the national level was fed in through a Steering Committee, composed of national representatives and established to guide the preparation of this proposal.

An initial set of criteria was then produced, including such aspects as whether a substance is of concern to human health, whether there is evidence of human and/or environmental exposure at EU level and whether there are open policy questions. The financial and technical feasibility of monitoring the substances was also a criterion.

Substances proposed at both national and EU level were then systematically assessed against these criteria, based on information provided from both EU and national levels. This first prioritization exercise resulted in the nine substance groupings that will be the focus of EHBM activities in 2017 and 2018.

---

² From: <http://www.eea.europa.eu/themes/human/human-biomonitoring/prioritisation-and-substances>

The list of prioritised substance groups for 2017 in HBM4EU includes:

phthalates and Hexamoll® DINCH,
bisphenols,
per-/polyfluorinated compounds,
flame retardants,
cadmium and chromium,
PAHs,
aniline family,
chemical mixtures, and
emerging substances.

The consortium then compiled information on substance classification, policy-related research questions and research objectives, with the results captured in scoping documents for the prioritized substances. These scoping documents formed the basis for the development of activities for inclusion in the 2017 action plan for the HBM4EU.

Two additional rounds of prioritization will be conducted during the five years of the project, one from 2017 to 2018 and one from 2019 to 2020. The consortium will build on the experience gained with the first prioritization exercise, refine the approach to increase transparency and make it open to stakeholders.

Purpose and aim of the Nordic workshop

This Nordic Workshop will bring together scientists and regulatory specialist from the Nordic countries to:

- Discuss priority setting of which substances to include in the upcoming biomonitoring programs
- How to optimize the communication between scientists and authorities regarding use of HBM data in a regulatory context (e.g. REACH)
- Promote Nordic collaborations in science and training

This information will be a valuable contribution to feed in to the national advisory groups in the national hubs related to HBM4EU and subsequently be used as input for applications for EU funding.

A detailed agenda from the workshop is attached in Annex I.

The Nordic Workshop was granted by Nordic Risk Assessment Project (NORAP) and Nordic Exposure Group (NEXPO). More information on NORAP and NEXPO is attached in Annex II.

Further information regarding the HBM4EU is attached in Annex III.

Information regarding the Nordic Hubs is attached in Annex IV.

The list of participants is in Annex V and all abstracts available from the presenters are in Annex VI.

Participants presentations

Participants were invited to share short presentations on specific cases or issues that they find relevant to the following topics: Status of the HBM4EU in each country, Prioritization of chemicals, Nordic contribution to WP and/or Common Nordic interests. Abstracts (if available) of the presentations are attached in Annex VI. These presentations as PDF documents are available on the website

http://www.ifsv.ku.dk/afdelinger/ms/in_vitro_toksikologi_kopi/in_vitro_forskning/hbm4eu/hbm4eu-march-meeting-2017-in-copenhagen/

Participants

The workshop had 43 participants from the different Nordic countries (see list of participants in Annex V).

Table 1: Summary of workshop participants.

	Finland	Norway	Sweden	Iceland	Faroe Islands	Denmark	Total
Participants total	4	4	8	2	1	24	43
Authority	1	1	6	0	1	6	15
Academia	3	3	2	2	0	18	28

Table 2: Summary of Institutions represented at the workshop.

Institutions represented at the workshop (by country)	Participants
Finland	4
National Institute for Health and Welfare (THL)	2
Ministry of Social Affairs and Health	1
National Institute of Occupational Health	1
Iceland	2
Matís ohf. - Icelandic Food and Biotech R&D (Iceland)	1
University of Iceland	1
Faroe Islands	1
Faroe Health	1
Norway	4
Norwegian Institute of Public Health	3
Arbeidstilsynet	1
Sweden	8
Karolinske Institute	2
National Food Agency	2
Environment Protection Agency	2
Swedish Chemicals Agency	1
Swetox	1
Denmark	24
Dept. of Growth and Reproduction, Region H	3
National Research Centre for the Working Environment	4
University of Southern Denmark	2
University of Copenhagen	3
Danish Veterinary and Food Administration	1
Danish Environmental Protection Agency	3
Danish Agency for Science and Higher Education	1
TREALIV	1
Aarhus University	3
National Food Institute, Technical University of Denmark	2
Danish Working Environment Authority	1

Summary of discussions on prioritization of chemicals

Comments on prioritization, Inputs from group discussions, Monday 20th

Criteria for prioritization

Chemicals that are widely used and appear in both consumer products and occupational settings
Chemicals of high concern in the EU – those compounds where there is lack of knowledge
Persistence, Bioaccumulation potency
Toxicity, Endocrine disrupting properties
Exposure – using tonnage as a proxy for exposure – high volume chemicals
Possible use of in silico modeling of PBPK - Physiologically based pharmacokinetic modelling
Check list of substance of very high concern (SVHC) under REACH and use this as a basis for prioritization

Chemicals

Arsen
Biocides
Brominated flame retardants, new
Chemicals in textiles
Chlorinated parafins
Compounds in plastic products
EDCs
Emerging chemicals
Hygiene products
Markers of health: markers of oxidative stress/inflammation in human blood, that can be correlated with particulate air pollution
Metals can easily be measured together: arsenic, mercury, zinc
Mercury
Microplastics – as vehicles for POPs
Mixtures – ex vivo combined effect biomarkers, e.g. of oxidative stress
Nanomaterials, both intentional and unintentional use and exposure
Occupational exposures
Organophosphate – starting to be used as plasticisers
Pesticides: glyphosate, pyrifos, 2-4-D, pyrethroids
Phosphorous containing flame retardants
Poly and per fluorinated compounds
Replacement chemicals
Triclosan
UV filters
What we find in sewage treatment plants

Other

Check the Community Rolling Action Plan – identify leads on specific compounds

How to capture personal data and epidemiology in the data base?

ECHA – evaluation process – how can we contribute?

Groups, how can we group chemicals? By compound group or by use?

Include populations that are exposed by “everyday use” as well as populations that are occupationally exposed, as the latter rarely is included in population based biomonitoring studies. As Occupational Exposure Limits/DNELs for work often are derived using much lower uncertainty factors than for consumers and outer environment, occupational exposure may leave very little room for exposure outside of work – as well as the other way round.

Focus measurement on chemicals where there is a possibility for correlation for biomarkers of health, e.g. inflammatory markers.

Focus measurements in fewer populations as this will give an idea of cumulative exposure (without this even being an underlying aim). If this is done in populations, where correlations with biomarkers of health can also be done, it will enable assessment of how exposure to several chemicals interact to affect health (rather than how single chemicals in isolation may affect health).

Summarized input from general discussion to further prioritisation of substances/groups of chemicals

General prioritisation of substances

Toxicity concern

- Concern for CMR, ED, cardiovascular effects, asthma, COPD, allergies, neurological development
- Exposure concern (e.g. Use codes in REACH registrations)
- Tonnages (high volume)
- Also aggregated exposure to groups of substances (e.g. PFAS)
- Phys-Chem data relevant for higher exposure potential (e.g. vapour pressure for inhalation exposure), including nano-forms of substances

Persistency (+Bioaccumulation?)

Consider use of data for each substance?

Support new regulation, Substances with emerging concern

Substances with upcoming regulations? Dialogue with ECHA/EFSA/MS authorities?

Relevant CORAP substances

FAST TRACK procedure?

Understand effects in humans

including exposure to mixtures

Follow time trends of regulated substances, E.g. mercury

Correlation to other/“classic” estimations of exposure

Explore sources

Single substances or groups?

Substance groups – structural similarity

- (analytic methods will often capture structurally similar substances)
- Uses – functional similarity
- Tox knowledge/Mode of action

Considered substances/groups

- Additional metals, e.g. mercury, aluminium, arsenic, zinc
- Triclosan (main purpose: Finding sources to exposure)
- Nanomaterials, both intentional and unintentional
- Microplastics – as vehicles for POPs
- Poly and perfluorinated substances
- Chemical UV filters
- Pesticides?: Glyphosate, pyrifos, 2,4-D
- Phosphorous containing flame retardants
- Organophosphates – starting to be used as plasticisers
- Preservatives
- Particles

Substances of emerging concern

How to identify? (5 parallel considerations, with a relevant scoring system?)

How to define? – agreement on emerging concern.

Exposure

- Use (e.g. Use codes in REACH registrations)
- Tonnages (high volume)
- Also aggregated exposure to groups of substances (e.g. PFAS)
- Non target screening

Toxicity

- (Concern for CMR, ED, cardiovascular, asthma, COPD, allergies, neurological development)
- In vitro activity (e.g. ED) in human samples + identifying substances inducing effects?
- Human samples
- Persistency and bioaccumulation

Prioritised substances:

- Relevant CORAP substances (REACH)
  - How to contribute to REACH evaluation process? Dialogue with relevant Member States?
  - Alternatives to regulated substances with toxicological concern
- Relevant (concerning) alternatives to phthalates
- Relevant (concerning) alternatives to BPA
- Relevant (concerning) alternative PFAS

Further input

- How to capture personal data and epidemiology in database?
- ADME data should be highly prioritised
  - Possible use of in silico modelling
- Occupational health
- Mixtures are of high priority when investigating associations between exposure and effects
  - (ex vivo combined effect biomarkers, e.g. of oxidative stress + mixtures of substances with special effects/MoA, e.g. EDCs)

Overall conclusions from the workshop

The aim of the workshop was to bring together scientists and regulatory specialist from the Nordic countries to discuss priority setting of which substances to include in the biomonitoring programs and how to optimize the communication between scientists and authorities regarding use of HBM data in a regulatory context (e.g. REACH). Overall, the following main conclusions were drawn based on discussions during the workshop and will provide the basis for moving forward in future Nordic collaboration and contribution to HBM4EU.

- The prioritization of substances should be made with the concern of toxicity, exposure and persistency in mind.
- For use of data for each substances there should be considerations on how it can support new regulations, will it provide better understanding on the effect in humans (including exposure to mixtures), is there a time trend in regulated substances, and does it correlate to other estimations of exposure.
- On the subject of whether the substances should be single substances or groups of substances, it is important to consider if the substance groups have structural similarity, the functional similarity and the mode of action
- The substances or groups of substances that the participants find to be most important in the HBM4EU is additional metals, triclosan, nanomaterials, microplastics, poly- and perfluorinated substances, chemical UV-filters, pesticides, phosphorous containing flame retardants, organophosphates, preservatives and particles.
- There is also a need to look at substances of emerging concern. Mostly there is a need to look at how to identify these, how to define these, how great is the exposure, toxicity, and how these are prioritised.
- Further inputs from the discussions are related to how to capture personal data and epidemiology in database, that ADME data should be highly prioritized, that occupational health is a good place to start, and that mixtures are of high priority when investigating associations between exposure and effects

This information is a valuable contribution to feed in to the national advisory groups in the national hubs and subsequently be used as input for applications for EU funding.

