HBM4EU TRAINING SCHOOL 2018-1

Ljubljana, Slovenia

The 1st training school will be provided June, 18th – 22nd in Ljubljana, Slovenia. You can combine one or more of the courses provided from the following options. If you would like to spend the whole week in training you should decide which of the laboratory skills training you would like to follow on Friday.

Date	Level	Code	Title
18-19 June	Basic	B01	HBM4EU basic training
20 June	Advanced	A01	Ethics
21 June	Advanced	A02	Data management and basics of data analysis
22 June	Advanced	A03	HBM in occupational health: applications to chromium
22 June	Advanced	A04	Quality requirements, validation and implementation of analytical methods in HBM programmes
22 June	Advanced	A05	Biomarkers of effect

B01 HBM4EU basic training

Date: June 18-19th, 2018

Location: Jožef Stefan Institute, Reactor Center, Brinje 40, Ljubljana, Slovenia

Instructors

Alenka Franka, University Medical Centre Ljubljana, Slovenia; Janja Snoj Tratnik, Department of Environmental Sciences, Jožef Stefan Institute, Ljubljana, Slovenia; Lisbeth Knudsen, Department of Public Health, University of Copenhagen, Denmark; Marta Esteban, Instituto de Salud Carlos III, Madrid, Spain; Holger Koch, IPA, Germany; Milena Horvat, Department of Environmental Sciences, Jožef Stefan Institute, Ljubljana, Slovenia; Paul Scheepers, Radboudumc, Nijmegen The Netherlands, Sylvie Remy, VITO, Mol, Belgium; Hanna Tolonen, National Institute for Health and Welfare (THL), Department of Public Health Solutions Health Monitoring Unit, Helsinki, Finland; Ulrike Fiddicke, Umweltbundesamt, Berlin, Germany

Description

The basic training tries to provide an overview of the most relevant aspects of HBM and wherever possible specifically for HBM4EU at a basic level. We encourage participants to take their own projects ideas to the course. For some participants it may be possible to apply some of the acquired knowledge and skills immediately to implementation of national HBM4EU studies.

Learning objectives

The participant is familiar with applications of HBM and is aware of the societal context.
The participant is aware of the ethics implications and the required approval of study protocols
The participant can implement the harmonized HBM4EU methodology in his/her own country

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733032.

Info: hbm4eutraining.hev@radboudumc.nl

Day-1 Monday, June 18th

08:30 Registration of participants and coffee/tea
09:00 Welcome by representative of HBM4EU management board and local organizers
09:10 Quick round to become acquainted with participants and instructors

Session 1: introduction of the course and the topic

09:20 Introduction to the course and introduction to the learning objectives (Paul Scheepers)
09:30 Concepts and principles of HBM (Paul Scheepers)
10:00 Overview of HBM initiatives around the globe and brief history of HBM4EU (Hanna Tolonen)
10:30 HBM in a societal context and policy interactions (Paul Scheepers)
11:00 Break

Session 2: Orientation on the design HBM4EU studies

11:15 Objectives and research questions: science and society (Paul Scheepers)
11:45 A structured approach to the HBM4EU harmonized study protocol for reference values (Ulrike Fiddicke)
12:15 Ethics and approval of study protocol: what is required and how to arrange it (Berit Faber)
12:45 Taking a representative sample for all age groups (Hanna Tolonen)
13:15 Lunch

Session 3: information and recruitment of participants

14:00 Selection of participants (inclusion/exclusion criteria) (Hanna Tolonen)
14:30 Information, invitation and informed consent (Berit Faber)
15:00 Data management and save-guarding privacy (/Sylvie Remy)
15:30 Collection of person and contextual information by questionnaire (Ulrike Fiddicke)
16:00 Break

