Deliverable Number: D6.10

Deliverable Title: Synopsis of Policy-Rules for Collecting Biomarkers in Social Surveys

Work Package: WP6

Deliverable Type: Report

Dissemination Status: Public

Submitted by: MEA (MPG) – SHARE-ERIC

Author: Daniel Schmidutz

Submission Date: July 2016

This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under grant agreement No 654221.

Synopsis of Policy-Rules for Collecting Biomarkers in Social Surveys

–

Field Report on the Collection of Dried Blood Spot Samples in SHARE

CONTENT

1 Introduction 4

2 The Collection of Dried Blood Spots in SHARE 6

2.1 Background and Aims of Collecting Dried Blood Spots 6

2.2 Piloting the Method and Logistics of DBS Sampling in SHARE 7

2.3 Preparing the Full-scale Implementation 8

3 Ethics and Legal Requirements by Country 10

3.1 AT – Austria 11

3.2 BE – Belgium 12

3.3 CH – Switzerland 15

3.4 CZ – Czech Republic 19

3.5 DE – Germany 20

3.6 DK – Denmark 23

3.7 EE – Estonia 26

3.8 ES – Spain 28

3.9 FR – France 30

3.10 GR – Greece 33

3.11 HR – Croatia 36

3.12 HU – Hungary 38

3.13 IL – Israel 41

3.14 IT – Italy 43
3.15 LU – Luxembourg 47
3.16 NL – The Netherlands 50
3.17 PL – Poland 54
3.18 PT – Portugal 57
3.19 SE – Sweden 59
3.20 SI – Slovenia 63
4 Summary and Concluding Remarks 67
5 References 71
6 Annex 72
6.1 Acronyms and Abbreviations 72
6.2 List of Tables 73
6.3 Transnational Inquiry on Ethics Committee Approvals 74

1 Introduction

Modern research in the social sciences requires recording much more innovative variables, such as objective health information or precise data on the financial status of respondents. In this regard, for instance, the inclusion of so-called biomarkers, i.e. objective measures of biological and physical functions, and the linkage of survey data with administrative records recently gained in importance for field surveys in terms of supplementing 'traditional' self-reported survey data.

Since health is a major concern for ageing societies it is essential to better understand underlying processes and pathways of the development of certain diseases. Combining self-reported information on health with objective health measures helps to overcome typical biases caused by individual perceptions and to improve the precision of health measurement. Therefore, the *Survey of Health, Ageing and Retirement in Europe (SHARE)*[1] started to expand its already existing collection of objective physical biomarkers (such as grip strength, lung force, etc.) by collecting biological biomarkers, using the method of dried blood spot (DBS) sampling, in the fourth wave of the panel study. After a successful initial testing of the logistics of the DBS collection in a pilot study in Germany and its successful expansion to six countries in the pretest of SHARE wave 5, it was decided to fully implement the DBS collection in SHARE wave 6.

While being able to complement population-based survey data collection with innovative variables such as biomarkers is of great value with regard to later scientific analyses and the socio-economic impact scientific findings of such analyses may have, the collection of these types of data is also associated with ethical and legal challenges. New methods of data collection such as the DBS sampling amplify the ethics issues which need to be addressed and extend the requirements for researchers in relation to legal provisions. Besides these challenges, cross-national research projects such as SHARE raise particular ethical and legal challenges to which researchers have to respond.

This Deliverable addresses central legal (as well as related administrative) requirements and ethics issues related to the collection of DBS samples and aims at providing a *Synopsis of Policy-Rules for Collecting Biomarkers in Social Surveys* in a cross-national perspective. Following a practical approach, by describing the experiences in relation to research ethics and the legislative and administrative regime(s) that have been made when implementing the collection of biological samples in various European countries and Israel in the context of the SHARE study, the current document also provides a *Field Report on the Collection of Dried Blood Spot Samples in SHARE*. At this, the aim of the Deliverable is to show the very

[1] The Survey of Health, Ageing and Retirement in Europe (SHARE) is a multidisciplinary and cross-national panel study that incorporates information regarding social, economic and health factors of more than 123,000 individuals from 20 European countries and Israel aged 50 or older as well as national institutional and social policy conditions. For more information please visit: http://www.share-eric.eu/.

concrete ethical and legal challenges of cross-national survey practice when combining traditional face-to-face interviewing with the collection of blood samples and to provide an overview of differences and similarities in this regard on a country-by-country basis.

The report starts off with a description of the background and aim of the DBS collection in SHARE and highlights advantages of the inclusion of biological biomarkers in population-based surveys including self-reported information on health (Chapter 2.1). It continues by giving an overview about initial experiences that have been made in SHARE when piloting and pretesting the DBS collection (Chapter 2.2) and highlighting a few important aspects of the preparation phase for the full-scale implementation of the DBS collection in wave 6 of the SHARE study (Chapter 2.3).