Workshop evaluation

After the workshop we have received positive feedback from many of the participants. Mostly the feedback has been that the Nordic collaboration has been improved, and that the participants have been inspired by other participants from the other Nordic countries. Also the participants believe that the Nordic expertise can ensure a Nordic influence on the outcome of the HBM4EU project as a whole and how all can benefit from the shared actions.

Next steps

There was a proposal to arrange a new Nordic workshop/meeting in 2-3 years.

Acknowledgements

This workshop was made possible by grants from Nordic Risk Assessment Project (NORAP) and NEXPO. We would like to sincerely thank all the participants for contributing their time and expertise. We would thank Pernille Danielsen, Department of Public Health for proof reading.

References

<http://www.eea.europa.eu/themes/human/human-biomonitoring>

<http://www.eea.europa.eu/themes/human/human-biomonitoring/prioritisation-and-substances>

Appendix I – Workshop program

Day 1 10.00-16.30

9.00-10.00: Registration and breakfast/coffee at the hotel Lounge Upstairs

1. 10.00-10.15: Welcome and introduction, news from the consortium (Lisbeth E. Knudsen)

- a. 10.10-10.45: Catherine Ganzleben: Status of HBM4EU

2. 10.45-12.00: Status of HBM4EU in each country (chair: Anna-Maria Andersson)

- a. 10.45-10.55: Hanna Tolonen (FIN): The Finnish HBM4EU Hub
- b. 10.55-11.05: Britta Hedlund (S): Health related environmental monitoring in Sweden – Data for HBM4EU
- c. 11.05-11.15: Cathrine Thomsen (N): Biomonitoring projects and analyses work we are conducting in Norway/NIPH which might contribute to HBM4EU
- d. 11.15-11.25: Thorhallur Halldorsson (IS): The Icelandic Hub
- e. 11.25-11.35: Lisbeth E. Knudsen (DK): The Danish Hub
- f. 11.35-11.45: Pal Weihe (FO): The Faroe Island cases

12.00-13.00: Lunch at the hotel at Restaurant La Rocca

3. 13.30-16.30: Prioritization of chemicals (chair: Britta Hedlund)

- a. 13.00-13.20: Anna Karin Lindroos (S): Collecting biomarkers in a national dietary survey
- b. 13.20-13.40: Marie Louise Holmer (DK): Use of human biomonitoring data in regulation of chemicals
- c. **13.40-15.30: Discussion on prioritization of chemicals in groups**

14.30-15.00: Break (coffee/tea and cake)

- d. 15.30-16.00: Summing up of group discussions
- e. 16.00-16.05: Helle Margrete Meltzer (N): Establishing a network on biomonitoring in Russian Karelia
- f. 16.05-16.15: Johan Lindberg (S): Biomarker discovery/qualification for liver-toxicity
- g. 16.15-16.30: Tina Kold Jensen (DK): The Odense Child Cohort

4. 18.30-20 Dinner at the hotel at Restaurant Pinxtos

Day 2 9-15

5. Nordic contributions to WP (chair: Helle Margrete Meltzer)

- a. 9.00-9.10: Marika Berglund (S): Swedish contributions to WP8: Targeted field work surveys and alignment at EU level
- b. 9.10-9.25: Agneta Åkesson (S): The Central Sweden Cohorts & Biobank a National Research Infrastructure
- c. 9.25-9.40: Hanna Tolonen (FIN): WP11 – Linking HBM and health studies, and register data. Nordic involvement now and in future.
- d. 9.40-9.50: Cathrine Thomsen (N): The Norwegian Institute of Public Health's contribution in HBM4EU

9.50-10.00: Break (coffee/tea and cake)

- e. 10.00-10.10: Anna-Maria Andersson (DK): The Capital region of Denmark participation in HBM4EU: focus on linking HBM to health studies and health effects
- f. 10.10-10.20: Hanne Frederiksen (DK): Non-persistent EDCs in Danes: Presentation of HBM-data in present and future studies
- g. 10.20-10.30: Eva Cecilie Bonefeld-Jørgensen (DK): Biomarkers of exposure and effects & Molecular Epidemiology: DK and Greenlandic birth cohorts
- h. 10.30-10.40: Anne Marie Vinggaard (DK): DTU's contribution to HBM4EU
- i. 10.40-10.50: Ulla Birgitte Vogel (DK): NRCWE contributions and interests
- j. 10.50-11.00: Torben Sigsgaard (DK): NorDoc

6. 11.00-12.00: Discussion on prioritization of chemicals (Marie Louise Holmer and Mette Holm)

12.00-13.00: Lunch at the hotel at Restaurant La Rocca

7. 13.00-14.00 Common Nordic interests (chair: Marika Berglund)

- a. 13.00-13.20: Lisbeth E. Knudsen (DK): Ethics in HBM4EU and Training
- b. 13.20-13.40: Kim Kryger (DK): Future funding in EU
- c. 13.40-14.00: Anne Thoustrup Saber (DK): BIOBRAND and BIOTRACK - two ongoing biomonitoring studies of firefighters and train conductors
- d. 14.00-14.15: Marie Frederiksen (DK): Flame retardants and PCB HBM-studies from Denmark
- e. 14.15-14.30: Tiina Santonen (FIN): How to engage Nordic occupational health
- f. 14.30-15.00 Wrap up (chair: Lisbeth E. Knudsen)

Appendix II – Description of NORAP and NEXPO

Nordic Risk Assessment Project – NORAP:

Risk and hazard assessment and risk management with chemicals, including endocrine disruptors, combination effects and social costs. The group develops methods, guidelines and instructions in connection with the implementation of EU and international chemicals regulation. Chair: Lena Höglund DK, e-mail: lemah@mst.dk

Nordic Exposure Group – NEXPO:

Use of chemicals and the exposure of people (at work, as consumers, the general population, both directly and indirectly via the environment) and the environment to chemicals. The group's work includes assessing exposure scenarios, the development and harmonisation of methods, strategies, guidelines, instructions, education and training in methods of exposure assessment, IT tools and databases. The group works at Nordic, European (primarily in the EU/EEA on REACH) and global level (OECD). Chair: Marianne van der Hagen NO, e-mail: marianne.vanderhagen@miljodir.no

Appendix III – HBM4EU partners, governing structure, substances and work packages

Priority substances to start with in the 1st year

Chemical family/Substances	Goals
Phthalates & Hexamoll®DINCH®	time trends, focus on substitutes
Poly/per-fluorinated compounds	baselines, time trends, support regulation, biomarkers of exposure and effect
Brominated & organophosphate flame retardants	baselines, time trends, support regulation, research on health impact
Bisphenol A, S and F	overall human exposure and exposure sources, possible further regulation
Cadmium and Chromium(VI)	overall human exposure and exposure sources, Cr(VI): possible geogr. variation
8 carcinogenic PAHs in REACH, 16 USEPA priority PAHs	overall human exposure, impact of PAHs on public health
Aniline derivatives	exposure of workers
Mixtures	identification of chemical mixtures, assessment of effects
Emerging substances	screening for new substances, non-targeted analysis

Governing Structure of HBM4EU

Why do we need HBM4EU?

- To better understand the consequences of **human exposure to various chemicals**, a key aspect of environmental health
- To bridge the gap between **science and policy making**
- To share **evidence of use** from national programs
- **To share existing experience** in the EU and to share the burden
- To generate better evidence for **better regulation**
- To give better access by a new data-infrastructure - **IPChem**
- To **include aggregate exposure** in the health risk assessment

Appendix IV - The Nordic Hubs

Nordic HBM4EU National Hub Contact Points

Finnish National Hub Contact Point.	
Name of the organisation in your language:	In your language: Terveystieteiden tutkimuskeskus (THL)
	In English: National Institute for Health and Welfare
Contact name:	Hanna Tolonen
Email address:	hanna.tolonen@thl.fi
Telephone number:	+358 29 534 8638
Website address:	http://www.thl.fi
Please note that by providing a contact name and email address, you agree to them being included on the HBM4EU website.	
Work packages and tasks that the organisation is directly involved in: WP1, WP2, WP7, WP8, WP10, WP11, WP15	

HBM4EU partners in Finland.	
Name of the organisation:	In your language: Terveystieteiden tutkimuskeskus (THL)
	In English: National Institute for Health and Welfare
Website address:	https://www.thl.fi/
Work packages and tasks that the organisation is directly involved in: WP1 (Tasks 1.1, 1.2, 1.4, 1.5), WP2 (Tasks 2.2, 2.5), WP7 (Tasks 7.1, 7.3), WP8 (Task 8.3), WP10 (Tasks 10.4, 10.5), WP11 (WP leader, all tasks), WP15 (Tasks 15.1, 15.3)	
Name of the organisation:	In your language: Työterveyslaitos
	In English: Finnish Institute of Occupational Health

Website address:	http://www.ttl.fi/en/
Work packages and tasks that the organisation is directly involved in: WP2 (Task 2.5), WP4 (Task 4.2), WP5 (Task 5.3), WP7 (Task 7.1, 7.3), WP8 (Task 8.5), WP10 (Task 10.4, 10.5), WP11 (Task 11.1), WP12 (Task 12.1, 12.2, 12.3), WP13 (Task 13.2), WP15 (Task 15.3), WP16 (Task 16.1, 16.2, 16.3)	

No HBM4EU linked third parties in Finland

Key stakeholders that work on chemical issues in Finland	
Non-governmental organisations:	
Name of the organisation:	In your language: Turvallisuus- ja kemikaalivirasto (Tukes)
	In English: Finnish Safety and Chemical Agency
Website address:	http://www.tukes.fi
No Industrial federations:	

Icelandic National Hub Contact Point.	
Name of the organisation in your language:	In your language: Háskóli Íslands
	In English: University of Iceland
Contact name:	Thorhallur Ingi Halldorsson
Email address:	tih@hi.is
Telephone number:	+354 5438407
Website address:	http://english.hi.is/
Please note that by providing a contact name and email address, you agree to them being included on the HBM4EU website.	
Work packages and tasks that the organisation is directly involved in: University of Iceland coordinates the National Hub and is directly involved the WP 13, task 13.2 and WP 10 task 10.2.	

