Report from EU Bridge Health Horisontal activity 7 on ethical issues.

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Questionnaire survey

As part of the general survey a number of questions were specifically asked related to ethics as seen in table with the general question of 'Have you been hampered (should have been challenged) in your project by ethical or legal issues?'

Results

When initiating human biomonitoring (HBM) studies in EU you have to apply to national and EU-regulations on Human participation in studies including description of: Study persons/tissues, who, where, how, Informed consent, data privacy, bio banking, and secondary use. Applications for approvals of HBM studies to national ethics committees are not uniform as the ethics committees include national and local elements which are discussed and prioritized from the cultural and moral/ethics background of the ethics committee. Thus a harmonization within EU is not practicable, though it has been discussed for decades to aim at more uniform requirements.

Summary of the questionnaire

The horizontal issue in legal and ethics is to survey current practices, upcoming regulations and obstacles for cross country studies. In this HA study 18 project participants participated. The following section will cover the experiences from ethics issues in these different respondents by including the questions the researchers were asked, who did answer these and what did they answer. Furthermore, this section will include advices from the researchers to upcoming projects in relation to ethical and legal issues and how these could be useful for Bridge Health.

Table 1 shows the topics related to ethical or legal issues the researchers had been hampered in the project and how many researchers it was relevant for. As shown in table 1, the major ethical or legal issues the researchers had been hampered in the project were secondary use of data, storage and transport of samples/data, data protection and cross country exchange.

Topic	Case(s) / total	Cases
Recruitment	3/18	(H.T; JM.R; A.J)
Information to participants about project	2/18	(JM.R; A.J)
Informed Consent	3/18	(W.R; JM.R; A.J)
Sampling	1/18	(A.J.)
Information about results	3/18	(E.B; U.H; A.J)
Incidental findings	1/18	(A.J)
Vulnerable groups	1/17	(JM.R)

Minors and withdraw	0	
Secondary use of data	7/18	(R.L; S.G; J.Z; E.B; J.Z; JM.R; A.J)
Storage and transport of samples/data	5/18	(W.R; E.B; U.H; JM.R, A.J)
Data protection	6/18	(W.R; J.Z; E.B; U.H, G.K; A.J)
Sampling frame	1/17	JM.R
Cross country exchange	7/18	(R.L; S.G; J.Z; E.B; U.H, J.Z; A.J)
Insurance	0	

The researchers were asked to elaborate the problem and how it was solved. In general, the problem that repeated in several countries was local ethics and privacy regulations e.g. in the different countries, and these different rules were preventable for pooling data in the countries. Researchers from several countries indicate the design of the informed consent was challenging and different rules had to be followed between member states. In some of the countries the researchers solved those problems by different methods, which gave them the agreement to complete the study, but in some other countries the problem couldn't be solved which caused limitations.

The researchers were required to give their advice to upcoming projects in relation to ethical or legal issues, and how this could be useful for Bridge Health. It looks like there is a consensus about the difficulty to get clear information about the rules in participating countries and it would therefore be extremely helpful to have a resource for this on the European level. At this point it is important to implement the project in accordance with the rules in each country regarding ethic committees, data protection and providing individual level data
A new EU Data Protection Regulation could be useful in the development of a structure which systematically brings together information on MS level in relation to ethical and legal issues, one starting point could be Health Data Navigator (HDN), which is one of the major instruments of EU data protection law and aims at achieving a minimum level of data protection in the Member States. This is expressed by six main principles, which is:

- Legitimacy to collect data for
- Limited purposes
- Transparency for the data subject
- Proportionality in relation to the purpose
- Security of processing
- Control by data protection authorities.

(More detailed information is available on: http://www.healthdatanavigator.eu/data-management/data-protection)

Another advice is that experiences of COPHES/DEMOCOPHES should be taken into account. The European pilot project DEMOCOPHES was developed to test the feasibility of a harmonized Human Biomonitoring (HBM) project in Europe with the possibilities to compare exposure levels

across borders and support environment, health and chemical policies (WP6). Detailed information is available on the website: http://www.eu-hbm.info/cophes and the table 2 in the publication by Casteleyn et al. shows the diversity within countries:

Table 2: Table on the different documents to be submitted to 17 countries in the DEMOCOPHES project

Table 3
Overview of documents submitted to ethics committees.