Then, a detailed description of the experiences in relation to research ethics and the legislative and administrative regime(s) that have been made during the implementation process in SHARE is given (Chapter 3). At this, particular importance is placed on a country-by-country documentation of information on ethics issues and legal requirements that has been collected as part of the practical administration of the survey during the years 2012 to 2014.

Finally, the main general legal and ethical issues that have been experienced are briefly summarised and the outcomes for the implementation of the blood collection in SHARE wave 6 are highlighted (Chapter 4).

2 The Collection of Dried Blood Spots in SHARE

2.1 Background and Aims of Collecting Dried Blood Spots

The Survey of Health, Ageing and Retirement in Europe (SHARE) is a cross-national and multidisciplinary panel study incorporating individual self-reported information regarding social, economic and health factors as well as national institutional and social policy conditions in order to understand how we age differently within Europe. These factors are well-known determinants of healthy ageing in its broad definition which includes adequate economic and social support as well as good health.[2]

Self-reported information on health is important as it reflects subjective impressions. When collected in different countries, however, it is typically biased because individual perceptions vary across countries as much as socio-cultural factors. This bias can be overcome through objective measures of biological and physical functions, so-called biomarkers. For this reason, biomarkers, serving as indicators of the objective state of health, are increasingly used in epidemiological and socio-economic research.

Already from its beginning, SHARE has used objective physical biomarkers well-known for their prediction of adverse health outcomes, e.g. grip strength and lung force. But even though these physical biomarkers provide some valuable insights about potential health risks, they provide indirect information only and do not allow an understanding of the underlying processes and pathways. This knowledge gap can be filled with the aid of certain biological biomarkers, which are strongly correlated with health.[3]

In many clinical and medical epidemiological studies, biomarkers have been collected through venipuncture and venous blood analyses. Such a methodology, however, is extremely expensive when used in field surveys such as SHARE. As an alternative, the method of dried blood spot sampling has been introduced to the research field (cf. McDade et al. 2007). DBS sampling means that several drops of blood are taken by pricking, e.g. a finger, and collecting the capillary blood drops on a filter-paper card. The blood spots are left to dry and the cards are then shipped by ordinary postal mail to a biobank, where they are stored in freezers until analyses are performed. DBS samples, in principle (i.e. if there are no legal restrictions), can easily be collected in surveys employing trained laypersons (interviewers).

[2] For further information see the website of the SHARE project: http://www.share-eric.eu/.

[3] Biomarkers as collected in SHARE so far include: a) Physical biomarkers: grip strength, lung force/peak flow, walking speed, chair stand, height, waist circumference, blood pressure (physical and performance measures taken in SHARE) – b) Biological biomarkers: HbA1c, total cholesterol, C-reactive protein and Vitamin D (values gained from the analysis of dried blood spots in the SHARE pilots; please see Chapter 2.2)

Present biotechnology allows DBS samples to be used to determine various lipoprotein or protein structures as well as tracer elements (e.g. heavy metals) in the individual. Among them, the more well-known biological markers, like glycated haemoglobin (HbA1c), a marker of diabetes, and C-reactive protein (CRP) and other cytokines, markers of inflammation and associated with atherosclerosis, hypertension and cardiovascular diseases, have reliably been measured in DBS samples. More recently, DBS assays for the measurement of Vitamin D and cholesterol have been developed and validated. Low values of Vitamin D are associated with a loss of muscle mass, muscle weakness and functional decline, as well as elevated risk of osteoporosis and fracture. Cholesterol is a marker for the risk of cardiovascular diseases. Furthermore, DBS assays for other biomarkers, which will have huge potentials in future studies, are under development.[4]

The inclusion of biomarkers in the SHARE study is expected to give novel insights into the relations between chronic conditions common in old age and behavioural and environmental risk factors under various socio-economic conditions. The collection of DBS samples in SHARE will therefore not only enrich the SHARE database but also support multidisciplinary scientific research. Furthermore, a fundamental advantage of including biomarkers into a large-scale survey such as SHARE is the simultaneous availability of biological and socio-demographic data in a representative (i.e. non-clinical) population. Using these data, manifold research areas can be investigated, e.g. the implications of recent public policy interventions on the health of older citizens, the causal link between biological aging processes with socially and economically induced health behaviours, or the future costs of typical chronic diseases in old age, such as diabetes.

