HBM4EU TRAINING SCHOOL 2018-2, Nijmegen, The Netherlands

The 2nd training school will be provided November, 19th – 23rd in Nijmegen, The Netherlands. 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 advanced training courses you would like to follow on Thu-Nov-22 and Fri-Nov-23.

Please notice that the programme may be subject to minor changes.

Programme outline

Date	Level	Code	Title
19-20 November	Basic	B02	HBM4EU basic training
21 November	Advanced	A06	Interpretation of and access to human biomonitoring data in HBM4EU
22 November	Advanced	A07	Workshop on the alignment of studies in the frame of HBM4EU
22 November	Advanced	A08	Mycotoxins and pesticides biomarker analysis
23 November	Advanced	A09	Integrated exposure modelling/HBM data assimilation
23 November	Advanced	A10	Mixtures and related data analysis
23 November	Advanced	A11	Determination of phthalate/DINCH and alkylpyrrolidone metabolites in urine

Detailed Programme

Below the programme is shown, using the same format as used for the 1st HBM4EU Training School. Input was provided directly from the WPs. For some courses A9, A10 and A11 titles of lectures will become available later.

B02 HBM4EU basic training

Date: 19-20th November 2018

Location: Room 'De Beelkamer' Huize Heyendael, Geert Grooteplein Noord 9, 6525 EZ Nijmegen Phone +31-24-3611282. Note: On Tuesday after lunch 'De Beelkamer' will not be available. The session will continue in the 'Van Agt Room' (restaurant).

Instructors

Alenka Franko, University Medical Centre Ljubljana, Slovenia; Lisbeth E. Knudsen, Department of Public Health, University of Copenhagen, Denmark; Milena Horvat, Department of Environmental Sciences, Jožef Stefan Institute, Ljubljana, Slovenia; Holger Koch, IPA, Germany; Paul Scheepers, Radboudumc, Nijmegen, The Netherlands, Jos Bessems, Sylvie Remy, Greet Schoeters, VITO, Mol, Belgium; Hanna Tolonen, National Institute for Health and Welfare (THL), Department of Public Health Solutions Health Monitoring Unit, Helsinki, Finland;

Description

The basic training provides 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 project 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.

The participant is aware of the HBM4EU project structure and work packages contents

Day-1 Monday, November 19th

08:30 Registration of participants and coffee/tea

09:00 Welcome by representative of HBM4EU management board (Hanna Tolonen)

09:10 Quick round to become acquainted with participants and instructors

Session 1: Introduction of the course and the topic (Paul Scheepers/Hanna Tolonene)

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 (Greet Schoeters)

11:00 Break

Session 2: Sample collection (Holger Koch/Paul Scheepers)

11:15 Blood and urine: sample collection, aliquoting and storage (Paul Scheepers)

11:50 Human biomonitoring: from exposure biomarker identification to population studies: basic principles in matrix and biomarker selection (Holger Koch)

12:25 Quality assurance in the preanalytical phase (Holger Koch)

13:00 Lunch in 'De Hal' of Huize Heyendael

Session 3: Basic principles of laboratory analysis (Holger Koch/Milena Horvat)

14:00 Validation of analytical methods (Milena Horvat)

14:30 Use of (certified) reference materials (Milena Horvat)

15:00 HBM4EU laboratory quality assurance programme (Holger Koch)

15:30 Break

Session 4: Data analysis and interpretation (Paul Scheepers/Milena Horvat)

15:45 From raw data to information: adjustments, conversions and calculations (Paul Scheepers)

15:15 Eye balling and descriptive statistics (Paul Scheepers)

15:45 Basic principles of biokinetics (Paul Scheepers)

16:15 Break

Session 5: HBM4EU Programme structure and work packages contents

16:30 Pillar-1 Science to Policy: (WP4-WP5-WP6) (Greet Schoeters/Jos Bessems)

17:00 Pillar-2 European HMB Platform: (WP7-WP8-WP9-WP10) (Ovnair Sepai)

17:30 Pillar-3 Exposure and Health (WP11-WP12-WP13-WP14-WP15-WP16) (Erik Lebret, tbc)

