HBM4EU science and policy for a healthy future

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Criteria for the use of existing biological samples from health studies for HBM analysis

(Extracted from D11.1)

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2 Background

In health surveys, especially in health examination surveys (HES), biological samples are commonly collected and often also stored for future use. This provides a possibility to extend the health surveys also to HBM if underlying criteria for the sample collection and supporting information is met.

This document will provide a short overview of what is known about availability of stored samples in national HESs in Europe, what are the key criteria for samples when analysing the HBM4EU 1st priority chemicals, and what are the criteria for the use of stored biological samples from health studies for HBM analysis.

2.1 Stored biological samples from national HESs

In 2007-2017, a national HES was conducted in 14 EU Member States.[1] In all these surveys, blood samples (Figure 1[33]) were collected and all except one country also stored sample for future use (Figure 3[33]). Urine samples were collected in nine countries (Figure 2[33]). Two collected 24 hour urine and eight spot urine samples. In four countries also urine samples were stored for future use (Figure 3[33]).

Figure 1. Blood sample collection

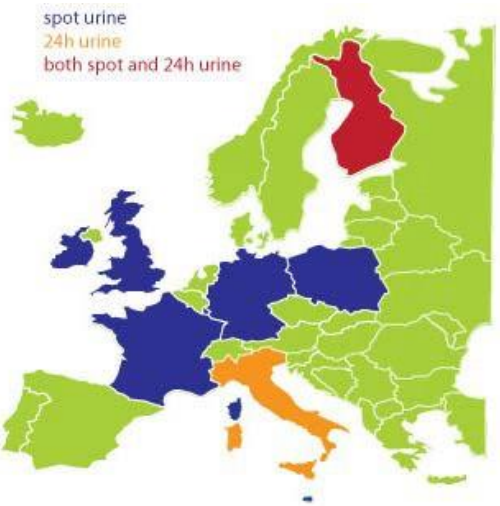

Figure 2. Urine sample collection

[1] Tolonen H, Paalanen L, Sääksjärvi K et al. Inequalities in availability of health information from national health examination surveys in EU Member States. October 2017. Available at: http://www.ehes.info/publications/Report_inequalities_health_information.pdf

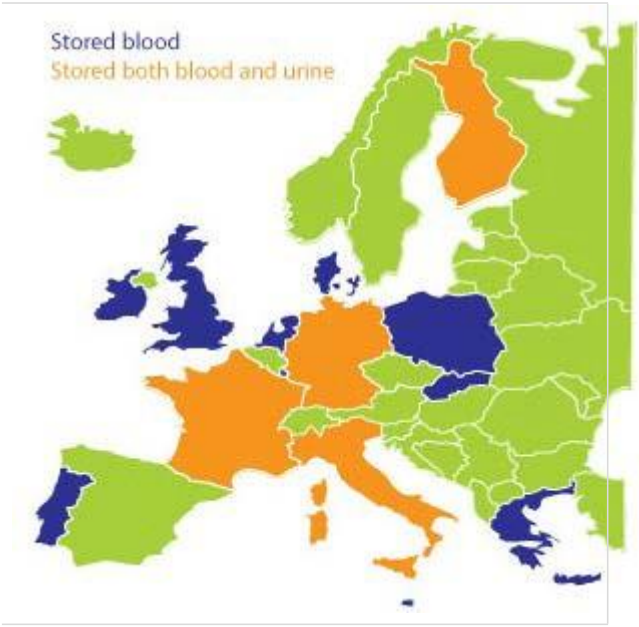

Figure 3. Samples stored for future use

Additional to these national HESs, several smaller regional and disease specific surveys have been conducted in most of the EU Member States. Many of these have also collected biological samples and stored them for future use.

2.2 Sample collection and handling in health studies

Sample collection and handling procedures vary between health studies. In EHES, basic guidelines for blood and urine sample collection were provided.[2] These are guidelines for procedures and don't provide any specification for types of sample collection and storage materials such as tubes. Obviously each individual national HES may have their own variations from these and they have used sample collection material available for them. Therefore, these guidelines provide only indicative procedures on how sample collection in health studies could go.

In principle, EHES recommendations to collect blood samples also allows for long term storage to be used in the future. Since in EHES, collection of urine (preferably 24 hour) is optional, collection of urine samples is voluntary but recommended whenever possible.

3 Requirements for 1st priority chemicals

Some chemicals are more prone for contamination during the sample collection, handling and storage than others. Table 1 provides a short overview of the key points to take into account during the sample collection and storage for HBM4EU 1st priority chemicals. Table 1 also provides sample type (preferred in bold) on which the chemical can be measured and minimum amount of sample needed.

Table 1. Sample type, amount of sample needed, storage and other special requirements for the HBM4EU 1st priority chemicals.