2.2 Piloting the Method and Logistics of DBS Sampling in SHARE

In the SHARE wave 4 main data collection, Germany served as a pilot country. Aiming at later full-scale implementation in SHARE, this pilot primarily served the purpose of determining whether and how an inclusion of a DBS collection could be realised in a population-based survey context within a European country and to test the logistics being associated with such a project. In order to design a training program for interviewers, SHARE representatives attended the interviewer training of the Health and Retirement Study (HRS) in the United States of America. HRS implemented the collection of biomarkers in its previous waves with great success. The SHARE interviewer training closely followed the HRS model in preparing the interviewers for their tasks. Interviewers were trained in depth for any eventualities, such as advising participants who take blood thinners or helping

[4] Further reading on applications and techniques of dried blood spot sampling: See *Li, W. and Lee, M.S. (Eds.) (2014): "Dried Blood Spots: Applications and Techniques." John Wiley & Sons, Hoboken, New Jersey.* The comprehensive anthology includes contributions on the history, principles, procedures, methodologies, applications, and emerging technologies related to DBS and is conceptualised as working guide for researchers.

participants, who do not bleed enough. The training on collecting biomarkers took about seven hours and the majority of this time was dedicated to supervised hands-on training sessions.

In the German pilot, all questions of the biomarker section, including the collection of DBS, were not integrated in the CAPI (computer-assisted personal interviewing) yet, but included in a paper-and-pencil booklet, which was filled in by the interviewers. After the interview, the interviewers sent the booklet to the survey agency. The three different data sources (booklet, laboratory analyses data and CAPI data) were linked using a barcode system later on: first the analyses data was linked to the booklet and finally this merged dataset was linked to the SHARE survey data.

In the following pretest of SHARE wave 5 the DBS pilot study was extended. At this stage the biomarker section was included in the CAPI (BS_module). Six countries volunteered to participate in the DBS collection in the pretest of this wave: Belgium, Denmark, Germany, Italy, Portugal, and Switzerland. The strategy was based on the experiences from collecting DBS in the German SHARE wave 4 and experiences from the Danish SHARE Country Team, which has extensive knowledge of DBS collection in population-based interview surveys among old and oldest old people in Denmark (cf. Christensen et al. 2007).

A coordinating SHARE biomarker team was set up consisting of members of the central SHARE coordination, the German and Danish SHARE Country Teams. The overall aim was to identify further methodological and logistical challenges, but also to get a better understanding of the legal and ethics related administrative frameworks. The pretest net sample was set to 150 in each country, which also was the DBS target population. The SHARE biomarker team developed an instruction manual with step-by-step instructions as well as a short video showing both the DBS collection including the handling of the DBS card on-site and its shipment, arrival and handling at the SHARE Biobank in Odense, Denmark. The respective Country Teams and their survey agencies were thoroughly trained prior to the pretest.

2.3 Preparing the Full-scale Implementation

After the (successful) implementation of the of DBS collection in the pilot projects in SHARE waves 4 and 5, it was decided to implement the DBS collection in all countries participating in wave 6 of the SHARE study. Based on the experiences of the pilot projects in SHARE waves 4 and 5, all necessary preparations for the full-scale implementation of the DBS collection in the SHARE project were made.

As experienced in the pilot projects, the collection of DBS gives rise to various concerns from all parties involved (researchers, survey agencies, interviewers and participants) since it is considered to be an invasive method (albeit only minimally invasive). These concerns not

only had to be addressed in an appropriate manner, but also make ethics committee approval necessary. Therefore particular importance was placed on addressing all concerns that had been experienced so far and on how to best prepare all relevant information and documents needed for ethics review.

One of the main lessons learned from the previous DBS collections in SHARE was that the process of obtaining ethics approval, including the collection of all relevant information with regard to national legal, administrative and ethical requirements and the careful preparation of the application documents (which also includes field documents such as consent forms and information leaflets already), takes a lot of time. For this reason the preparations were started long before the actual fieldwork phase of wave 6. As a first step, a transnational systematic inquiry regarding national legal requirements and ethics committee approval procedures with regard to the collection of biomarkers derived from DBS samples has been carried out by the central SHARE coordination team[5] making use of the SHARE research network (see Annex 6.3).[6] The aim of this inquiry was to gather all relevant information about national ethics committees' approval procedures (including responsibilities, application procedures, documents, etc.), to identify the most important legal requirements (consent, data privacy, liabilities and other country-specific issues) and, furthermore, to identify probable requirements/restrictions of the responsible ethics committees (previous recommendations, opinions, etc.) with regard to the DBS collection. Besides avoiding unpleasant surprises and time delays or even serious problems, it was intended to evaluate the practical and financial feasibility in the light of this information.

In a second step, based on the information gathered from the inquiry, generic versions of the questionnaire, consent documents (information leaflet and consent forms) and other training and field documents (such as interviewer instructions, etc.) as well as a "survey protocol" (that could be submitted to the various ethics committees) have been prepared centrally. At this, all known legal requirements/restrictions and potential ethics issues as well as the national institutional and administrative frameworks have been taken into account in order to enable an ex-ante harmonisation of the DBS collection across the participating countries.[7] These documents then had to be translated into the respective national languages and, depending on the requirements of each country, compiled, adapted, extended and finally presented to the responsible national ethics committees and – in some cases – other authorities (such as data protection authorities).