18:00 Closure

Session 6: Orientation on the design of HBM4EU studies (Lisbeth E. Knudsen)

09:00 Objectives and research questions: science and society (Paul Scheepers)

09:30 Ethics and approval of study protocol: what is required and how to arrange it (Lisbeth. E. Knudsen)

10:00 Taking a representative sample for all age groups – Part A. General sampling theory (Hanna Tolonen)

10:30 Break

Session 7: information and recruitment of participants (Lisbeth E. Knudsen/Hanna Tolonen)

10:45 Taking a representative sample for all age groups – Part B. Sample selection for HBM4EU (Hanna Tolonen)

11:15 Information, invitation and informed consent (Lisbeth E. Knudsen)

11:45 Data management and save-guarding privacy (Lisbeth Knudsen)

12:15 Lunch in 'De Hal' of Huize Heyendael

Session 8: Reporting and communication; HBM4EU data repository; integration into IPCHEM (Sylvie Remy/Lisbeth Knudsen)

13:15 Communication of HBM results to groups and individuals (Paul Scheepers)

13:45 HBM4EU data inventory and data management (Sylvie Remy)

14:15 Basic introduction to reporting and submission of data to IPCHEM database (Sylvie Remy)

14:45 Break

Session 9: Exercise and discussion (Paul Scheepers/Lisbeth Knudsen)

15:00 Instruction for break out session (Paul Scheepers)

15:15 Exercises on implementation of different aspects of HBM4EU methodology in break out groups (Paul Scheepers/Lisbeth Knudsen/Hanna Tolonen/Milena Horvat/Alenka Franko)

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

A06 Interpretation of and access to human biomonitoring data in HBM4EU (Sylvie Remy/Eva Govarts)

Date: Wednesday 21 November 2018

Location: Room 'De Marijnenkamer' Huize Heyendael, Geert Grooteplein Noord 9, Nijmegen,

Instructors

Jos Bessems, Liese Gilles, Eva Govarts, and Sylvie Remy, VITO, Mol, Belgiuml; Nina Vogel, UBA, Berlin, Germany; Loïc Rambaud, ANSP, Saint-Maurice, France; Lubica Murinova, SZU, Bratislava, Slovakia

Description

The target group for this course is data providers and data users. The participants will learn how to integrate Human Biomonitoring (HBM) data into IPCHEM and how to exchange them with HBM4EU partners. The participants will also learn how to use IPCHEM to find HBM data. More information about IPCHEM can be found on https://ipchem.jrc.ec.europa.eu/ .

In an hands-on R-session, the participants will learn how to harmonise and aggregate HBM data (derive descriptive statistics) using simulated data. This excercise will enable the participants to analyze their own data in a way they can be compared with other data in HBM4EU.

The participants will learn different statistical methods that are applied in the field of HBM, such as: calculation of European reference values, identification of determinants, analysis of time trends, analysis of health effects.

Important note: for this course the applications 'R' and 'R-studio' should be pre-installed on a notebook or laptop computer that is brought to the course. Instructions of how to install the software will be provided as soon as the registration for this course is completed.

Learning objectives

Exchanging HBM data in HBM4EU: The participant wil learn to transfer HBM data to IPCHEM and exchange of data between partners.

Harmonizing data to enable comparison between datasets in HBM4EU: the articipant will learn to prepare data using the HBM4EU data template and codebook; deriving aggregated data using R-script

The participant will learn how to use IPCHEM to find and obtain access to HBM data

The participant will learn how to use HBM data for risk assessment

Regarding statistical analyses of HBM data, we will present some case studies, to show the participants how HBM data can and will be used within the project.