HBM4EU partners in Iceland.	
Name of the organisation:	In your language: Landlæknir
	In English: Directorate of Health
Website address:	http://www.landlaeknir.is/english/
Work packages and tasks that the organisation is directly involved in: The Directorate of Health is one of the partners of the Icelandic National Hub	
Name of the organisation:	In your language: Matvælastofnun
	In English: Icelandic Food and Veterinary Authority
Website address:	http://www.mast.is/english
Work packages and tasks that the organisation is directly involved in: The Icelandic Food and Veterinary Authority is one of the partners of the Icelandic National Hub	
Name of the organisation:	In your language: Umhverfisstofnun
	In English: The Environment Agency of Iceland
Website address:	http://www.ust.is/the-environment-agency-of-iceland/
Work packages and tasks that the organisation is directly involved in: The Environment Agency of Iceland is one of the partners of the Icelandic National Hub	
Name of the organisation:	In your language: Matís
	In English: Matís Ltd. - Icelandic Food and Biotech R&D
Website address:	http://www.matis.is/english/
<i>Please add more as required</i>	Matis is one of the partners of the Icelandic National Hub

In Iceland, human biomonitoring falls both directly and indirectly under the remit of three different governmental agencies: The Directorate of Health (under the Minister of Welfare), The Icelandic Food and Veterinary Authority (under the Ministry of Industries and Innovation) and The Environment Agency of Iceland (under the Ministry for the Environment). When it comes to human biomonitoring these agencies usually work closely with researcher at the University of Iceland and Matis both in terms of sharing of expertise and data. As a result the National Hub consists of these key partners. The

HBM4EU initiative provides an excellent opportunity for better sharing of resources and expertise which will lead to more focus and ambitious human biomonitoring projects being conducted in the future.

Norwegian National Hub Contact Point.	
Name of the organisation in your language:	In your language: Folkehelseinstituttet
	In English: Norwegian Institute of Public Health
Contact name:	Cathrine Thomsen
Email address:	Cathrine.Thomsen@fhi.no
Telephone number:	+47 21 07 65 46
Website address:	www.fhi.no
Please note that by providing a contact name and email address, you agree to them being included on the HBM4EU website.	
Work packages and tasks that the organisation is directly involved in: WP6 task 6.3, WP8 task 8.1 and 8.4, WP9 task 9.1, WP10 task 10.4 and 10.5, WP11 task 11.5, WP13 task 13.1 and 13.2 and WP14 task 14.2 and 14.3.	
Norwegian Institute of Public Health	

HBM4EU partners in Norway	
Name of the organisation:	In your language: Helse- og omsorgsdepartementet (PO)
	In English: Ministry of Health and Care Services
Website address:	https://www.regjeringen.no/en/dep/hod/id421/
Work packages and tasks that the organisation is directly involved in:	
Regjeringen.no	

The Norwegian Institute of Public Health (NIPH) is a governmental institution placed directly under the Ministry of Health and Care Services (PO). The institute is a national centre in the areas of epidemiology, mental health, infectious diseases control, environmental medicine and drug abuse. The NIPH is PM in HBM4EU and the National Hub Contact Point in Norway.

NIPH will be involved in all Pillars of HBM4EU where we will act as advisors and co-workers as to the handling, evaluation and interpretation of all biomonitoring data. In addition we foresee to be contributing to the chemical analyses to be undertaken in the course of the project, and furthermore, with samples and data from the Norwegian Environmental Biobank. NIPH will also contribute with toxicological expertise covering toxico-kinetics, adverse outcomes, mode of action, adverse outcome pathways and biomarker of effects development. NIPH's toxicology-, analyses- and nutrition experts have longstanding experience with all aspects of biomonitoring; from planning and implementing studies to clinical investigations, data handling, statistics and writing up and communicating results.

Please identify the **key stakeholders** that work on chemical issues in Norway.

Non-governmental organisations:

Name of the organisation:	In your language: Framtiden i våre hender
	In English:
Website address:	https://www.framtiden.no/
Name of the organisation:	In your language: Miljøstiftelsen Bellona
	In English: Bellona
Website address:	http://bellona.no/
Name of the organisation:	In your language: Greenpeace Norge
	In English: Greenpeace Norway
Website address:	http://www.greenpeace.org/norway/no/

Governmental organisations:

Name of the organisation:	In your language: Miljødirektoratet
	In English: Norwegian Environment Agency

Website address:	http://www.miljodirektoratet.no/
Name of the organisation:	In your language: Helsedirektoratet
	In English: Norwegian Directorate of Health
Website address:	https://helsedirektoratet.no/English
Name of the organisation:	In your language: Statens Arbeidsmiljøinstitutt
	In English: STAMI – The National Institute of Occupational Health
Website address:	https://stami.no/en/
Name of the organisation:	In your language: Mattilsynet
	In English: Norwegian Food Safety Authority
Website address:	https://www.mattilsynet.no/language/english/
Name of the organisation:	In your language: Vitenskapskomiteen for mattrygghet
	In English: Norwegian Scientific Committee for Food Safety
Website address:	http://www.english.vkm.no/

Swedish National Hub Contact Point.	
Name of the organisation in your language:	In your language: Naturvårdsverket
	In English: Swedish Environmental Protection Agency
Contact name:	Britta Hedlund, Karin Norström, Linda Linderholm
Email address:	forename.lastname@swedishepa.se
Telephone number:	+46 8 698 10 00
Website address:	www.naturvardsverket.se (in Swedish) http://www.swedishepa.se/ (in English)
Please note that by providing a contact name and email address, you agree to them being included on the HBM4EU website.	
Work packages and tasks that the organisation is directly involved in: As a National Hub Contact Point we are involved in WP 1-2, WP 4-7, WP 9-11, WP 15	

Please provide us with details of all HBM4EU partners in Sweden.	
Name of the organisation:	In your language: Kemikalieinspektionen In English: Swedish Chemicals Agency
Website address: 	http://www.kemi.se (in Swedish) http://www.kemi.se/en (in English)
Work packages and tasks that the organisation is directly involved in: Member of the National Hub	
Name of the organisation:	In your language: Livsmedelsverket In English: National Food Agency
Website address: Livsmedelsverket NATIONAL FOOD AGENCY, SWEDEN	http://www.livsmedelsverket.se (in Swedish) http://www.livsmedelsverket.se/en/ (in English)
Work packages and tasks that the organisation is directly involved in: Member of the National Hub	
Name of the organisation:	In your language: Forskningsrådet Formas In English: The Swedish Research Council Formas
Website address: The Swedish Research Council Formas Committed to excellence in research for sustainable development	http://www.formas.se (in Swedish) http://www.formas.se/en (in English)
Work packages and tasks that the organisation is directly involved in: Invited to the National Hub	
Name of the organisation:	In your language: Arbetsmiljöverket In English: Swedish Work Environment Authority
Website address: SWEDISH WORK ENVIRONMENT AUTHORITY	http://www.av.se (in Swedish) http://www.av.se/en (in English)
Work packages and tasks that the organisation is directly involved in:	

Invited to the National Hub	
Name of the organisation:	In your language: Folkhälsomyndigheten
	In English: The Public Health Agency of Sweden
Website address:	http://www.folkhalsomyndigheten.se (in Swedish) https://www.folkhalsomyndigheten.se/the-public-health-agency-of-sweden/ (in English)
The Public Health Agency of Sweden	
Work packages and tasks that the organisation is directly involved in:	
Member of the National Hub	

HBM4EU linked third parties in Sweden.	
Name of the organisation:	In your language: Karolinska Institutet
	In English: Karolinska Institute
Website address:	http://ki.se (in Swedish) http://ki.se/en/startpage (in English) Links to the departments involved: Institute for Environmental medicine: http://ki.se/imm/start (in Swedish) http://ki.se/en/imm/startpage (in English) SWETOX: http://swetox.se (in Swedish) http://swetox.se/en/ (in English)
Karolinska Institutet	
Work packages and tasks that the organisation is directly involved in:	
WP 7-11, WP 13, WP 15	
Name of the organisation:	In your language: Umeå Universitet
	In English: Umeå University
Website address:	http://www.umu.se (in Swedish) http://www.umu.se/english/?languageId=1 (in English)
Umeå Univers	
Link to the department involved:	
http://www.phmed.umu.se/enheter/envmed/ (in Swedish) http://www.phmed.umu.se/english/units/envmed/?languageId=1 (in English)	

Work packages and tasks that the organisation is directly involved in: WP 11	
Name of the organisation:	In your language: Lunds Universitet
	In English: Lund University
Website address: LUND UNIVERSITET	http://www.lu.se (in Swedish) http://www.lunduniversity.lu.se/ (in English) Link to the department involved: http://ammlund.se/ (in Swedish) http://ammlund.se/uk.html (in English)
Work packages and tasks that the organisation is directly involved in: WP 9	

The activities within the Swedish National Hub is in many ways connected to our national Health Related Monitoring Programme which is a part of the Monitoring programme coordinated by the Swedish EPA. Except this the HUB can gain experience from other research programmes that the partners and linked third parties and involved in.   Link to the data host for monitoring data: http://ki.se/en/imm/health-related-environmental-monitoring-hami

Key stakeholders that work on chemical issues in Sweden.	
Non-governmental organisations:	
Name of the organisation:	In your language: Naturskyddsföreningen
	In English: Swedish Society for Nature Conservation (SSNC)
Website address: Naturskyddsföreningen	http://www.naturskyddsforeningen.se (in Swedish) http://www.naturskyddsforeningen.se/in-english (in English)
Name of the organisation:	In your language: CHEMSEC
	In English: CHEMSEC - THE INTERNATIONAL CHEMICAL SECRETARIAT

Website address:	http://chemsec.org (in English)
Industrial federations:	
Name of the organisation:	In your language: IKEM Innovations- och kemiindustrierna i Sverige
	In English: Innovation and Chemical Industries in Sweden
Website address:	http://www.ikem.se (in Swedish) http://www.ikem.se/in_english (in English)
Name of the organisation:	In your language: Kosmetik- och Hygienföretagen
	In English: The Swedish Cosmetics, Detergents and Toiletries Association
Website address:	http://www.kohf.se (in Swedish) https://www.kohf.se/om-kohf/kohf-in-english/ (in English)
Trade union organisation:	
Name of the organisation:	In your language: Landsorganisationen i Sverige
	In English: The Swedish Trade Union Confederation
Website address:	http://www.lo.se (in Swedish) http://www.lo.se/english/startpage (in English)