[5] SHARE Central: the central SHARE coordination team is located at the Munich Center for the Economics of Aging (MEA) at the Max Planck Institute for Social Law and Social Policy (Max Planck Society for the Advancement of Science, MPG).

[6] First findings of this inquiry have already been presented in Section 7.1.2 "Dried Blood Spot Collection in Population-based Surveys (SSc)" of deliverable D6.1 of the DASISH project (Schmidutz et al. 2013; available at: http://dasish.eu/deliverables/).

[7] One of the conceptual cornerstones of SHARE is the ex-ante harmonisation of the study across countries.

3 Ethics and Legal Requirements by Country

The information presented in the following subchapters is based on the experiences in relation to research ethics and the legislative and administrative regime(s) that have been made in various European countries and Israel during the process of including the collection of biological samples, namely dried blood spots (DBS), in SHARE. Most of the information has been obtained as part of the practical administration of the survey, including all necessary preparatory steps, during the years 2012 to 2014.[8] The information has been collected in a decentralised fashion by members of the SHARE Country Teams, which are responsible for the implementation of the survey in each individual country. This process has been coordinated and supported by the central coordination team of SHARE (SHARE Central). All information provided as well as the outcomes with regard to possibility of including DBS sampling (including relevant restrictions) in population-based interview surveys such as SHARE has been centrally reviewed and documented and is summarised for each country. As far as possible this information has been double checked and, if deemed necessary, supplemented with information available on the internet at the time of writing (July 2015 until June 2016).[9]

Disclaimer:

The following summaries of the legal framework conditions and the ethics committee approval systems in the different countries are specifically focused on the collection of dried blood spots in population-based field surveys. The information contained herein may therefore not be applicable in all situations and the experiences made in the SHARE project do not necessarily generalise to other surveys. The information provided is for general informational and educational purposes only; it is not intended and should not be construed to constitute legal advice. Although reasonable efforts to include accurate and up-to-date information have been made, SERISS (including any person/party involved in creating, producing or delivering this document) makes no warranties (express or implied) or representations of any kind as to its accuracy, currency or completeness.

[8] Some of the information has been collected earlier during the piloting phase of DBS sampling in SHARE. This information has been reviewed and updated.

[9] **Please note**: At the time of the DBS collection in SHARE the central legislative instrument of EU data protection law was "Directive 95/46/EC of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data". The Directive includes a minimum set of provisions to be implemented by the Member States and had to be transposed into national law by the end of 1998. The Data Protection Directive (by definition) is not a self-executing legal instrument and therefore leaves the choice of form and methods to the national authorities. As a result, the provisions of the Directive have been implemented in different ways in the Member States, resulting in differences in the level of data protection, both on paper and in practice (Schmidutz et al. 2013).
Consequently, these national implementations of Directive 95/46/EC provide the basis of the present documentation and not the "General Data Protection Regulation" (GDPR, Regulation (EU) 2016/679 of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC), which has entered into force on 24 May 2016 and will directly apply from 25 May 2018 in all EU Member States.

3.1 AT – Austria

Legal Framework Conditions

In Austria, due to occupational restrictions it is completely forbidden for laypersons to perform any medical task or prick anybody in order to collect blood samples. According to the Austrian Medical Practitioners Act (Art. 2ff. "Ärztegesetz" [de]) and others (Art. 15 "Gesundheits- und Krankenpflegegesetz", Art. 9 "Sanitätergesetz"), only medical doctors and nurses under medical supervision are allowed to take blood from the capillary system. As an exception paramedics may take blood from the capillary system on their own, but only for the purpose of glucose measurements. Consequently, the collection of DBS by laypersons is prohibited in Austria.

Moreover, is also not allowed that participants take blood drops themselves from the capillary system and prick their own fingers ('self-pricking') as this would be considered as an attempt of bypassing the professional requirements of the Austrian legal system and therefore an illegal circumvention of the law.

➔ *Therefore, in Austria a DBS collection cannot be carried out in the context of SHARE.*

The central relevant data protection law with regard to the processing of personal data in Austria is the Federal Act concerning the Protection of Personal Data ("Datenschutzgesetz" [de, en]).

Furthermore, the following legal conditions would apply if DBS would be collected by medical professionals in accordance with the legal requirements described above: Verbal consent given to the medical doctor who takes the DBS sample is deemed sufficient. The amount of information a medical doctor needs to give his patients is specified in the Quality Assurance Ordinance of the medical association (Art. 19 "Qualitätssicherungsverordnung" [de]). Participants have to be informed about the analyses results of their DBS samples.

Regarding the shipment of DBS samples to another European Country no legal restrictions are known. Concerning the collection of DBS, however, a specific study participant insurance would be required since the insurance of Johannes Kepler University (SHARE Country Team's home institution) would not cover any damage that might arise from the DBS collection.