Session 1: HBM4EU Data Management

09:00 Welcome + tour de table

09:15 Data management plan and data policy (Sylvie Remy, Liese Gilles)

09:30 How to prepare your data for sharing (Sylvie Remy, Liese Gilles)

09:45 How to enable access to your data to other partners (Sylvie Remy, Liese Gilles)

Session 2: Hands on R-session on HBM4EU data harmonisation and data aggregation

10:00 Input data format: HBM4EU data template and codebook (Sylvie Remy)

10:30 Running the HBM4EU script in R with simulated data (Sylvie Remy)

11:00 Break

11:15 Interpretation of the outputs: descriptive statistics, stratification, handling of samples below LOD/LOQ (Sylvie Remy)

12:00 Lunch in 'De Hal' of Huize Heyendael

Session 3: IPCHEM: the Information platform for chemical monitoring

13:00 Introduction to IPCHEM (Liese Gilles)

13:15 How to find HBM and HBM4EU harmonized data in IPCHEM (Liese Gilles)

13:45 Overview of HBM4EU data integrated into IPCHEM (Liese Gilles)

Session 4: Analyses of HBM data in HBM4EU

14:00 Statistical analyses of HBM data in HBM4EU (Eva Govarts)

14:30 Break

14:45 Calculation of European reference values (Eva Govarts)

15:00 Use of HBM data for risk assessment (Jos Bessems)

15:30 Urinary levels of bisphenol A among European women and major determinants (Loïc Rambaud)

15:50 Time trends in Cat A phthalates in Danish and German young adults between 2000 and 2017 (Nina Vogel)

16:10 What are the PFAS levels and health effects in vulnerable population groups (Lubica Murinova)

17:00 Closure

A07 Workshop on the alignment of studies in the frame of HBM4EU (Greet Schoeters/Ovnair Sepai)

Date: Thursday 22nd November 2018

Locatio: Room 'De Beelkamer' Huize Heyendael, Geert Grooteplein Noord 9, 6525 EZ Nijmegen

Phone +31-24-3611282. For parallel sessions the Beelkamer 'De Hal' will also be available

Instructors

Liese Gilles, Eva Govarts, Sylvie Remy, Greet Schoeters, VITO, Mol, Belgium, Hanna Tolonen, National Institute of of Health and Welfare (THL), Helsinki, Finland, Ovnair Sepai, Public Health England, UK, London, UK; Argelia Castano, Marta Esteban, Instituto de Salud Carlos III; Madrid, Spain; Ulrike Fiddicke, Umsweltbundesamt, Berlin, Germany

Description

The workshop is organized for all partners who will be part of the alignment of HBM studies (WP8 Task 8.1) and feasibility studies (WP8 Task 8.4) and those who's samples will be collected for time trend analysis (WP8 Task 8.2) or those successful in the IC – 1. The workshop consists of interactive sessions discussing study design, sampling framework, ethics, recruitment procedure, communication with study participants (incl. reporting back results to participants), etc. This course will also address how to align these aspects across studies. In addition, analysis of priority substances under HBM4EU, data management, data analysis and future perspective for a sustainable HBM platform in Europe will also be discussed.

Learning objectives

The participants will obtain understanding how national HBM studies will be aligned on European level

The participants will learn how to use the study design, sampling framework, ethics principles, recruitment strategy and communication with the study participants

The participants will be aware of the analysis of priority substances and will know the basic skills to handle data management and data analysis.

Session 1: Interactive session »How to harmonize studies as far as possible«

09:00 Welcome and introduction to the parallel sessions (moderator to be assigned)

09:15 Parallel session 1.1 - Children 6-11 years (Ulrike Fiddicke)

09:15 Parallel session 2.2 - Teenagers 12-19 years (Greet Schoeters)

09:15 Parallel session 1.3 - Adults 20-39 years (Hanna Tolonen)

10:45 Presentation on sampling frame: who is participating, coverage (Liese Gilles)

11:15 Break

Session 2: Post-harmonization

11:30 How to transform questionnaire data and exposure data into harmonized variables (Eva Govarts)

12:00 Lunch in 'De Hal' of Huize Heyendael

Session 3: Interactive session »Next steps to take«

13:00 Introduction to the parallel sessions (moderator to be assigned)

13:05 Parallel session 3.1: Collect new samples (Greet Schoeters)

13:05 Parallel session 3.2: Make use of biobanked samples (Hanna Tolonen)

13:05 Parallel session 3.3: Access data (Eva Govarts)

14:00 Conclusion

14:15 Break

Session 4: Transport of samples / analysis: update and discussion

14:30 Analysis of priority substances under HBM4EU update of QA/QC programme (Argelia Castano/ Marta Esteban, tbc)