Danish National Hub Contact Point.	
Name of the organisation in your language:	In your language: Københavns Universitet
	In English: University of Copenhagen
Contact name:	Lisbeth E. Knudsen
Email address:	liek@sund.ku.dk
Telephone number:	+45 35327653
Website address:	www.ku.dk
Please note that by providing a contact name and email address, you agree to them being included on the HBM4EU website. I agree	
Work packages and tasks that the organisation is directly involved in: WP1 Task 1.6 WP2 Task 2.8	
UNIVERSITY OF COPENHAGEN	

HBM4EU partners in Denmark.	
Name of the organisation:	In your language: Region Hovedstaden (Region H)
	In English: Capital Region of Copenhagen
Website address:	www.regionh.dk
Work packages and tasks that the organisation is directly involved in: WP 8-13	
Name of the organisation:	In your language: Det Nationale Forskningscenter for arbejdsmiljø
	In English: National Research Centre for the Working Environment
Website address:	www.nrcwe.dk
Work packages and tasks that the organisation is directly involved in: WP14	
Name of the organisation:	In your language: DTU Fødevareinstituttet
	In English: National Food Institute

Website address:	http://www.food.dtu.dk/
Work packages and tasks that the organisation is directly involved in: WP5, WP14, WP15 & WP16	

The Capital Region
of Denmark

NATIONAL RESEARCH CENTRE
FOR THE WORKING ENVIRONMENT

Please provide us with details of all HBM4EU linked third parties in your country.	
Name of the organisation:	In your language: Københavns Universitet In English: University of Copenhagen
Website address:	www.ku.dk
Work packages and tasks that the organisation is directly involved in: WP1, WP2 Task 1.6, task 2.8	
Name of the organisation:	In your language: Syddansk Universitet (SDU) In English: University of Southern Denmark
Website address:	www.SDU.dk
Work packages and tasks that the organisation is directly involved in: WP10,11,13	
Name of the organisation:	In your language: Århus Universitet In English: Aarhus University
Website address:	http://www.au.dk/
Work packages and tasks that the organisation is directly involved in: WP9 (Laboratory analyses and quality ass.) and WP14 (Effect Biomarkers)	

Key stakeholders that work on chemical issues in Denmark.	
Governmental organisations:	
Name of the organisation:	In your language: Miljøstyrelsen
	In English: Environmental Protection Agency
Website address:	www.mst.dk
Name of the organisation:	In your language: Fødevarestyrelsen
	In English: Danish Veterinary and Food Administration
Website address:	www.foedevarestyrelsen.dk
Name of the organisation:	In your language: Arbejdstilsynet
	In English: Danish Working Environment Authority
Website address:	www.at.dk
Name of the organisation:	In your language: Sundhedsstyrelsen
	In English: Danish Health Authority
Website address:	www.sst.dk/
Name of the organisation:	Styrelsen for Forskning og Uddannelse (Observer)
	Danish Agency for Science and Higher Education (Observer)
Website address:	http://ufm.dk/en/the-minister-and-the-ministry/organisation/danish-agency-for-science-and-higher-education?set_language=en&cl=en (page in English)

Appendix V – List of participants

Country/Name	Institution	Email address	WP
Finland			
Kiviranta, Hannu	National Institute for Health and Welfare (THL)	Hannu.Kiviranta@thl.fi	
Korhonen, Hanna	Ministry of Social Affairs and Health	hanna.korhonen@stm.fi	Ministerial Adviser, responsible for REACH and CLP
Santonen, Tiina	National Institute of Occupational Health	Tiina.Santonen@ttl.fi	Occupational Health
Tolonen, Hanna	National Institute for Health and Welfare (THL)	hanna.tolonen@thl.fi	WP11 leader; Member of Management Board, Member of Ethics Board; Partner in WP7: tasks 7.1 and 7.3; Partner in WP8: task 8.4
Iceland			
Jörundsdóttir, Hrönn Ólína	Matís ohf. - Icelandic Food and Biotech R&D	hronn@matis.is	
Halldórsson, Þórhallur Ingi	University of Iceland	tih@hi.is	National Hub Contact Person Partner in 10.2A
Faroe Islands			
Pál Weihe	Faroe Health	pal@health.fo	
Norway			
Cequier, Enrique Mancinereas	Norwegian Institute of Public Health	EnriqueMancinereas.Cequier@fhi.no	Partner WP9, WP10 and WP11
Meltzer, Helle Margrete	Norwegian Institute of Public Health	HelleMargrete.Meltzer@fhi.no	Partner WP8 and WP11, task leader WP11.5.
Suleiman, Abdulqadir	Arbeidstilsynet	abdulqadir.suleiman@arbeidstilsynet.no	
Thomsen, Cathrine	Norwegian Institute of Public Health	Cathrine.Thomsen@fhi.no	National Hub Contact Person, Governing board as Technical person, Partner in WP9 and WP10, task leader WP9.1
Sweden			
Berglund, Marika	Karolinska Institute	Marika.Berglund@ki.se	WP 7 (7.2, 7.4), 8 (8.1, 8.2 task lead), 9.1, 10.4, 11.5, 13.2 and 15.2
Darnerud, Per Ola	National Food Agency	PerOla.Darnerud@slv.se	
Hedlund, Britta	Environment Protection Agency	Britta.Hedlund@naturvardsverket.se	National Hub Contact Person
Lindberg, Johan	Swetox	johan.lindberg@swetox.se	
Lindroos, Anna Karin	National Food Agency	AnnaKarin.Lindroos@slv.se	
Norstrom, Karin	Environment Protection	Karin.Norstrom@Naturvardsverket.se	

	Agency		
Warholm, Margareta	Swedish Chemicals Agency	Margareta.Warholm@kemi.se	
Åkesson, Agneta	Karolinska Institute	agneta.akesson@ki.se	WP 7 (7.2, 7.4), 8 (8.1, 8.2 task lead), 9.1, 10.4, 11.5, 13.2 and 15.2
Denmark			
Andersson, Anna-Maria	Dept. of Growth and Reproduction, Region H	Anna-Maria.Andersson@regionh.dk	WP 8-13, Governing board as Technical person
Bonefeld-Jørgensen, Eva Cecilie	Centre for Arctic Health & Molecular Epidemiology, Aarhus University, Aarhus	ebj@ph.au.dk mailto:	WP14
Frederiksen, Hanne	Dept. of Growth and Reproduction, Region H	Hanne.Frederiksen@regionh.dk	WP 8-10
Frederiksen, Marie	National Research Centre for the Working Environment	mef@arbejdsmiljoforskning.dk	WP14
Grandjean, Philippe	University of Southern Denmark	PGrandjean@health.sdu.dk	W11
Hansen, Heidi Katrine	University of Copenhagen	heidihan@sund.ku.dk	
Hansen, Pernille Winton	University of Copenhagen	pwha@sund.ku.dk	
Holm, Mette	Danish Veterinary and Food Administration	METH@fvst.dk	Governing board as member
Holmboe, Stine Agergaard	Dept. of Growth and Reproduction, Region H	stine.agergaard.holmboe@regionh.dk	WP11
Holmer, Marie Louise	Danish Environmental Protection Agency	mlh@mst.dk	
Hougård, Karin Sørig	National Research Centre for the Working Environment	ksh@arbejdsmiljoforskning.dk	WP14
Höglund, Lena Marianne	Danish Environmental Protection Agency	lemah@mst.dk	
Jensen, Tina Kold	University of Southern Denmark	tkjensen@health.sdu.dk	WP11
Klint, Mikala	Danish Environmental Protection Agency	mkl@mst.dk	
Knudsen, Lisbeth E.	University of Copenhagen	liek@sund.ku.dk	National Hub Contact Person WP1: Ethics, WP2 Training
Kryger, Kim	Danish Agency for Science and Higher Education	klk@fi.dk	
Nørmark, Susanne	TREALIV	info@trealiv.com	
Saber, Anne T	National Research Centre	ats@arbejdsmiljoforskning.dk	WP14

	for the Working Environment		
Sigsgård, Torben	Aarhus University	ts@ph.au.dk	
Svingen, Terje	National Food Institute, Technical University of Denmark	tesv@food.dtu.dk	
Vind, Nanna Rosted	Danish Working Environment Authority	nrv@at.dk	
Vinggaard, Anne Marie	National Food Institute, Technical University of Denmark	annv@food.dtu.dk	WP14
Vogel, Ulla Birgitte	National Research Centre for the Working Environment	UBV@arbejdsmiljoforskning.dk	WP14
Vorkamp, Katrin	Aarhus University	kvo@envs.au.dk	WP9

Appendix VI – Abstracts of presentations

Status of the HBM4EU in each country

Hanna Tolunen (FIN): The Finnish HBM4EU Hub

Finnish National Hub is been established during the spring 2017. In current plan, Finnish National Hub would include the Ministry of Social Affairs and Health (STM), the National Institute for Health and Welfare (THL), the Finnish Institute of Occupational Health (FIOH) and the Finnish Safety and Chemicals Agency (Tukes).

STM (<http://stm.fi/en/frontpage>) is charge of planning, steering and implementation of social and health policy. Their goal is to ensure that everyone has an equal opportunity to lead a healthy and socially secure life. STM is the project owner for Finland in HBM4EU.

THL (<https://www.thl.fi/en/web/thlfi-en>) and development institute under the Finnish Ministry of Social Affairs and Health aiming to promote health and welfare in Finland. They provide reliable information on health and welfare for use in decision-making and activities in the field. Provided information is based on research on population health and welfare, effectiveness of health and welfare policies and services, as well as environmental health and social problems. THL has large data resources such as population based health examination surveys which have biobanked samples together with wide selection of physical health measurements and questionnaire information, and possibility for follow-up (mortality and morbidity) through register linkage to support this research. THL is the project manager in HBM4EU.

FIOH (<https://www.ttl.fi/en/>) is specialized in well-being at work, research, advisory services and training and they operate under the Ministry of Social Affairs and Health. FIOH targets their activities so that they create improved well-being at workplaces and help extend working careers. Proposed solutions are based on research evidence and reliable methods that work in practice. FIOH has long traditions in the biomonitoring of occupational exposure. It conducts both research related to biomonitoring and provides biomonitoring services to workplaces. FIOH is the project manager in HBM4EU.

Tukes (<http://tukes.fi/en/>) supervises and promotes the technical safety and conformity, together with the consumer and chemicals safety in Finland. They supervise products, services and production systems in their branches, and enforce the relevant legislation.