Session 4: Samples collection

16:15 Human biomonitoring: from exposure biomarker identification to population studies: basic principles in matrix and biomarker selection (Holger Koch)
16:45 Specifics on blood fractions and urine voids (Paul Scheepers)
17:00 Sample collection materials, techniques and instructions (Paul Scheepers)
17:15 Aliquoting, temporary storage, and biobanking of samples (Paul Scheepers)
17:30 Quality assurance in the preanalytical phase (Marta Esteban),
18:00 Closure

Day-2 Tuesday June 19th

Session 5: Basic principles of laboratory analysis

09:00 HBM4EU laboratory quality assurance programme (Marta Esteban)
09:30 Validation of analytical methods (Janja Snoj Tratnik)
10:00 Use of (certified) reference materials (Milena Horvat)
10:30 Setting the laboratory analytical quality performance requirements (Janja Snoj Tratnik)
11:00 Break

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Session 6: Data analysis and interpretation

11:15 From raw data to information: adjustments, conversions and calculations (Paul Scheepers)
11:45 Eye balling and descriptive statistics (Lisbeth E. Knudsen)
12:15 Basic principles of biokinetics (Paul Scheepers)
12:45 Lunch

Session 7: Reporting and communication; HBM4EU data repository and integration into IPCHEM

13:30 Communication of HBM results to groups and individuals (Paul Scheepers)
14:00 HBM4EU data inventory and data management (Sylvie Remy)
14:30 Basic introduction to reporting and submission of data to IPCHEM database (Sylvie Remy)
15:00 Break

Session 8: Exercise and discussion

15:15 Instruction for break out session (Paul Scheepers)
15:30 Exercises on implementation of different aspects of HBM4EU methodology in break-out groups (Ulrike Fiddicke/Paul Scheepers/Lisbeth Knudsen/Hanna Tolonen/Milena Horvat)
16:30 Short presentations by participants and discussion (Paul Scheepers)
17:30 Plenary course evaluation of the two-day basic training (Paul Scheepers)
18:00 Closure

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A01 **Ethics**
Date: Wednesday, June 20st, 2018
Location: Jožef Stefan Institute, Reactor Center, Brinje 40, Ljubljana, Slovenia

Instructors
Lisbeth E. Knudsen, Berit Faber, Hanna Tolonen, National Institute for Health and Welfare (THL), Department of Public Health Solutions Health Monitoring Unit, Helsinki, Finland

Learning objectives
The participant has an overview of ethics requirements for HBM4EU studies
The participant can apply these principles and requirement to his/her own HBM4EU study

Description
The participants will get a solid overview of requests related to HBM studies in EU and for the HBM4EU programme specifically. Critical issues of information, consent, feed-back of study results, data protection and forward of individual data to IPCHEM will be covered. The participants will actively contribute with own experiences/studies, solving cases and developing information and consent material.

Programme
09:00 – 12:00 Morning session

1. Ethics in general and with a focus on HBM4EU, Policy paper (Lisbeth E. Knudsen/Berit Faber)
2. Cases (Lisbeth E. Knudsen)
3. Ethics and health information including genetic testing (Hanna Tolonen/Berit Faber)
4. Biobanking (Berit Faber/Hanna Tolonen)
5. HBM4EU templates and how to handle these (Lisbeth E. Knudsen)
6. Participants presentations/questions

12:00 – 13:00 Lunch break

13:00 – 17:00 Afternoon session

1. How to serve the participants (Lisbeth E. Knudsen):
   - Information
   - Consent – specific, broad, dynamic
   - Feed-back
   - Forward of results
2. Contractual demands (Lisbeth E. Knudsen, Berit Faber):
   - Data protection
   - Data and sample transfer
   - Sample exchange
3. Conclusions and recommendations (Lisbeth E. Knudsen, Berit Faber)

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A02 Data management and basics of data analysis
Date: Thursday, June 21st, 2018
Location: Reactor Center, Brinje 40, Ljubljana, Slovenia