[2] Tolonen H (Ed.) EHES Manual. Part B. Section 6. Collection of biological samples. 2nd edition. National Institute for Health and Welfare. 2016. Directions 2016_14. URN:ISBN:978-952-302-701-5. URL: http://urn.fi/URN:ISBN:978-952-302-701-5

Chemical	Sample	Amount of sample	Storage	Accepted materials	Special requirements
Phthalates/DINCH	**urine**/ spot or 24-h	0.25-0.50 ml	at least -20ºC	PP- and PE-plastic	Phthalate-containing materials must be avoided
Bisphenols	**urine**/ spot or 24-h	0.25-0.50 ml	at least -20ºC	PP- and PE-plastic	
Per-/Poly-fluorinated compounds	**serum**	0.25-0.50 ml	at least -20ºC	PP- and PE-plastic	No special requirement, except fluorinated materials must be avoided
Flame Retardants	**urine**/ spot or 24-h, serum	5-10 ml urine, 1-2 ml serum	at least -20ºC	PP- and PE-plastic	Potential target compound contamination by sampling devices should be explored before sampling if possible
Cd, Cr	urine/spot	20 ml urine	at least -20ºC	PP- and PE-plastic	Special-washed containers have to be used, and no preservatives may be added. Specimen is prone to contamination.
Cd	blood	5 ml whole blood	at least -20ºC	A heparinized vacuum tube (e.g. Vanosafe®, Vacuette ® trace element)	Specimen is prone to contamination.
PAHs and air pollutants	**urine**/ spot or 24-h	5-10 ml	at least -20ºC	PP- and PE-plastic	
Anilin family: Aniline, 4.4'-MDA, MOCA	urine/spot	20 ml	at least -20ºC	PP- and PE-plastic	Specimens (Aniline, 4.4'-MDA and MOCA) are prone to contamination. Aniline: no preservative 4.4'-MDA: sulfamic acid added as preservative MOCA: no preervative
Chemical mixtures	**urine**/ spot or 24-h, serum	5-10 ml urine, 1-2 ml serum	at least -20ºC	PP- and PE-plastic	Potential target compound contamination by sampling devices should be explored before sampling if possible
Emerging	**urine**/ spot	5-10 ml	at least	PP- and	Potential target compound

Chemical	Sample	Amount of sample	Storage	Accepted materials	Special requirements
chemicals	or 24-h, serum	urine, 1-2 ml serum	-20ºC	PE-plastic	contamination by sampling devices should be explored before sampling if possible

4 Criteria

Since in many health studies biological samples, mainly blood and sometimes also urine, are collected and stored for future use, these provide a potential also for further analysis of HBM biomarkers. To be able to use stored samples from health studies for HBM analysis, following key points has to be checked and clarified:

Ethics

Does the ethical approval and informed consent used for original data collection cover the secondary use of stored samples for HBM analysis?

Depending on national guidelines and practices, samples collected in health studies may be used broadly for any public health purposes, for studies on specific diseases etc. If original ethical approval and informed consent doesn't allow the use of stored samples for HBM analysis, it may be possible to obtain new ethical approval for this secondary use of samples.

Study population

Does the target population of the health study correspond to one needed for HBM analysis?

When samples and data are used for the secondary purposes, we cannot change the definition and selection of the target population anymore. Therefore, it has to be assessed if the target population for the health survey is adequate for the needs of the HBM analysis.

Information collected by questionnaire(s)/health measurements

What kind of information has been collected by questionnaire(s) about background, lifestyles and possible exposures in health studies, and are there any relevant health measurements included?

Health surveys always have questionnaire(s) and health measurements to support and amend the results obtained from biological samples. Questionnaire(s) tend to have socio-demographic background information, information about diagnosed diseases and general health and also some lifestyle topics such as smoking, alcohol use and diet. Extent of the questionnaire(s) varies considerably between the surveys.

Since similar information is also needed to support interpretation of the HBM analysis, it should be checked that all the relevant information is available and if not, does that limit the use of biological samples for HBM analysis.

Type of available samples

What type of samples is available for the secondary analysis?

In most of the health studies, blood (serum and/or plasma) is stored for future use. Collection of urine, especially 24 hour urine samples, is rarer in health studies. Therefore, availability of the samples may already set limitations for what could be measured.

Amount of available samples

How much of the samples are available for the secondary analysis?

Since each of the HBM analysis has a minimum requirement for the amount of sample needed, it should be checked how much of the sample(s) is available for the secondary analysis and is that enough for the planned HBM analysis.

Sample collection materials

What type of materials was used for sample collection?

If possible and information is available, it should be checked what kind of materials were used for sample collection to avoid possible contamination by the target compounds. In health studies, field blanks recommended for HBM studies are not usually used.

Sample handling procedures

How samples were handled and processed on the field?

Survey protocols should include details about sample handling and processing in the field. These should be checked to ensure that samples are handled the way that it does not result in problems for HBM analysis, including possible contamination with target compounds after collection of the samples.

Sample storage

On what type of tubes and on which temperature samples were stored?

Sample storage environment is essential for preservation of the biological samples and for what they can be used for in the future. Therefore, before making the decision about the use of stored samples, it should be checked on which type of tubes they are stored, on which temperature, have the samples been thawed and re-frozen, and does that affect the usability of samples for HBM analysis.

Access to the samples

How one can get access to the sample and does that cost something?

Usually every study has their own protocol and rules on how and for which types of analysis they provide access to the stored samples. When samples of interest have been identified, the conditions for access have to be agreed with the principle investigator or management board of that specific health study. It varies between countries and studies whether samples can be accessed without cost or whether the interested party has to pay for accessing the samples.