Britta Hedlund (S): Health related environmental monitoring in Sweden – Data for HBM4EU

Britta Hedlund and Karin Norström, Swedish Environmental Protection Agency

The Swedish EPA has the overall responsibility for coordinating national and regional environmental monitoring which includes ten program areas. One of these areas is the program for Health Related Environmental Monitoring – HÄMI. Studies concerning the relationship regarding environmental factors and effects on human health started in 1993. The Institute of Environmental Medicine (IMM) at the Karolinska institute is the host for data collected in national and regional health-related environmental monitoring.

HÄMI should on a long term basis monitor factors in the environment that can affect the human health. The focus of the programme is to estimate exposure of hazardous substances from the environment and to follow indicators of human exposure. Studies are also performed to link exposure to possible health effects by evaluating certain health indicators. The results that are gained within HÄMI should be able to show trends in human exposure and to show possible effects of actions, e.g. from regulatory work. The results are also used for international environmental reporting.

Ongoing investigations are analyses of hazardous substances in blood, mother's milk, urine and hair and both metals and organic pollutants are considered depending on the matrix. For mother's milk, blood and urine there are number of time trends available. Also pollutants in air are studied to make correlations with e. g. asthma, as well as exposure studies with personal sampling. Exposure of noise is also an example of data generated by HÄMI.

Concerning the substances initially prioritized within HBM4EU, we have Swedish data for "classic" PFAS, phthalates, bisphenols, brominated flame retardants and cadmium for different matrices. We also have data on PAH regarding personal sampling of air exposure. Populations where these groups of substances have been studied are e.g. first time mothers in Uppsala, men and women from the south and northern parts of Sweden, young children, mother and child pairs, as well as the general population. These data will be briefly presented in the presentation given.

Further, in an ongoing study, children from several areas in Sweden will be analysed for new brominated flame retardants and for less well known PFAS, such as precursors and replacement PFAS.

Cathrine Thomsen (N): Biomonitoring projects and analyses work we are conducting in Norway/NIPH which might contribute to HBM4EU

Cathrine Thomsen, Helle Margrete Meltzer, Norwegian Institute of Public Health

The Norwegian Institute of Public Health (NIPH) has long experience in exposure characterisation of environmental toxicants and runs a well-equipped laboratory for chemical analyses, primarily focussed towards human biomonitoring. We have recently started the “Norwegian Environmental Biobank” nested within the Norwegian Mother and Child Cohort study (MoBa) and are presently finishing a sample collection where we have recruited family triads (mother, father, child $n \approx 500-650$). The main goal is to obtain an overview of the population’s exposure to environmental pollutants over time and assess the impact of this exposure on a number of health outcomes. As all Norwegians have their unique personal identification number, we have the possibility to link this cohort to the numerous questionnaires already collected in MoBa as well as to other national health registries. MoBa (see www.fhi.no/morogbarn) is a nationwide pregnancy cohort of approximately 114,500 children. Women were recruited between 1999 and 2008 through a postal invitation in connection with a routine ultrasound examination offered to all pregnant women in Norway during weeks 17–18 of gestation. The participation rate was 41 %. Biological samples from mother, father and child were collected and stored in a state-of-the-art biobank in Oslo, Norway. The mothers filled in a comprehensive food frequency questionnaire (FFQ) and other questionnaires including exposure and potential confounders, and information has also been collected from the father. The mothers and children are followed up through questionnaires during childhood. Pregnancy and birth records from the Medical Birth Registry of Norway (MBRN) are linked to the MoBa database.

The Department of Environmental Exposure and Epidemiology at NIPH performs chemical analytical research on human exposure to persistent and non-persistent organic pollutants with a focus on biomonitoring of breast milk, blood and urine. We have long-term experience with human biomonitoring of environmental pollutants and have at present validated and published methods for numerous of the compounds that will be under focus the first years in HBM4EU. State of the art instrumental methods available include automated solid phase extraction and clean-up, GC-LRMS, GC-MS/MS, LC-MS/MS using online extraction and clean-up methods, as well as an LC-QToF that can be used both for targeted and non-targeted analyses and used in e.g. metabolomic approaches.

NIPH is presently involved in the HELIX-project; The Human Early Life Exposome, funded through FP7 (308333). The HELIX ‘early-life exposome approach involves combining all environmental hazards that mothers and children are exposed to and linking these to the health, growth and development of the children. In-utero and early life exposure to a wide range of environmental contaminants across six European cohorts has been assessed through biomonitoring performed at our laboratory; these data are likely to be a valuable contribution to the HBM4EU project.

Thorhallur Halldorsson (IS): The Icelandic Hub

Lisbeth E. Knudsen (DK): The Danish Hub

Pál Weihe (FO): Temporal tendencies of developmental exposures in Faroese birth cohorts

Pál Weihe: The Faroese Hospital System and The University of Faroe Islands

Introduction

In order to study long-term health effects of prenatal and postnatal exposure to pollutants a longitudinal study was initiated on the Faroe Islands in 1986. Given the advantages of conducting such research in the Faroe Islands, four prospective Faroese Birth Cohorts have since then been established with multiple follow-up examinations at different intervals and ages.

Methods and results

The first cohort was established in 1986-1987 and includes 1022 singleton births assembled from consecutive deliveries at the three Faroese Hospitals (75% of all births). The mean (geometric mean) mercury concentration in cord blood was 22.3 µg/L and 4.17 µg/g in hair, PCB concentration in cord blood was 1.8 µg/L (adjusted to a mean lipid concentration of 3 g/L, the PCB concentration was 0.6 µg/g lipid) while DDE levels were 0.3 µg/L (lipid adjusted, DDE concentration was 0.1 µg/g lipid). The perfluorinated alkylate substances (PFASs) were also measured. The GM of perfluorooctanesulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) in cord blood were 2.7 µg/L and 1.8 µg/L respectively.

As a follow-up, Cohort 2 was established in 1994-1995 and included 182 singleton term births at the hospital in Tórshavn, Faroe Islands (64% of all births). In this cohort, the mean MeHg concentration in cord blood was 21.0 µg/L and 4.1 µg/g in maternal hair. The GM for maternal serum PCB was 1.1 µg/g lipid and mean serum-DDE concentration was 0.7 µg/g lipid.

New insight into health risks caused by environmental pollutants and changing exposure patterns in the Faroes led to the formation of Cohort 3 in 1997-2000 including 656 children (~ 60% of all pregnancies). In Cohort 3, the MeHg and DDE exposure had declined – the mean MeHg concentration in cord blood was 12.4 µg/L, in hair 2.1 µg/g and mean serum-DDE concentration was 0.5 µg/g lipid. However, the PCB levels were still high with mean maternal serum-PCB concentration of 1.2 µg/g lipid. The GM of PFOS and PFOA in maternal serum were 27.4 µg/L and 3.2 µg/L respectively.

The most recent of Faroese cohort, Cohort 5, was established in 2007-2009 and included 490 singleton births (~ 70% of births in that period). In cohort 5, the Hg exposure had declined substantially, with the GM being 4.8 µg/L in cord blood and 0.7 µg/g hair. The PCB, DDE and some PFASs had also begun to decline. The GM for serum-PCB was 0.4 µg/g lipid and mean serum-DDE concentration was 0.1 µg/g lipid while maternal GM for serum PFOS and PFOA were 8.0 µg/L and 1.4 µg/L respectively.

Discussion

While Hg levels in pilot whales have not decreased over the last three decades, concentrations in the blood of pregnant women have decreased significantly. While a dietary shift can be caused by several factors, it is likely that the risk communication undertaken in the Faroe Islands was the driving force for the decreases in human tissue levels of Hg, PCB and PFOS/PFOA for several reasons.

Prioritization of chemicals

Anna Karin Lindroos (S): Collecting biomarkers in a national dietary survey

Anna Karin Lindroos, PhD, Risk- and Benefit Assessment Department, the National Food Agency, Sweden

Sweden has conducted several national dietary surveys since the 1980s where detailed information on food intake has been collected. The detailed information is used to monitor food consumption patterns, identify nutrients at risk of being too low and form a base for to assessment of exposure of unwanted substances from foods. Collecting blood and urine together with detailed information on food intake makes it possible to study the sources of the unwanted substances, identify groups at risk of nutrition deficiency or high exposure of unwanted substances and thus go beyond simple descriptive differences. In the Swedish adult survey in 2010-11 it was therefore decided to also collect blood and urine samples in a sub-group. This additional data collection was made possible through support from the Swedish Environmental Protection Agency. Although the data analyses were somewhat limited by the small sample size (around 300 participants), the results on PCBs and chloropesticides, heavy metals, PFAS and phthalates gave informative results on associations between levels of contaminants in biological matrices and dietary and life style factors.

In the next Swedish national dietary survey it was decided to include human biomonitoring (HBM) in a bigger study group. During the school year 2016 and 2017 the NFA is conducting a national dietary survey in adolescents- The Riksmaten Adolescent Survey. Children and adolescents in grade 5 (aged 11-12 years), grade 8 (14-15 years) and 2nd year of high school (17-18 years) are recruited through randomly selected schools around Sweden. The aim is to examine at least 3000 students. In the survey participants report all foods and drinks consumed together with detailed portion size description for three days, in new web-based web-application. They also complete on-line questionnaires on socioeconomy, demographics, health dietary supplements and frequencies of infrequently eaten food s. Weight and height are measured and physical activity measured for 7 days. In addition 1200 students are asked to donate blood and urine. The blood and urine collection is done in collaboration with Occupational and Environmental Medicine clinics in Sweden (Linköping, Lund, Gothenburg, Stockholm, Umeå). At the examination day, field workers from the Riksmaten Adolescent survey and the Occupational and Environmental Medicine clinics visit the school together. The blood and urine collection has sometimes been a challenge as rooms and conditions for blood and urine sampling differ greatly between schools. The different, and sometimes difficult conditions, has made it possible to use the survey as a training opportunity for a crises situation when it is necessary to rapidly set up an organisation for collecting blood and urine in field. This part of the work has therefore been supported by the Swedish Civil Contingencies Agency. The data collection has so far been successful, and in March 2017 over 2500 students have participated in the survey and blood and urine has been collected from around 850 students of the participants. We expect that the HBM part of the Riksmaten study will generate important information on levels of a number of contaminants in Swedish adolescents, and on their possible associations with a number of life style and environmental factors.