14:45 Transport of samples under HBM4EU SOP's (name instructor to be added)

15:00 Break

Session 5: Data processing / data analysis

15:15 How to harmonize your data and integrate data into IPCHEM (Sylvie Remy)

15:45 Calculating European reference values and analyse determinants of exposure (Eva Govarts)

Session 6: Way forward - discussion

16:15 Discuss obstacles and issues (moderator to be assigned)

17:00 Future perspectives: Interactive discussion of plans/ideas for 2020 and 2021 (Ovnair Sepai)

17:30 Concluding session (Greet Schoeters)

18:00 Closure

A08 Mycotoxins and pesticides biomarker analysis

Date: Thursday, 22nd November, 2018

Location: RIKILT - Wageningen University & Research Center, Wageningen, The Netherlands

Instructors

Mycotoxins: Marthe De Boevre, Arnau Vidal, Centre of Excellence in Mycotoxicology & Public Health, Ghent University, Ghent, Belgium; Hans Mol, RIKILT Wageningen University & Research, Wageningen, The Netherlands.

Pesticides: Hans Mol, Rosalie Nijssen, Paul Zomer, RIKILT Wageningen University & Research, Wageningen, The Netherlands

Description

The second list of HBM4EU Priority Substances was established in May 2018 and includes the compound groups "mycotoxins" and "pesticides". This calls for analytical methods for the determination of biomarkers of exposure for these compounds. This one-day course will focus on chemical analysis based on LC-MS (MS/MS, HRMS).

General aspects: after a brief update on developments in instrumental analysis, validation and analytical quality control will be addressed, taking into account the well-established EU guidance documents for pesticides and mycotoxins analysis from the food safety domain.

Mycotoxins: first a general introduction on mycotoxins and their biomarkers will be given, and general approaches for their analysis. Then we will zoom in on HBM4EU-prioritised mycotoxins: first on aflatoxins biomarkers, the various biomarker matrix options, and in detail methods for their determination. Second, on deoxynivalenol in urine, with details on quantitative analysis. Applications of the methods in HBM studies in the presenters' laboratories will be shown and discussed.

Pesticides: here emphasis will be on non-persistent pesticides and urine as biological matrix. Topics will include suspect screening using non-target measurement (LC-HRMS), the general workflow for setting up an analytical method, possibilities and limitations of multi-analyte analyte methods, and challenges in quantification. Applications of the methods in HBM studies in the presenters' laboratories will be covered in the presentations.

Learning objectives Mycotoxin biomarkers of exposure

Basic knowledge on mycotoxins and their biomarkers

Specific knowledge on aflatoxins biomonitoring: the right biomarker, options for quantitative analysis, including the validation and lab quality control

Specific knowledge on deoxynivalenol (and related compounds) biomonitoring: target biomarker, options for quantitative analysis, including the validation and lab quality control

Learning objectives Pesticide biomarkers of exposure

Knowlegde on approaches for metabolite screening using LC-full scan HRMS

Knowledge on how to set up a (multi) method for pesticide biomarkers

Basic understanding of the quantitative analysis of selected urinary biomarkers of pesticides, including validation and laboratory quality control

Session 1: General aspects

09:30 Welcome/introduction (Hans Mol)

09:45 Developments in chromatography/mass spectrometry (Hans Mol)

HBM meets food residue analysis: EU-guidance documents on validation and analytical quality control in the fields of pesticides and mycotoxins

To be or not to be...sense and nonsense about LOD, LOQ, LOI

10:30 Break

Session 2: Mycotoxins biomarker analysis

10:45 Genenal introduction to mycotoxin biomarkers (Marthe De Boevre/Hans Mol)

11:15 Determination of aflatoxin biomarkers for acute and chronic exposure (Marthe De Boevre)

11:45 Determination of deoxynivalenol and zearalenone urinary biomarkers (Hans Mol)

12:15 Lab tour and Luch break

13:15 Methods applied:

- Metabolism and excretion of dexoynivalenol/DON-glucoside, a human volunteer study (Arnau Vidal)
- Biomarkers in 24-h urine vs. mycotoxins in 24-h duplicate diet (Hans Mol)

Session 3: Pesticides biomarker analysis

14:00 Biomarker discovery/verification and suspect screening of pesticide biomarkers using LC-HRMS (Rosalie Nijssen)

14:30 Target (multi)analyte methods of pesticide biomarkers incl. pyrethroids in urine (Hans Mol)

15:00 Tea break

15:15 Determination of glyphosate, methods and application (Paul Zomer, tbc)

15:45 Hair: an alternative matrix for HBM of pesticides? (Rosalie Nijssen)

16:15 Closure

A09 Integrated exposure modelling/HBM data assimilation (Denis Sarigriannis/ Spyros Karakitsios)

Date: Friday 23 November 2018

Location: Room ‚Robert Regoutkamer', Huize Heyendael, Geert Grooteplein Noord 9, 6525 EZ Nijmegen

Phone +31-24-3611282

Instructors

Denis Sarigiannis[1,2]/Spyros Karakitsios[1,2]. [1]HERACLES Research Center on the Exposome and Health – Center for Interdisciplinary Research and Innovation, Aristotle University of Thessaloniki, Greece, [2]Environmental Engineering Laboratory, Department of Chemical Engineering, Aristotle University of Thessaloniki, Greece.

Description

The aim of this course is to help the trainees to understand the logical workflow and the mathematical framework that describe the continuum of the life-cycle of chemicals and how it relates to environmental, consumer, dietary exposure and get translated into biomonitoring data. A key component towards this direction is the internal dose modelling, materialized by the physiology based toxicokinetic (PBTK) models. In recent years PBTK–based models keep gaining ground in regulatory exposure and risk assessment, describing in quantitative terms the absorption, metabolism, distribution and elimination (ADME) processes in the human body, with a focus on the effective dose at the expected target site. In addition, integrated exposure models that incorporate PBTK models also offer the opportunity to assimilate biomonitoring data through exposure reconstruction. In this reverse dosimetry approach, exposure components are quantified and are related to the observed biomarkers concentrations.

Learning objectives

Understanding of the life cycle of chemicals and the processes of emission of different compound classes into the environment

Understanding of multimedia fate into the environment

Understanding of key exposure concepts such as exposure scenarios, dose, intake, uptake, pathways and routes

Understanding of internal dosimetry principles and basic toxicokinetic concepts

Understanding of the methods of exposure reconstruction based on toxicokinetics data

Understanding of uncertainty and sensitivity analysis in toxicokinetic models

Get familiar with integrated exposure/toxicokinetics models in real-life exposure scenarios

Session 1: [Title]

hh:mm [title (name instructor)]

hh:mm [title (name instructor)]

hh:mm [title (name instructor)]

hh:mm Break [15 min]

Session 2: [Title]

hh:mm [title (name instructor)]

hh:mm [title (name instructor)]

hh:mm [title (name instructor)]

hh:mm Lunch [60 min]

Session 3: [Title]

hh:mm [title (name instructor)]

hh:mm [title (name instructor)]

hh:mm [title (name instructor)]

hh:mm Closure [note: room is available untill 16:00]

A10 Mixtures and related data analysis (Jelle Vlaanderen/Erik Lebret)

Date: Friday 23 November 2018

Location: Room 'De Marijnenkamer' Huize Heyendael, Geert Grooteplein Noord 9, 6525 EZ Nijmegen, Phone +31-24-3611282

Instructors

Jelle Vlaanderen, Division of Environmental Epidemiology, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, The Netherlands; Ilse Ottenbros, Erik Lebret, National Institute of Public Health and the Environment, Bilthoven, The Netherlands

Description

Analyzing mixtures of exposures is a recognized challenge in environmental epidemiology. In this training we will introduce and provide an R script for several statistical approaches to describe mixture patterns and for modeling of mixture data, including circosplots, network analysis, sparse partial least squares regression and (Bayesian) penalized regression. The training will start with an introduction into the concepts related to the analysis of mixture data and available approaches, and will involve a large practical component. The training will end with a reflection on the acquired insights of the applied approaches and their relevance to HBM4EU. Note: for this course prior knowledge of the software application R is required. You need to install these applications on a notebook or laptop computer that is brought to the course.