Ethics Committee Approval System

In Austria, ethics committees are organised at an institutional level. The competent ethics committee for SHARE Austria is located at the Johannes Kepler University. However, according to the Medicines Act (Art. 40 "Arzneimittelgesetz" [de]), only clinical trials are required to apply for ethics committee approval in Austria. According to the Medical Devices Act, with regard to clinical trials the criteria of the Declaration of Helsinki have to be met (Art. 41 "Medizinproduktegesetz"). A clinical trial defined as "a systematic trial to examine the effect of a medicament on a person [...]" (Art. 2a "Arzneimittelgesetz").

➔ *Since the DBS collection in SHARE would not be considered as a clinical trial, obtaining ethics approval would not be mandatory.*

TABLE 1: OVERVIEW – AT

Type of ethics committee (EC)	Medical EC (about 27 ECs at institutional levels)
Number of ethics committees to be consulted	n/a
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	No ethics approval needed
Special requirements regarding ethics committee approval	n/a
Required form of consent	Verbal informed consent
Special requirements regarding consent	None
Special data privacy requirements	None known
Shipment of biological samples (DBS)	No restrictions known
Medical risks related requirements	DBS collection only by medical professionals
Feedback of blood (DBS) analyses results to the participants	Required
Relevant national legislation	Ärztegesetz (Art. 2ff.) [de] Arzneimittelgesetz (Art. 40) [de] Gesundheits- und Krankenpflegegesetz (Art. 15) Sanitätergesetz (Art. 9) Qualitätssicherungsverordnung (Art. 19) [de] Datenschutzgesetz [de, en]
Relevant ethical guidance	Declaration of Helsinki
Fees of ethics approval	n/a
Duration of ethics approval procedure	n/a
Other requirements	n/a
Similarities to other countries	- As in CZ, PL (and probably LU) only medical personnel are allowed to take blood samples and participants are not allowed to prick their own fingers. - As in DK, HR, NL, PL (and maybe LU) the participants have to be informed about certain analyses results.

3.2 BE – Belgium

Legal Framework Conditions

Regarding the collection of DBS there are no special legal constraints in Belgium. As a matter of principle, with regard to the sampling of a survey a permission (to ask the National Register to draw names and addresses) of the Commission for the Protection of Privacy (Privacy Commission, CPP) has to be obtained. During the preparation phase of the DBS collection in SHARE, it has been argued by lawyers that for the collection of DBS an additional permission of the national Privacy Commission would be needed. This however turned out not to be the case. When the Belgian SHARE Country Team contacted the Privacy

Commission, they were told that they would have to contact the Sectorial Committee on Health, which in turn told the Belgian Country Team to contact the ethics committee of the respective university.

In order to conduct a collection of DBS in Belgium informed written consent is necessary. At this, participants must be fully informed about the aims and methods of the study.

There are no major legal restrictions concerning the shipment or storage of DBS samples. They may be sent to other countries and the storage duration is not limited in principle. However, it is not clear whether signed consent forms can be sent to another institution.

The main legal source of data protection in Belgium is the Royal Decree implementing the Act of 8 December 1992 on the protection of privacy in relation to the processing of personal data (Data Protection Act), which implements the European Data Protection Directive (95/46/EC).

Ethics Committee Approval System

Currently there are more than 200 research ethics committees (RECs) in Belgium of which 20 are non-hospital based. There is a central Consultative Committee for Bioethics acting only in a consultative way. Hospitals, university faculties and companies have their own local ethics committees. In Belgium every university has its own local ethics committee.

Multicentre studies are treated differently compared to single centre studies. In the Belgian case the DBS collection in SHARE is considered as a multicentre study within Belgium, since there are two SHARE partner institutions involved in Belgium (the University of Antwerp and the University of Liège). If the study takes place in more than one institution, one central ethics committee has to be chosen. In the pretest of SHARE wave 5 as well as the pretest and main data collection of wave 6 the ethics committee of the University of Antwerp, namely the Ethics Committee of Antwerp University Hospital (Committee for Medical Ethics UZA-UA), was chosen by the Belgian County Team.

When submitting an application to the central ethics committee all documents and materials concerning the study must be handed in. In the case of SHARE, the following documents had to be prepared (in Dutch and French): a cover letter, an information form containing basic information about the study (i.e. about involved persons, the aim and methods of the study, the source of funding, participant numbers, characteristics of the participants and the way of recruitment, about possible risks and about how informed consent is ensured), the informed consent forms (in Dutch and French), the definitive protocol of the study, a summary of the protocol, questionnaires and all other fieldwork materials, copies of all research contracts, an insurance form, CVs (résumé) of all researchers involved and a list of all local ethical committees involved in Belgium (i.e. for SHARE the Comité d'Ethique Hospitalo-Facultaire de Liège).