Marie Louise Holmer (DK): Use of human biomonitoring data in regulation of chemicals

Marie Louise Holmer, Danish Environmental Protection Agency

In regulation of chemicals, human biomonitoring data can be used for prioritization of substances for further scrutiny, to support risk assessment of substances, to aid in the assessment of costs for society of exposure to substances, and as a follow up to evaluate the effects of regulatory actions. Human biomonitoring data provide specific information about exposure for decision makers. However, human biomonitoring data are not a prerequisite for regulation of chemical substances, and several issues complicate the use of these data. For example adequate knowledge for regulatory use is most often not available for each specific substance. This includes knowledge about metabolism (are all metabolites measured and is the substance maybe a metabolite of another substance), what does the measured (e.g. urinary) level mean in relation to which level people are/have been exposed to (requires thorough knowledge of absorption, distribution, metabolism and excretion of each substance, which may also differ between ages and genders) and what are the sources for exposure (to guide proper regulatory action). These advantages and challenges will be illustrated by use of some recent regulatory cases.

Johan Lindberg (S): Biomarker discovery/qualification for liver-toxicity.

Untargeted monitoring of low molecular analytes in various biological matrixes using HR-LC/MS is a powerful method to discover novel biomarkers. Data from preclinical studies, clinical studies and in vitro models will be shown to illustrate how novel biomarkers can be further qualified/validated for clinical usage.

Tina Kold Jensen (DK): The Odense Child Cohort

Jensen TK^{1,2}, Kyhl H^{1,4}, Barington T^{3,4}, Buhl S⁵, Jørgensen JS⁶, Christesen HT¹, Høst A¹, Husby S¹.

1. Hans Christian Andersen Children's Hospital; 2. Department of Environmental Medicine, University of Southern Denmark; 3. Department of Clinical Immunology, Odense University Hospital; 4. Odense Patient data Explorative Network (OPEN); 5. Odense City Government and Administration, Department for Child and Family, Centre for Health; 6. Department of Gynecology and Obstetrics, Odense University Hospital

The Odense Child Cohort (OCC) included newly pregnant women residing in the Municipality of Odense, Denmark, between 2010 and 2012 were recruited at a voluntary information meeting about ultrasound examinations, at first antenatal midwife visit, or at the ultrasound examination at Odense University Hospital at gestational age 8–16 weeks. Of the eligible population of 6,707 pregnant women, 4,017 women were informed about the study and 2,874 (42.9%) enrolled in the cohort; and 2,551 live life births are being followed up at age of 18 years. Women donated a blood sample before 16 completed weeks of gestation. At 28 weeks of gestation the women collected urine samples (spot and 24 hours) and some had an oral glucose tolerance test performed. At birth blood from the placenta and umbilical cord was collected. The children were and will be examined at 3 and 18 months and 3, 5, 7, 9, 12, 15, and 18 years of age. Weight, length, congenital malformations, blood pressure, skin fold thickness, skin colour and anogenital distance will be measured. On each occasion, parents are asked to give permission for a blood sample to be taken from their child. We have measure BPA, TCS, BP3, phthalates, PFAS and pyrethoid pesticide and organophosphate.

Nordic contributions to WP

Marika Berglund (S): Swedish contributions to WP8: Targeted field work surveys and alignment at EU level

Marika Berglund, Institute of Environmental Medicine, Karolinska Institutet

The Human biomonitoring for Europe (HBM4EU) project aims to develop a sustainable human biomonitoring programme to support chemical regulation and enhance knowledge of the relationship between exposure to chemicals in the daily environment and human health.

Several European countries already perform human biomonitoring activities for exposure monitoring, status and trend and risk assessment purposes, as well as for health research in the area of environmental medicine. One challenge of the HBM4EU project is to align ongoing and new studies, where feasible, to produce EU level data and to counteract fragmentation. The first step would be to make an inventory of ongoing activities for which harmonisation is possible, cost-effective and would lead to a larger database and increased knowledge.

Sweden has since long a health related environmental monitoring programme (HÄMI), coordinated and financed by the Swedish EPA. This programme is focused on exposure and human biomonitoring in small groups of the population, typically risk groups, for evaluation of time trends in environmental pollutants and chemicals, for follow up of the environmental goals, and minor focus on health effects. Currently, there is a strong support for increased resources for HÄMI and strengthening of the linkage between HÄMI and health research.

There are a number of candidate Swedish studies that could support the European initiative HBM4EU and that may benefit from alignment with other national and European activities. Examples are the Swedish national dietary survey in which 24 h dietary recall and biomonitoring is performed, as well as prospective population based cohort studies among adults and children, and health examination studies, with repeated biological sampling.

Thus, there is a possibility to benefit from already collected samples stored in biobanks for evaluation of past exposure and identification of data gaps on the EU level. These samples are typically linked with clinical and health data and other individual information, e.g. from disease and mortality cause registers. The challenge is to get access to these precious samples in large enough volumes to perform chemical analyses and link the results with the personal information.

Agneta Åkesson (S): The Central Sweden Cohorts & Biobank a National Research Infrastructure

Agneta Åkesson, Institute of Environmental Medicine, Karolinska Institutet.

The Central Sweden Cohorts & Biobank consist of two large population-based cohorts; the Swedish Mammography Cohort (SMC) consisting of more than 60 000 women born 1914-1948, and the cohort of Swedish Men (COSM) consisting of over 40 000 men born 1918-1952. The SMC was established in 1987–1990 (together with a mammography screening program) with the aim to explore dietary exposures in relation to breast cancer risk and has since been expanded to assess risk of various health outcomes. The participation rate was very high (74%). The COSM was established 10 years later, in 1997, with the aim to explore diet and lifestyle in relation to chronic diseases. Since then, additional questionnaire data have been collected and sub-cohorts with biological specimens have been established making these cohorts a valuable resource for the scientific community. Using each participant's Swedish personal identity number, the SMC and the COSM are linked annually to multiple registries to ensure up to date information on all participants' health status including prescribed drug use. A large number of incident diseases and deaths have been ascertained, ensuring high statistical power in studies. Disease information include cardiovascular diseases, cancers, diabetes, rheumatoid arthritis, fractures, cataract extraction, kidney stones, etc. A physical health examination was initiated in 2003 and more than 10 000 individuals have donated blood and urine samples to a biobank. Also fat biopsies, saliva and fecal sampling have been performed in subgroups. In addition to diet and other modifiable lifestyle factors, several environmental contaminants have been assessed, either estimated via the food frequency questionnaire or measured in blood or urine (including metals, PCBs, MeHg) and several validation studies have been performed. The cohorts could be expanded to include also information on occupational exposures via registers. More than 500 publications have been published. Principal investigator Prof Alicja Wolk

Webpages:

[http://ki.se/en/imm/the-swedish-mammography-cohort-smc;](http://ki.se/en/imm/the-swedish-mammography-cohort-smc)

[http://ki.se/en/imm/swedish-mammography-cohort-clinical-smc-c;](http://ki.se/en/imm/swedish-mammography-cohort-clinical-smc-c)

<http://ki.se/en/imm/cosm-a-cohort-of-50000-swedish-men>

<http://ki.se/en/imm/cohort-of-swedish-men-clinical-cosm-c>

Hanna Tolonen (FIN): WP11 – Linking HBM and health studies, and register data. Nordic involvement now and in future.

The objectives of the WP11 are:

- Evaluate opportunities and obstacles related to linking HBM, health surveys and administrative data sources.
- Evaluate of existing biological samples from health studies which could be used to analyse HBM biomarkers.
- Provide tools for linking HBM and health studies for improved cost-benefit and knowledge on human exposure-health outcome correlations.
- Provide broader HBM and health data on same individuals.

Work is organized in five tasks:

- Task 11.1 Opportunities and obstacles for linking HBM programme and health studies
- Task 11.2 Standard operating procedures and guidelines for use of existing biological samples, linking HBM and health studies
- Task 11.3 Workshop on opportunities and obstacles to combine HBM and health studies
- Task 11.4 Feasibility studies
- Task 11.5 Linking HBM to administrative registers

The WP is led by Hanna Tolonen (FIN, THL) and she is also leading tasks 11.2 and 11.4 and from Nordic countries Denmark, Norway and Sweden are involved. From Denmark Anna-Maria Andresson (Dept. of Growth and Reproduction) is leading Task 11.1 and from Norway Helle Margrete Meltzer (National Institute of Public Health) task 11.5. In all tasks at least one Nordic partner is involved.

In coming years and future Annual Work Plans, Nordic contribution for all activities should be ensured and possible contribution for feasibility studies explored.

Cathrine Thomsen (N): The Norwegian Institute of Public Health's contribution in HBM4EU

Cathrine Thomsen, Helle Margrete Meltzer, Norwegian Institute of Public Health

The Norwegian Institute of Public Health (NIPH) is a governmental institution placed directly under the Ministry of Health and Care Services. The institute is a national centre of excellence in the areas of epidemiology, mental health, infectious diseases control, environmental medicine and drug abuse. Approximately 100 people work within the field of Environmental Medicine. The primary deliverable of the institute is to give science-based advice to the Norwegian government. The environmental groups work within a number of areas including food safety and nutrition, effects on the immune system, air pollution and noise, environmental exposure, water hygiene, and the impact of consumer chemicals on health. The groups are strongly involved in research collaborations, both nationally and internationally, including the EU projects Helix and Euromix.

NIPH has long experience in exposure characterisation of environmental toxicants and run a well-equipped laboratory for chemical analyses, primarily focussed towards human biomonitoring. We have recently started up the "Norwegian Environmental Biobank" nested within MoBa (the Norwegian Mother and Child Cohort study), and are presently finishing the sample collection. In addition, NIPH has a long experience in conducting toxicological research and the institute runs a number of well-equipped *in vivo* and *in vitro* laboratories. Scientists in this group are involved in performing risk assessments for the Norwegian Scientific Committee for Food Safety, EFSA, ECHA and WHO.

NIPH will be involved in all Pillars of HBM4EU where we will act as advisors and co-workers as to the handling, evaluation and interpretation of all biomonitoring data. In addition we foresee to be contributing to the chemical analyses to be undertaken in the course of the project, and furthermore, with samples and data from the Norwegian Environmental Biobank. NIPH will also contribute with toxicological expertise covering toxico-kinetics, adverse outcomes, mode of action, adverse outcome pathways and biomarker of effects development. NIPH's toxicology-, analyses- and nutrition experts have longstanding experience with all aspects of biomonitoring; from planning and implementing studies to clinical investigations, data handling, statistics and writing up and communicating results. The NIPH is PM in HBM4EU and the National Hub Contact Point in Norway.