Learning objectives

Be able to describe mixture patterns in HBM data

Awareness of statistical methods that are available to analyze mixture data

Know how to apply these methods on a real dataset

Session 1: [Title]

hh:mm [title (name instructor)]

hh:mm Break [15 min]

hh:mm [title (name instructor)]

hh:mm Lunch [Note the room for the lunch is available 12:30 – 13:30

Session 2: [Title]

hh:mm [title (name instructor)]

hh:mm [title (name instructor)]

hh:mm Closure [note room is available until 16:00]

A11 Determination of phthalate/DINCH and alkylpyrrolidone metabolites in urine

Date: 23rd November 2018

Location: Institute for Prevention and Occupational Medicine of the German Social Accident Insurance - Institute of the Ruhr-Universität-Bochum (IPA), Bürkle-de-la-Camp-Platz 1, 44789 Bochum (Germany)

Instructors

Phthalate/DINCH: Holger M. Koch, Claudia Pälmke, Institute for Prevention and Occupational Medicine of the German Social Accident Insurance - Institute of the Ruhr-Universität-Bochum (IPA), Bochum, Germany

Alkylpyrrolidones: Daniel Bury, Holger M. Koch, Institute for Prevention and Occupational Medicine of the German Social Accident Insurance - Institute of the Ruhr-Universität-Bochum (IPA), Bochum, Germany

Description

Phthalate/DINCH: In this theoretical training course, the determination of phthalate and DINCH metabolites in urine via online-SPE-LC-MS/MS is presented. The analysis procedure is explained and critical steps are pointed out (e.g. choice of enzyme). For isomeric phthalates (and DINCH) specific focus will be put on correct/harmonized integration of isomeric peaks by exemplary chromatograms. The confirmatory power of using more than one metabolite for one target analyte is explained, including the use of oxidised metabolites. Several approaches for a robust in lab quality assurance/control in the quantitative analysis of phthalates and DINCH are explained. Finally, exemplary studies are presented.

Alkylpyrrolidones: In this theoretical training course, the determination of urinary N-methyl-2-pyrrolidone (NMP) and N-ethyl-2-pyrrolidone (NEP) metabolites (2-hydroxy-N-methylsuccinimide (2-HMSI), and 5-Hydroxy-N-methyl-2-pyrrolidone (5-HNMP) in case of NMP and 2-hydroxy-N-ethylsuccinimide (2-HESI) and 5-Hydroxy-N-ethyl-2-pyrrolidone (5-HNEP) in case of NEP) via GC-EI-MS/MS after solid phase extraction (SPE) and derivatization (silylation) is presented. The analysis procedure is explained and critical steps and pitfalls are pointed out. Exemplary chromatograms are shown and the quantitative analysis is explained. Finally, exemplary studies are presented.

Learning objectives for the morning (phthalates/DINCH)

Knowledge of specific phthalate and DINCH metabolites to be analyzed in urine samples.

Understanding of sample preparation using enzymatic hydrolyses and online SPE–LC coupling.

Understanding of analytical procedure, including harmonized peak integration of isomeric peaks.

Quantitative analysis, including in lab quality assurance based on analytical data (including multiple metabolites).

Learning objectives for afternoon (alkylpyrrolidones)

Knowledge of specific NMP and NEP metabolites (including their formation) to be analyzed in urine samples.

Understanding of sample preparation using SPE.

Understanding of analytical procedure, including derivatization.

Quantitative analysis based on analytical data.

Calculation of external doses (reverse dosimetry) based on analytical data.

Session 1: Determination of phthalate and DINCH metabolites in urine

09:00 [Lab tour (name instructor)]

09:30 title (name instructor)]

10:30 Break [15 min]

10:45 [title (name instructor)]

12:00 Lunch

Session 2: Determination of alkylpyrrolidone (NMP, NEP) metabolites in urine

13:00 [title (name instructor)]

15:30 Break

15:45 Lab tour (name instructor)]

16:30 Closure