Instructors
Sylvie Remy, VITO, Mol, Belgium; Eva Govarts, VITO, Mol, Belgium

Description
The focus of this course is management and use of data on human subjects within HBM4EU. The HBM4EU data management plan and data policy have been developed to reach the highest level of EU General Data Protection Regulation (GDPR) compliance. To share data on human subjects between HBM4EU partners, a secure platform has been established: the HBM4EU repository. The metadata of all datasets that are used for HBM4EU research will be directly integrated into IPCHEM (https://ipchem.jrc.ec.europa.eu/), the Information Platform for Chemical Monitoring. This will allow researchers beyond HBM4EU and policy makers to contact the Data Owner/Data Provider to request access to use the data. Furthermore, integration of aggregated and single measurement data into IPCHEM is stimulated, while respecting the ethico–legal framework. More information on HBM4EU data management is available at: https://www.hbm4eu.eu/data-management/

Learning objective
The participant knows how:
to integrate data collections into HBM4EU;
the data are structured in the HBM4EU repository;
to perform basic statistical analysis;
to find, extract, and use the information and data that are available via IPCHEM.

Programme
09:00-12:00 Morning session

1. Practical considerations concerning the general data protection regulation (GDPR):
   - Types of data: personal data, sensitive data, anonymous versus pseudonymous data
   - HBM4EU repository
   - HBM4EU tutorial
   - HBM4EU repository: harmonization of the data: HBM4EU codebook and HBM4EU data template
   - HBM4EU statistical analysis plan
   - Exercises: Basic statistical analyses of HBM4EU data using R

12:00-13:00 Lunch break

13:00-17:00 Afternoon session

2. IPCHEM tutorial
   - Guidance for data owners/providers: transfer of Introduction to the IPCHEM platform
   - Query the metadata
   - Case studies

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4. Data to HBM4EU and integration into IPCHEM
5. Guidance for data users: requesting access to data for HBM4EU research

A03 HBM in occupational health studies: applications to chromium
Date: Friday, June 22nd, 2018
Location: Jožef Stefan institute, Reactor Center, Brinje 40, Ljubljana, Slovenia

Instructors
Tiina Santonen, Mirja Kiilunen, Finnish Institute of Occupational Health, Helsinki, Finland; Kate Jones, Liz Leese, Health & Safety Laboratory, Health & Safety Executive, Buxton, UK, (*to be confirmed)*; Karen Galea, Institute of Occupational Medicine, Edinburgh, UK (*to be confirmed*); Radu Duca, KU Leuven, Belgium; Thomas Göen, University of Erlangen-Nürnberg, Germany; Sophie Ndaw, INRS, Vandoeuvre, France; Maria João Silva, National Institute of Health Dr. Ricardo Jorge, Lisbon, Portugal

Description
A study is prepared to determine the occupational exposure of workers to chromium. For those participants who take part in this project or have an interest in HBM applied to occupational health are invited to take part in fine tuning and implementation of draft study protocols, including questionnaires, informed consent forms, etc. This will be a work session that also address technical/practical skills regarding e.g. collection of samples of exhaled breath condensate.

Learning objective
The participant understands the specific requirements to apply HBM in an occupational setting
The participant obtained specific knowledge and skills regarding sample collection methods

Programme (tentative)
09:00-09:30 Introduction of HBM in occupational health – how HBM4EU aims to improve the use of HBM in occupational health (Tiina Santonen)
09:30-10:00 Outline of occupational health study on worker's exposure to chromium (Sophie Ndaw)
10:00-11:00 Discussion on fine tuning and implementation of informed consent, questionnaire on gathering contextual data (Tiina Santonen)
11.00-12.00 Sample collection procedures; industrial hygiene samples and wipe samples (Radu Duca, Karen Galea, *to be confirmed*)
12:00-13:00 Break
13:00-15:00 Training on the collection of exhaled breath condensate (Liz Leese, *to be confirmed*)
15:00-16:00 Collection and treatment of blood samples, effect markers (Maria João Silva)
16.00-17-00 The analysis of biomarkers in the chromium study (Thomas Göen)