The committee reviews the documents and requests changes or makes remarks when considered necessary. The criteria of the Declaration of Helsinki have to be met by the research project. In case that any issues are raised by the ethics committee, the ethics committee will give a final approval (in a formal letter) if/as soon as they are solved in a satisfactory manner. The ethics committee in Antwerp meets every Monday (except holidays). Requests or answers to remarks of the ethics committee must be submitted by Thursday of the previous week. In accordance with our experiences from SHARE waves 5 and 6, the entire process approximately takes two months, until the final approval is granted.

For the DBS collection, the ethics committee may require that specific study participant insurance is taken to cover the specific risks of the research project (which was the case for the DBS part of the SHARE study).

The preparation is time consuming and the whole process should not be taken lightly. Clearing things between the ethics committee/s and the applying university/Country Team took about two months until the DBS collection has been approved. Some of the remarks that were made by the central ethics committee in the first instance (when applying before the pretest of SHARE wave 5), such as calling participants before visiting them, may be due to that fact that the ethics committee is a medical ethics committee, which mainly reviews clinical or medical epidemiological studies. Careful explanation why such things were impracticable in the case of a large study such as SHARE was necessary in order to deal with these remarks. In the context of the ethics approval of the DBS collection in SHARE wave 5, in the first round of the application process, it was even the case that the ethics committee of the University of Antwerp did not approve the application initially, while the ethics committee of the University of Liège approved exactly the same application straight away. Since the latter was picked as the central committee the study had to be put on hold in both parts of the country. However, eventually the DBS collection was approved by both ethics committees. For the DBS collection in wave 6 approval of both committees was granted straight away.

➔ *Final conditions of the approval of the DBS collection in SHARE wave 6 are that the results of the study and any adverse events have to be reported back to the central ethics committee in Antwerp and that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before such analyses may be carried out. DNA analyses of DBS samples were excluded from the application in Belgium from the very beginning.*

TABLE 2: OVERVIEW – BE

Type of ethics committee (EC)	Medical REC (200+ RECs organised at an institutional level)
Number of ethics committees to be consulted	2; in the case of a multicentre study several RECs have to be consulted and one central committee has to be chosen

Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS collection
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee; DNA analyses of DBS samples were excluded (self-restriction)
Required form of consent	Informed written consent
Special requirements regarding consent	None
Special data privacy requirements	Permission to draw names and addresses from the National Register of the Belgian Privacy Commission (CPP) needed
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	Specific study participant insurance required (covering specific risks of DBS collection)
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Data Protection Act [en, fr]
Relevant ethical guidance	Declaration of Helsinki
Fees of ethics approval	No fees
Duration of ethics approval procedure	About 2 months
Other requirements	Documents have to be submitted in French and Dutch to the ethics committee/s; Results of the study and any adverse events have to be reported back to the ethics committee
Similarities to other countries	- As in CH, NL and SI SHARE is considered as a multicentre study. - As in CH, DK, EE, ES, FR, IT, LU, PT, SE and SI additional ethics committee approval for further analyses of the DBS samples is needed. - As in CH, FR, HU, IL, LU and NL a specific study participant insurance is required. - As in DE, FR, IL, IT, LU, PL, PT, SE and SI DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

3.3 CH – Switzerland

Legal Framework Conditions

In Switzerland, all research on human subjects has to be approved by an ethics committee according to the Ordinance on Human Research with the Exception of Clinical Trials (Human Research Ordinance, HRO). In general, research on human subjects is regulated in Switzerland by the Federal Act on Research involving Human Beings (Human Research Act, HRA).

➔ *Therefore, not only the DBS collection but the entire SHARE study is subject to ethical review in Switzerland.*

With regard to the DBS collection no special legal constraints apply in Switzerland. In order to conduct a DBS collection in Switzerland informed written consent is necessary. It is important that consent information and the blood samples are strictly separated from the very beginning.

Besides the data protection provisions given in the Human Research Ordinance (cf. Chapter 3 on the further use of biological material and health-related personal data for research), the main legal source of data protection in Switzerland is the Federal Act on Data Protection (FADP). Further information on data protection in Switzerland can be found on the official website of the Federal Data Protection and Information Commissioner (FDPIC).

Concerning the collection of DBS a specific study participant insurance is required in order to cover potential harm (e.g. private liability insurance or a hospital liability insurance, which, however, requires that the principal investigator of the DBS part of the study is a medical doctor and that a nurse is present during the interviewer training).

Ethics Committee Approval System

In Switzerland, ethics committees are organised at cantonal level. Some cantons have their own ethics committee whereas other cantons are organised in a consortium. An overview of the ethics committees in Switzerland can be found on the website of the Association of Swiss Ethics Committees on research involving humans (swissethics). If a research project is conducted in more than one canton it is classified as multicentre research. Since SHARE is a trans-regional study with participants in several (more than five) cantons, SHARE was considered as a multicentre study.