Anna-Maria Andersson (DK): The Capital region of Denmark participation in HBM4EU: focus on linking HBM to health studies and health effects

Anna-Maria Andersson, Dept. of Growth and Reproduction, Rigshospitalet

The Capital region of Denmark (RegionH) is one of the Danish partners³ in the European joint project on human biomonitoring - HBM4EU. RegionH is the main health care provider in the region of Greater Copenhagen. Participation of RegionH in the HBM4EU project is motivated by the obvious societal gains from prevention of non-communicable diseases caused by environmental factors, including exposures to chemicals with harmful effects on human health. Thus, from RegionH's point of view an important aspect of HBM4EU is the inclusion of workpackages, which have the overarching aims of improving how HBM data can be used to provide new knowledge on exposure-health associations and adverse outcome pathways (mainly in Pillar 3: "Exposure and Health". However, we also acknowledge that valid and reliable biomarkers of exposure are an important prerequisite and therefore also the importance of the work carried out in pillar 2.

RegionH's participation in the HBM4EU project is nested in the research group of Dept. of Growth and Reproduction at Rigshospitalet, which has a longstanding clinical and scientific interest in the impact of lifestyle and environmental factors on human development, growth and reproduction. RegionH has University of Southern Denmark (SDU) as a linked third party (LTP) in the HBM4EU project. The participation of LTP SDU is nested in the research group at Dept. of Environmental medicine, the focus of which also is on the impact of environmental factors on human health. Our focus on human health is also reflected in our involvement in HBM4EU, which is concentrated in WP11: "Linking HBM, Health surveys and registers" and WP12: "From HBM to exposure" with minor roles also in WP8, 9, 10 and 13. LTP SDU main involvement is in WP13: "Establishing exposure health relationships".

The Nordic countries have a long tradition for research-driven targeted human health studies – often with HBM included, while state-driven HBM surveys (like e.g. that of the Federal Institute for Risk Assessment (BfR) in Germany) or human health surveys (as e.g. NHANES of Center for Disease Control and Prevention in USA) have generally not been conducted. From a Nordic point of view it is therefore key that involvement of researcher-driven studies is facilitated in HBM4EU. Our involvement in WP11 is 1) aimed at promoting that HBM is linked to health surveys and studies for the added value of being able to link HBM data to health outcomes but also to 2) facilitate the involvement of researcher-driven health studies in HBM4EU and thereby hopefully promote the contribution of Nordic health studies/surveys in HBM4EU.

---

³ RegionH participates in HBM4EU as both programme owner and programme manager and as such co-fund RegionH activities in the HBM4EU project – mainly in the form of in kind person-months. Scientific contact person is research director Anna-Maria Andersson Cand.Scient, Ph.D. Scientific contact person for LTP SDU is prof. Tina Kold Jensen, MD Ph.D (tkjensen@health.sdu.dk).

Hanne Frederiksen (DK): Non-persistent endocrine disrupting chemicals (EDCs) in Danes: Presentation of HBM-data in present and future studies

Hanne Frederiksen, Dept. of Growth and Reproduction, Rigshospitalet

Several non-persistent industrial chemicals have shown endocrine disrupting effects in animal studies, and are suspected to be involved in human reproductive problems. Among the non-persistent chemicals, which have been most in focus, are the phthalates because of their anti-androgenic effects. Possible endocrine disrupting effects of other non-persistent chemicals like bisphenol A, triclosan, benzophenone-3 and parabens have also been discussed intensively during the past years.

We are all in contact with non-persistent chemicals in our daily life and get exposed by inhalation, through the skin and through our diet. Phthalates are plastizers that are used in numerous industrial products. Bisphenol A is the main component of polycarbonate plastics. Parabens and triclosan are anti-microbial preservatives, benzophenone-3 and other benzophenones act as UV screener in sunscreens, but also as UV absorber in industrial products, while chloro-phenols and phenyl phenols are used as pesticides in agriculture.

In spite of the widespread use of industrial chemicals, knowledge about exposure sources and human biomonitoring studies among different segments of the population are still in general limited. However, based on thousands of urine samples collected from different cohorts; The Copenhagen Mother-Child Cohort, The Copenhagen Puberty Study, the cohort of Danish men from the general population, Odense Child Cohort and minor collections from kindergarten children and mother-child pairs (Demochophes Study) we have now a broad overview of the Dane's exposure to some of the most widely discussed EDCs.

Our study shows that nearly all Danes were exposed to the five most common phthalates, bisphenol A, triclosan and benzophenone-3 and to at least two of the parabens. The exposure to other non-persistent chemicals was also widespread. Furthermore, a high individual exposure to one chemical was often associated with a high exposure to other chemicals and the possibility of combination effects of multiple exposures cannot be excluded.

A summary of the Danish HBM data including trends over time, age and gender differences will be presented as well as wishes for future HBM studies in the Danish population.

Eva Cecilie Bonefeld-Jørgensen (DK): Biomarkers of exposure and effects & Molecular Epidemiology: DK and Greenlandic birth cohorts

Eva Cecilie Bonefeld-Jørgensen, Centre for Arctic Health & Molecular Epidemiology, Aarhus University, Denmark

Humans are exposed to a wide variety of environmental compounds. Some compounds e.g. phthalates and Bisphenol A are relatively easily excreted from the body while others such as e.g. amphiphilic perfluorinated alkylacids (PFAAs) and lipophilic persistent organic pollutants (POPs, e.g. Polychlorinated biphenyls (PCBs), Organochlorine Pesticides (OCP), Brominated and organophosphate flame retardants (BRF)) and metals e.g. Mercury, Lead, are more persistent. The persistent compounds, having long half-life bio-accumulating in the human body, cause a lifelong continual exposure that can be further critical upon additional daily exposure to the compounds more easily excreted. Several studies have found that some compounds can interact and causing additive and/or synergistic bio-effects. Thus the combined mixture effects can be different from the effect of single compounds. The toxicological studies of single PFAAs and simple mixtures might be insufficient to predict how the actual complex mixtures of environmental compounds may affect humans. In humans, exposure to e.g. PFAAs and lipPOP have been associated with lower birth weight and longer time to pregnancy which might be related to disruptions of various hormonal systems.

To evaluate the actual serum mixture effects, we have developed methods to extract the actual complex serum mixtures of PFAAs, lipPOP and dioxin-like compounds (DL-POP) from human serum. Furthermore, we have saved serum fractions expected to contain e.g. BPA, phthalates, endogenous hormones etc. and it would be possible to further elaborate on these fractions.

For instance, we have in vitro data as well as ex vivo data showing that the actual complex serum mixture fractions of PFAAs, lipPOP and DL-POPs can affect the estrogen receptor (ER), the androgen receptor (AR), the thyroid hormone and Aryl-hydrocarbon receptor functions. Moreover, the compounds also showed cellular oxidative stress potential. The methods, exposure and some biomarker effect data and relations to reproduction and birth outcome will be presented.

Anne Marie Vinggaard (DK): DTU's contribution to HBM4EU

Anne Marie Vinggaard, Julie Boberg, Terje Svingen, Camilla Taxvig, Ulla Hass, Marianne Dybdahl and other colleagues in the Research Group for Molecular and Reproductive Toxicology, DTU Food

A major aim of HBM4EU is to develop and improve tools for risk assessment of chemicals by the use of human data, with the end goal that they are to be used by the authorities when risk managing chemicals. DTU Food has a long tradition for providing risk assessments of chemicals to the Danish national authorities and work closely with EFSA, ECHA and OECD. Consequently, our group has developed substantial know-how regarding the needs for risk assessment of chemicals. This knowledge can contribute to WP5 of HBM4EU, which deals with the implementation of human biomonitoring data in chemical risk assessment.

We have a long track record of investigating mixture effects of chemicals using various experimental strategies, including cell cultures, whole animals and mathematical modeling of effects – a knowledge that can be directly translated into mixture risk assessment using human samples. On the pragmatic side, we are currently developing a computational interface for mixture risk assessment; a 'Cocktail Effect Calculator' that includes hazard and exposure information from food and non-food sources. This assessment tool can be directly applied for mixture risk assessment of chemicals. This expertise is the background of DTU Food's involvement in WP15 of HBM4EU, which deals with mixture effects.

Another important research field at DTU Food is the use of bioassays for the identification of either emerging chemicals in complex matrices such as human samples, or food packaging materials. Our panel of bioassays has been used for identification of emerging chemicals in food packaging materials and similar approaches can be applied on human samples, which is intended in WP16 of HBM4EU dealing with emerging chemicals. In contrast to the traditional approach of analyzing one chemical at a time, the application of a top-down approach using bioassays will allow for an evaluation of the integrated toxicological hazard in the sample that also accounts for mixture effects. Furthermore, as yet unknown chemicals for which we are not aware can be identified by this approach.

The bioassays can also play a significant role in the identification of human biomarkers and we have already shown that for instance AhR activity in human milk can be used as a proxy measure for the total integrated exposure to organochlorines such as PCBs and dioxins. Approaches like this will be used in WP14 of HBM4EU, which deals with biomarkers of effect.

We welcome the HBM4EU initiative and look forward to contribute to this multinational collaborative effort.

Ulla Birgitte Vogel (DK): NRCWE contributions and interests

Common Nordic interests

Lisbeth E. Knudsen (DK): HBM4EU and ethics

Lisbeth E. Knudsen, University of Copenhagen

An ethics review was performed by the Commission prior to the contract negotiations of the proposal 733032 – HBM4EU under the call H2020-SC1-2016-RTD, a COFUND-EJP action with deadline of 13 April 2016. A 16 page Ethics review (assessment) report (CR) was issued⁴ and submitted to the coordinator for comments via the scientific officer. The document included an ethics analysis, and 9 Ethics requirements, which were all commented leaving some issues and specific approvals to be handled during the 5 year project period. Ethics is dynamic and many questions have to be resolved while work is being planned.