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A04 **Quality requirements, validation, and implementation of analytical methods in HBM programmes**

Date: Friday, June 22nd, 2018

Location: Jožef Stefan Institute, Reactor Center, Brinje 40, Ljubljana, Slovenia

Instructors

Milena Horvat, Janja Snoj Tratnik, Darja Mazej, Department of Environmental Sciences, Jožef Stefan Institute, Ljubljana, Slovenia; Marta Esteban, CNSA, ISCIII, Spain; Holger Koch, IPA, Germany (*to be confirmed*)

Learning objective

The participants will become acquainted with the principles and practical examples of the quality assurance and quality control adopted in the framework of HBM4EU. Moreover, the participants will be able to understand the importance of analytical method performance in the planning stage of the HBM programme, collection and storage of samples, day-to-day maintenance and quality control of analytical methods used for chemical analysis in human samples.

Description

The first part of the training will be dedicated to the outcomes and planning of QA/QC for HBM4EU. The validation part of the programme will cover the analytical quality parameters (LODs, LOQs, proper use of CRMs, reproducibility, repeatability, inter-laboratory comparisons) and assessment of measurement of uncertainty according to international standards. Practical examples from laboratory practice in HBM programme will be used. Participants will be encouraged to share their practical examples, especially for the proper evaluation of uncertainty.

Programme

09:00 – 10:00	Specific QA/QC requirements within HBM4EU
10:00 – 10:30	Assessment of the analytical quality performance during the planning stage
10:30 – 12:00	Quality performance characteristics: LOD, LOQ, reproducibility, repeatability, use of RM and CRMs, interlaboratory comparison
12:00 – 13:00	Lunch break
14:00 – 17:00	Uncertainty evaluation with practical examples for Cd, Cr, and bisphenols in urine

Note

It is recommended that participants bring their own notebook computers for use in exercises related to uncertainty evaluation.

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A05 Biomarkers of effect

Date: Friday, June 22nd, 2018
Location: Institute of Biochemistry, Faculty of Medicine, University of Ljubljana, Vrazov trg
Ljubljana, Slovenia

Instructors
Vita Dolzan, Alenka Franko, Metka Lenassi, Katja Goricar, University Medical Centre Ljubljana, Slovenia; Marieta Fernandez, UGR, Granada, Spain

Learning objectives
The participant knows how biomarkers are used in the clinic
The participant understands the role of biomarkers in research of gene-environment interactions

Description
The use of different types of biomarkers in a clinical practice and research will be illustrated. The application of biomarkers in diagnostic procedures is discussed as well as the use of different types of biomarkers in research of gene-environment interactions.

Programme

09:00–09:20	Biomarkers in human biological monitoring (Vita Dolzan)
09:20–09-40	Serum biomarkers in asbestos related diseases (Alenka Franko)
09:40–10:00	Genetic variability in human biological monitoring (Vita Dolzan)
10:00–10:20	Genetic variability and the risk of developing asbestos related diseases (Katja Goricar)
10:20–10:40	Coffee Break
10:40–11:00	Gene-environment interactions: the case of asbestosis (Alenka Franko)
11:00–11:20	Extracellular vesicles as novel biomarkers for monitoring human disease (Metka Lenassi)
11:20–11:40	The application of extracellular vesicles in malignant mesothelioma diagnosis (Metka Lenassi)
11:40–12:00	Biomarkers and ethics (Lisbeth E. Knudsen)
12:00–13:00	Lunch break
13:00–15:00	Demonstration of DNA genotyping methods and miRNA analysis (Pharmacogenetics Laboratory, Institute of Biochemistry, Faculty of Medicine, University of Ljubljana)
15:00–17:00	Demonstration of methods for isolation and characterization of extracellular vesicles (Institute of Biochemistry, Faculty of Medicine, University of Ljubljana)

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