Country	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17	
Document/ English (E) Translated (T)	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T	E	T
1. Submission letter		X			X	X	X				X	X			X		X						X	X			X				X	X	X	X
2. Specific application form		X			X		X				X				X		X			X			X	X			X				X	X	X	X
3. Summary of the project		X		X	X		X	X			X		X		X		X	X	X			X	X	X			X	X	X	X	X	X	X
4. EU protocol	X	X			X		X		X			X					X	X			X		X		X			X	X	X			X	
5. Addition to the protocol		X			X		X				X	X					X				X		X		X									X
6. Policy fact sheet	X			X	X	X					X		X					X							X									
7. Invitation (1st) letter	X			X	X	X	X	X			X		X		X		X			X	X	X	X		X	X			X	X	X	X		
8. Information leaflet	X				X	X	X	X			X		X		X		X			X	X		X		X	X			X	X	X	X		
9. Information leaflet for children					X	X					X		X				X			X	X		X						X	X				
10. Reply card					X	X					X		X		X		X						X						X	X	X	X		
11. Reminder letter					X	X					X		X		X		X													X	X			
12. Appointment (2nd) letter					X	X					X		X				X													X	X			
13. Informed Consent form		X		X	X	X	X	X			X		X		X		X			X	X	X	X		X			X	X	X	X		X	
14. Informed Assent for children					X	X					X				X		X			X			X					X	X				X	
15. Withdrawal letter		X			X	X					X		X		X		X						X							X	X		X	
16. Letter of thanks					X	X					X		X		X		X								X					X	X			
17. Pre-visit (3rd) letter					X						X				X		X													X	X			
18. Instruction leaflet on how to provide the urine samples					X						X				X		X								X									
19. Chemical fact sheets	X			X	X						X		X				X				X				X					X	X			
20. Letter informing on the results	X				X						X		X				X				X		X		X					X	X	X		
21. Procedure for informing on high results					X						X												X				X							
22. Basic questionnaire				X	X	X	X	X			X		X		X		X		X		X		X		X			X	X	X				X
23. Hair and urine questionnaires					X						X		X		X		X		X		X				X					X				X
24. Recruitment interview					X						X		X		X		X		X		X							X	X	X				X
25. Non responder questionnaire				X	X	X					X		X				X		X		X							X	X	X				X
26. Attestation of insurance											X	X									X		X											
27. Other				X			X	X	X					X	X	X			X	X			X		X			X	X	X	X			X

It was suggested to encourage DG Santes establishing a TF on harmonizing ethical rules for date collection and transfer and this TF working in coordination with BRIDGE 1 and BRIDGE 2 (the follower).

Discussion at the GA in Brussels April 2016

The recommendation at the GA in Brussels April 2016 was to include reference to issued papers by OECD, WHO and Eurostat. It was also recommended to keep trace on changes from the new legislation related to data protection and registries. In the WP 7 (Reproductive, maternal, newborn, child and adolescent health) and WP10 (Platform for administrative data on health care) ethics is specifically considered and exchange of documents/information about meetings and courses is recommended.

Data protection (from HA4)

Personal data are defined as any information relating to an individual, whether it relates to his or her private, professional or public life and can be anything from a name, photo, email address, bank details, material on social network sites, medical information or a computer's IP address.

Health data is always considered as sensitive information and therefore safeguarding the privacy of individuals has an important role when handling this type of data. If raw, individual level data is used and whenever data is transferred from one entity to the other, it is important to ensure the privacy of the individuals through anonymization.

There is a wide range of data anonymization techniques; substitution, shuffling, number variance, data variance, character masking, cryptographic techniques, public key techniques, message digest techniques, partial sensitivity and partial masking, masking based on external dependency, auxiliary anonymization techniques, alternative classification of data anonymization techniques and leveraging data anonymization techniques

Every time individual level data is shared, a special attention is paid to requirements set on national legislation. Written data transfer agreements must be prepared between data owner and organization managing the centralized database.

Under EU law, personal data can only be gathered legally under strict conditions and for a legitimate purpose. Persons and organizations that collect and manage personal information are under an obligation to protect it from misuse and protect the rights of the data owners. Consent is generally required for the processing of personal data.

In January 2012, the European Commission proposed a comprehensive reform of data protection rules in the EU.

On 4 May 2016, the official text of the Regulation 679 has been published in the EU Official Journal in all the official languages. While the Regulation entered into force on 24 May 2016, it shall apply from **25 May 2018**.

The objective of this new set of rules is to give citizens back control over of their personal data, and to simplify the regulatory environment for business. The data protection reform is a key enabler of the Digital Single Market which the Commission has prioritized. The reform will allow European citizens and businesses to fully benefit from the digital economy.

Under EU law, personal data can only be gathered legally under strict conditions, for a legitimate purpose. Furthermore, persons or organizations which collect and manage your personal information must protect it from misuse and must respect certain rights of the data owners which are guaranteed by EU law.

Every day within the EU, businesses, public authorities and individuals transfer vast amounts of personal data across borders. Conflicting data protection rules in different countries would disrupt international exchanges. Individuals might also be unwilling to transfer personal data abroad if they were uncertain about the level of protection in other countries.

Therefore, common EU rules have been established to ensure that your personal data enjoys a high standard of protection everywhere in the EU. You have the right to complain and obtain redress if your data is misused anywhere within the EU.

Ethical considerations in consent

In all current studies – research as well as surveillance HBM - participants are recruited following a study protocol detailing the purpose of the study and the handling of data. Informed consent is required as well as a procedure for feed-back of individual results, respecting the individual's right to know and not to know.