The scopes of responsibility of the ethics committees and procedures for application are regulated in the Human Research Act (cf. Chapter 8). The application documents have to be submitted to the so-called "leading committee", which for multicentre research projects is the ethics committee which is responsible at the site of activity of the project coordinator. The leading committee (in the case of SHARE: the Ethics Committee of the Canton of Vaud, CER-VD) contacts the ethics committees of other cantons in which the research is also carried out and asks for their opinion. According to the HRA it is bound by their opinion. At this, since the legislation on research involving humans has been changed in January 2014[10], the application procedure for multicentre research projects has been significantly simplified (i.e., only after the pretest of SHARE wave 5): until December 2013, after having obtained approval of the leading committee, the research protocol of a multicentre research project had to be submitted again to local committees in all cantons in which the research project was carried out. Even though the review procedure at the local committees was simplified, this did not necessarily mean that the application was processed much faster.

[10] The website of the Swizz Coordination office for research involving humans (Kofam) provides further information on the new legislation.

In the SHARE wave 5 pretest, participants came from five different cantons: Vaud, Zurich, Fribourg, Valais and Tessin. The Swiss SHARE Country Team first submitted the DBS research proposal to the Ethics Committee of the Canton of Vaud (CER-VD), which became the leading committee. Initially, DBS was planned to be conducted in all pretest cantons. However, due to complexity of the submission procedure, the very short deadlines and the slowness of each administrative step, the Swiss Country Team had to decide to limit the DBS experiment to Vaud and Fribourg (Fribourg being related to CER-VD), since submissions to the local committees would have been too time consuming. Although the DBS pilot was limited to Vaud and Fribourg, the working process of other ethics committees (Zurich, Tessin and Valais) was investigated. The Swizz SHARE Country Team learned that each ethics committee has its own working habits: the calendar of their meetings, the number of committee members, the time it takes to get a decision on a specific research proposal and the language in which the documents had to be submitted varied from one committee to another. With regard to the ethics committee application for SHARE wave 6 the Swizz Country Team was able to benefit from the new legislation on research involving humans that came into force in January 2014 and, therefore, only had to make one submission (again to CER-VD) for the DBS collection in Switzerland (covering the entire country).

Regarding the wave 6 application in Switzerland, one of the new principles in the legislation, namely in the Human Research Ordinance, has been of particular importance: the classification of research projects involving measures for sampling of biological material or collection of health-related personal data from persons on the basis of the risks and burdens for the individuals participating in them (Art. 7, HRO). Based on this classification, the ethics committee either makes its decision under "the regular procedure" (Category B, more that minimal risks) or under a "simplified procedure" (Category A: minimal risks) in accordance with the Ordinance on Organisational Aspects of the Human Research Act (HRA Organisation Ordinance, OrgO-HRA), which regulates the organisation of the ethics committees in terms of their composition and the procedural provisions. Furthermore, the requirement for documentation to be submitted with the application, for liability guarantees and for notification varies according to the classification (cf. HRO). The application documents that have to be submitted to the responsible ethics committee are specified in Annex 2 of the Human Research Ordinance. For the DBS collection in SHARE Switzerland, which has been classified as Category A research project, the following documents had to be prepared: a motivation letter, the research protocol in English and French, a general submission form, information documents for the participants, consent forms, insurance police, contract with the survey agency, CVs of all collaborators involved, an overview of the SHARE questionnaire, the biobank regulations, information on how data are collected, processed and anonymised and official approvals of other ethics committees.

Besides highlighting the fact that the criteria of the Declaration of Helsinki had to be met by the research project, the ethics committee stressed that special attention has to be paid with regard to cognitively impaired and deceased persons.

➔ *Final conditions of the approval of the DBS collection in SHARE wave 6 are that an advance letter has to be sent to survey participants (informing them about the project and providing them with the consent documents) and that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before they may be carried out. Moreover, a specific study participant insurance was required by the ethics committee. The Swizz SHARE Country Team was able to meet this requirement by means of the liability insurance fund of the University Hospital of Lausanne, Vaud (CHUV). For this reason, further requirements are that the principal investigator (PI) of the DBS part of the study is a medical doctor and that a nurse is present during the interviewer training (in accordance with CHUV regulations).*