The ethics analysis, detailed in¹, stressed the following elements:

- Recruitment and informed consent from new and existing collections of samples and data
- Data protection and confidentiality
- Compliance with relevant EU legislation of the non-EU countries Norway, Switzerland, Turkey, Serbia and Israel.
- Results from animal studies only from studies approved by the National Authorities and in compliance with the 3Rs
- Installation of measures to avoid stigmatisation of particular social groups, political or financial retaliation, and malevolent use. HBM4EU should be aware of potential detrimental socioeconomic disadvantages

Ethics was alerted at all possible instances during the kick off and many partners have engaged in the finalisation of Deliverable D1.1: The 1st ethics report addressing the ethics requirements for the work of year 1 as set out in the 1st AWP for each WP. Since final decision of use of available data/biological samples will depend on gap analysis conducted under WP7 (due M8), explicit answers for some WPs cannot be provided at this state (10 March 2017). The 2nd ethics report is due in M9 to accompany the 2nd AWP for the year 2018. Some tasks in the 1st AWP depend on the outcome of the gap analysis in WP7 (M8) before they can define their work. Therefore the 2nd ethics report will cover also ethics issues related to work resulting from the gap analysis and to be carried out in M10-12 of Y1.

Two policy papers will be issued

D 10.1 – Data management plan (M6) (lead by VITO);

D 1.5 – Legal and Ethics Policy document (M8)(lead by UCPH)

The preliminary Ethics Board (D1.4 Establishment of Ethics Board (UCPH); M6) has been established with the following internal members:

Lisbeth E. Knudsen, University of Copenhagen, Denmark (Chair)

Ulrike Doyle, UBA, Germany

Paul Scheepers, University of Nijmegen, Netherlands

Hanna Tollonen, THL, Finland

Ilse Loots, University of Antwerp, Belgium

---

⁴ Ethics IR/CR/SR: ETHICS REVIEW (ASSESSMENT) REPORT CR Proposal 733032-HBM4EU between 27/6/2016 and 4/7/2016

And the following external board members

Prof. Dr. David (D.M.R.) Townend, University of Maastricht, Netherlands

At the kick off meeting the WP leaders were asked to provide detailed information about ethics and data protection issues and provide ethics documents asap as the scientific officer requested access to these.

WP9 will make use of archived samples, eventually from the DEMOCOPHES project and the contact persons in each participating country will be approached for information about availability of samples and conditions for use.

Some WPs have declared which data to include the first year, some cohorts already identified however much work only initiated and a major effort will be necessary coming months.

When existing data to be included have been identified, ethics and data protection issues must be resolved according to the two policy papers

For new samplings templates will be developed to meets all the EU requirements related to informed consent, sampling, storage, data protection, feedback.

A webinar was hosted by UCPH after this meeting <https://c.deic.dk/hbm4euethics>

Lisbeth E. Knudsen (DK): HBM4EU and training

WP2 of HBM4EU includes training and an inventory of ongoing activities as well as requested/needed/wished activities is mapped. As the Nordic community has special opportunities I suggest our Hubs to develop a course program and approach NorDoc.

Mission Statement of NorDoc - Nordic Doctoral Training in Health Sciences

At a meeting in Helsinki on 28th September 2016 representatives of the seven doctoral schools/ faculties of health sciences, Aarhus University, the University of Bergen, the University of Copenhagen, the University of Gothenburg, the University of Helsinki, the University of Iceland and Karolinska Institutet, decided to establish a Nordic network of doctoral education in health sciences. It is the intention of the seven founding members to invite all doctoral schools/faculties of health sciences in the Nordic countries to participate in the network and contribute to its activities. <https://www.nordoehealth.net/about>

Membership

All Nordic doctoral schools/faculties of health sciences who accept this mission statement are invited to be members of NorDoc - Nordic Doctoral Training in Health Sciences.

Target audience and aim

The activities of NorDoc - Nordic Doctoral Training in Health Sciences aims to initiate, facilitate and intensify collaboration among the Nordic doctoral schools/faculties in all relevant fields for the benefit of Nordic doctoral candidates and their supervisors in order to support and ensure the highest possible quality in doctoral education in health sciences. Furthermore it is the aim of the network to initiate and facilitate relevant joint actions of the Nordic doctoral schools specifically in terms of

- removing barriers to cross-border collaboration between doctoral schools in the Nordic countries
- acknowledgement of Nordic doctoral education
- providing free access for Nordic doctoral candidates to current research courses offered by the members of the network
- exploiting common existing resources and capacities for the benefit of arranging doctoral courses in all relevant fields of research at the highest possible scientific level
- attracting international scientific resources and capacities for such activities
- promoting and encouraging mobility of doctoral candidates and researchers in and between the Nordic countries
- arranging conferences, seminars etc. on topics of common interest
- providing international (e.g. Nordic and European) funding for common research projects and other relevant joint activities as i.e. those mentioned above
- providing policy-makers in Nordic countries and international organisations (e.g. the European Union) with information on matters concerning doctoral education in health sciences
- expand knowledge of and understanding for doctoral education in the Nordic countries
- detecting and sharing best practices.

Anne Thoustrup Saber (DK): BIOBRAND and BIOTRACK - two ongoing biomonitoring studies of firefighters and train conductors

Anne Thoustrup Saber*(1), Maria Helena Andersen (2), Per Axel Clausen (1), Niels Ebbenhøj (3), Julie Elbæk (3), Anne Helene Garde (1,2), Åse Marie Hansen (1,2), Ismo Koponen (1), Eva-Carina Nørskov (3), Peter Bøgh Pedersen (3), Steffen Loft (2), Peter Møller (2), and Ulla Vogel (1,4)

(1) National Research Centre for the Working Environment, Denmark, (2) University of Copenhagen, Denmark, (3) Danish Technological Institute, Denmark, (4) Department of Micro- and Nanotechnology Technical University of Denmark, Denmark

Fire smoke contains many different carcinogens and firefighting is classified as possibly carcinogenic to humans (2B) by the International Agency for Research on Cancer (1). Danish train conductors working in the ME and MR-driven regional trains are exposed to significantly higher concentrations of diesel exhaust than by constant stay on very busy streets (2) and the International Agency for Research on Cancer (IARC) has classified diesel engine exhaust as carcinogenic to humans (group 1) (3). Furthermore, human exposure to particles may increase the risk of cardiovascular disease. So far there is very little knowledge on adverse health effects among Danish firefighters and train conductors.

In the two ongoing biomonitoring studies BIOBRAND and BIOTRACK we aim at obtaining more knowledge on to what extent Danish firefighters and Danish train conductors are exposed to particles and the adverse health effects thereof. We measure biomarkers of cancer (DNA strand breaks in peripheral lymphocytes) and cardiovascular disease (e.g. C-reactive protein and serum amyloid A) in blood samples from volunteers acting as train conductors, on recruits under education to fire-fighters and on a group of firefighters. As a marker of exposure to PAHs, 1-hydroxypyrene is measured in urine. Furthermore lung function and vascular function is assessed. Endpoints are assessed before and after exposure.

The BIOTRACK project is a Ph.d. project led by Ph.d. student Maria Helena Guerra Andersen. The project is implemented in close collaboration with DSB. The BIOBRAND project involves scientists from the National Research Centre for the Working Environment, Department of Occupational and Environmental Medicine, Bispebjerg Hospital, University of Copenhagen and the Danish Technological Institute. The project is implemented in close collaboration with the Danish Emergency Management Agency and Copenhagen Fire Brigade. A National Advisory Board including stakeholders from e.g. fire brigades, trade unions and The Danish Emergency Management Agency has been established. The National Advisory Board is involved in the overall study design and will be involved in the dissemination of the results to stakeholders. The National Advisory Board is also reference group for our sister project EPIBRAND which is an epidemiological registry study assessing possible health risks for Danish firemen. BIOBRAND and BIOTRACK are supported by the Working Environment Research Fund and Danish Centre for Nanosafety 2.

(1) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Painting, Firefighting, and Shiftwork, Volume 98, 2010.

(2) Karottki G, Loft S. Rapport vedrørende måling af udsættelse for ultrafine partikler blandt ansatte i DSB. In. DSB ed; 2015. pp. 1-48.

(3) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Diesel and Gasoline Engine Exhausts and Some Nitroarenes, Volume 105, 2014.

Marie Frederiksen (DK): Flame retardants and PCB HBM-studies from Denmark

Flame retardants have been extensively studied in a small study population of pregnant women in Denmark. The study included maternal and fetal blood, breast milk and placental tissue as well as external exposure parameters. Data is available for PBDEs in all matrices and for NBFRs in milk and dust. The HBM-data revealed the indoor environment was a significant source of PBDE-exposure and that the placenta provides limited protection of the fetus for these types of compounds. The study also revealed that the congener pattern had shifted from primary source congeners towards more persistent congeners. Finally, the study provides valuable information on comparison of between various tissues from the same individuals.

A study on PCB-exposure, showed that exposure from contaminated buildings can be a significant source of PCB even today. In a housing estate constructed in sections with and without PCB, PCB-28 was found in 100 times higher levels in blood of people living in the contaminated vs. non-contaminated apartments. Currently, a similar study investigating more exposure parameters is underway.

Tiina Santonen (FIN): How to engage Nordic occupational health

Tiina Santonen/Finnish Institute of Occupational Health

Biomonitoring has been used in occupational health for decades to assess the exposure and early effects at exposed workers. Although HBM4EU is largely based on concerns related to general population exposure, the project includes also occupational exposures and occupational biomonitoring. Occupational aspects has been included in almost all WPs; for example in WP8 there is a specific task related to targeted occupational surveys with EU added value.

One of the aims of HBM4EU is to impact policy making and regulatory risk assessment in Europe. One of the main policies related to the chemicals is EU chemical legislation (REACH). REACH includes exposure to chemicals via the environment, from consumer products and at workplaces. For example, in REACH authorization process the main concerns are often related to occupational exposure. Although the exposure models have improved during the recent years, especially dermal exposure assessment is still problematic, and may result in severe uncertainties in exposure assessment. Biomonitoring is important in decreasing uncertainty related to the dermal exposure modeling. Also in the case of recent restriction proposal of bisphenol A in thermal papers, occupational exposure of cashiers was the key issue and the few biomonitoring studies available on cashier's exposure proved to be extremely valuable. In addition, occupational exposure may also be a cause for variability in exposure levels in general population HBM studies and needs to be identified.

HBM4EU project involves some institutes/university departments with primary interest in occupational biomonitoring either as partners or (more often) as linked third parties. From Nordic countries Finnish Institute of Occupational Health (FIOH) and Danish National Research Centre for the Working Environment (NRCWE) are involved as partners. Occupational aspects and occupational institutes are, however, not very visible at the overall project plan. It should be discussed how to strengthen the role of occupational biomonitoring in HBM4EU and engage OSH experts also from other Nordic countries to the project. What are the interests of Nordic countries in this area? Are there common occupational exposures of interests which we should prioritize? Could we together strengthen the role of occupational biomonitoring at the project?