The protocol and information material has to be approved by the local/national Ethics committee and Data Protection issues are also part of the requested approval. For research activities supported by the EU commission a specific system is set up requesting information about specific issues of:

a) Recruitment, informed consent, collection, handling and sharing of health related information and other sensitive data included in the HBM studies (existing as well as new);

b) Biobanking and sharing of samples, also across countries, in HBM studies;

c) Data processing, dissemination and privacy including incidental findings;

d) Transfer of individualised data to databases ensuring privacy and IPR.

A development towards focus on individualised HBM is seen by requests for individual HBM data from lay persons and more specific information about individual risks by e.g. pregnant mothers and other sensitive groups. In a reaction to these developments, ethics evaluation panels also ask for measures to be taken to avoid vulnerability/stigmatization of individual groups. Measures to prevent potential detrimental socioeconomic disadvantages of individuals who want their individual results and measures to avoid stigmatization of particular social groups, political or financial retaliation and malevolent use are requested increasingly as part of ethics evaluations. It is important to explore how trust in the research team, which includes the the right to withdraw at any time, is respected as well as data protection This often depend on social and cultural factors, which is important to consider, during the planning of studies (Toccaceli V. et Al. 2014; Toccaceli et Al. 2016). Finally, despite a tendency towards the participants' use of and interest in individual results, the altruistic aspect of providing data for the benefit of the society will be investigated.

Ethical research guidelines promote the following four basic principles of biomedical ethics: autonomy, beneficence, nonmaleficence, and justice, and define the responsibilities of researchers to protect research participants and guarantee their rights and safety.

Autonomy is related to respect for the person, and is commonly understood as his/her right to know or not to know, and as his/her freedom in making decisions (to participate in or not to participate in, or withdraw from, the research). The principles of beneficence and nonmaleficence imply the obligation of maximizing possible benefits, protecting participants from potential/predictable harm, and securing their well-being. Justice addresses the issue of fairness of the distribution of research benefits and risks. Only reasons strictly related to research objectives, and not their easy availability or other population-specific characteristics (e.g., ethnic minorities, the socioeconomically less advantaged, gender, etc.), should define the criteria for selection of participants. In environmental as well as therapeutic research, justice is directly linked to the validity of the study, and to the possibility of extrapolating research findings from the study sample to the target population.

Dynamic consent vs broad consent

Informed consent is the process by which an adequately informed person can participate in choices about his/her health care and participation in research. Its purpose is to enable potential participants to make informed choices about themselves and to safeguard their own best interests, in the full knowledge of risks versus potential benefits. The traditional version of the consent, that has to be given from the participants every time their data or biomaterial is used in new projects, is time consuming requesting renewed approval by the Ethics Committee. Another way of obtaining consent is discussed. Broad consent is consent to a range of research questions within certain limits, including upcoming research questions. Dynamic consent is an alternative to broad consent placing the participants in the center. The dynamic consent is an ongoing process facilitated by modern communication strategies to inform, involve, and obtain consent for every research question based on biobank resources, thus giving the participants more control over “their” data and access to information about projects. The issue of dynamic consent is also considered a way of informing about results becoming available many years after sampling (Kaye et al., 2015; Steinsbekk et al., 2013; Johnsson and Eriksson, 2016; Spencer et al., 2016; Williams et al., 2015)..

Broad consent and dynamic consent is being debated worldwide with regard to ethical concerns. Some of the pros and cons are listed in table 3.

Table 3: The positive and negative opinions on dynamic consent versus broad consent. (sources: Kaye et al., 2015; Steinsbekk et al., 2013; Johnsson and Eriksson, 2016; Spencer et al., 2016; Williams et al., 2015, Grady et al., 2015).

Broad consent	**Dynamic consent**

Negative	*Positive*	*Negative*	*Positive*
Pragmatic	Some participants like that they only have to consent once	The amount of information makes it harder for the participants to distinguish between relevant and irrelevant information	Increased user participation
Not acceptable ethical solution due to participants agreeing to the material may be shared widely and used by many researchers	Allow individuals to control whether their samples are used for research and avoids the potential burden for researchers and donors of asking individuals to consider and make a decision for each new study	Greater involvement of participants lead to greater feeling of the research is to serve them directly -> therapeutic misconception is exacerbated	Participants get more committed to research interests and altruism
Paternalistic	The need for tech savvy participants is low	Participants may lose interest from overextension	Increased recruitment
Top down governance		Consent may lose meaning when it becomes repetitive,	Reduce dropout
Autonomy of participants not respected		Participants may need to be tech savvy	Reduce need for anonymization of data
Re-contact is expensive, time-consuming, may be difficult and can result in high drop-out rates			Educate the public
			Facilitate innovative research
			Sustain public confidence in the research enterprise

			Participants manage their own consent preferences
			Consent can securely travel along with the data and samples when shared with third parties
			Streamlined recruitment and more efficient re-contact

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