TABLE 3: OVERVIEW – CH

Type of ethics committee (EC)	Cantonal EC (9 ECs which are organised on a cantonal/regional level)
Number of ethics committees to be consulted	1 (if multicentre research in several cantons: "leading committee")
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	Entire survey (incl. DBS)
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee; An advance letter including the consent documents has to be sent to the participants
Required form of consent	Informed written consent (may also be in a non-written form if classified as Category A research)
Special requirements regarding consent	No
Special data privacy requirements	Consent forms and samples have to be shipped and stored separately
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	Liability insurance required; PI of the study has to be a medical doctor in the case of hospital liability insurance coverage; During the interviewer training a nurse must be present in the case of hospital liability insurance coverage
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Federal Act on Research involving Human Beings [en, de, fr, it] Human Research Ordinance [en, de, fr, it] Federal act on data protection [en, de, fr, it] HRA Organisation Ordinance [en, de, fr, it]
Relevant ethical guidance	Declaration of Helsinki; EU-ICH Guidelines GCP; CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subject (2002)
Fees of ethics approval	Leading committee: 1.000 CHF
Duration of ethics approval procedure	About 2 months (if documents are submitted on time: 2 weeks before a scheduled meeting)

Other requirements	Ethics committee applications need to be submitted in the language of the respective Canton
Similarities to other countries	- As in EE and SE the entire survey has to be approved. - As in BE, NL and SI SHARE is considered as a multicentre study. - As in DK, IT and SE an advance letter has to be sent to the participants. - As in BE, DK, EE, ES, FR, IT, LU, PT, SE and SI additional ethics committee approval for further analyses of the DBS samples is needed. - As in BE, FR, HU, IL, LU and NL a specific study participant insurance is required. - As in FR, IL, LU and SI the principal investigator of the study has to be a medical doctor.

3.4 CZ – Czech Republic

Legal Framework Conditions

In the Czech Republic, due to occupational restrictions it is forbidden for laypersons to do any medical task or to prick anybody in order to take a blood sample. According to the Act No. 372/2011 on health services (Healthcare Services Act [cz]) only certified medical personnel (such as medical doctors and nurses) are allowed to collect blood samples, including DBS samples. This restriction also implies that participants may not be instructed to prick their own fingers in order to collect blood samples in the context of a study such as SHARE. Furthermore, the collection of blood samples has to be carried out in a medical facility (or during a visit to the doctor).

➔ *Therefore, in the Czech Republic a DBS collection cannot be carried out in the context of SHARE.*

The central relevant data protection law with regard to the processing of personal data in the Czech Republic is the Act No. 101/2000 on the protection of personal data (Personal Data Protection Act, consolidated version).

Ethics Committee Approval System

According to the Act No. 378/2007 on pharmaceuticals (Act on Pharmaceuticals), there are two types of ethics committees, which are organised at an institutional level: there are about 100 local ethics committees established at healthcare institutions or research institutions, which review local research projects. Besides, several (9) ethics committees for the review of multicentre studies exist (cf. Veerus et al. 2013). These ethics committees, which play the role of central ethics committees, are also established at healthcare or

research institutions but are proposed by the State Institute for Drug Control (SÚKL) and approved by the Ministry of Health.

TABLE 4: OVERVIEW – CZ

Type of ethics committee (EC)	Medical EC (100+ at institutional levels)
Number of ethics committees to be consulted	n/a
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	n/a
Special requirements regarding ethics committee approval	n/a
Required form of consent	n/a
Special requirements regarding consent	n/a
Special data privacy requirements	n/a
Shipment of biological samples (DBS)	n/a
Medical risks related requirements	DBS collection only by medical professionals in medical facilities
Feedback of blood (DBS) analyses results to the participants	n/a
Relevant national legislation	Act No. 372/2011 Coll., Healthcare Services Act [cz] Act No. 101/2000 Coll., Personal Data Protection Act [en] Act No. 378/2007 Coll., Act on Pharmaceuticals [en]
Relevant ethical guidance	n/a
Fees of ethics approval	n/a
Duration of ethics approval procedure	n/a
Other requirements	n/a
Similarities to other countries	- As in AT, PL (and probably LU) only medical personnel are allowed to take blood samples and participants are not allowed to prick their own fingers.

3.5 DE – Germany

Legal Framework Conditions

Regarding the collection of DBS there are no special legal constraints in Germany. Neither are there legal restrictions with regard to the collection of DBS samples by trained laypersons nor concerning the shipment or storage of DBS samples. DBS samples as well as related consent forms may be sent to other countries and the storage duration is not limited in principle.

In order to conduct a collection of DBS in Germany informed written consent is necessary. Participants must be fully informed about the aims and methods of the study as well as about the processing of their samples and personal data and related rights.

In Germany, data protection is governed by numerous laws and regulations (federal and state legislation). On a national level data protection is regulated by the Federal Data Protection Act ("Bundesdatenschutzgesetz", BDSG) which implements the European Data Protection Directive (95/46/EC) and includes the most relevant provisions regarding the field of scientific research.

Ethics Committee Approval System

In Germany, research ethics committees are organised on an institutional level. There are 53 medical research ethics committees, which are legally competent to assess biomedical research, including clinical trials and drug research. However, ethics committees are not only established in the area of biomedical research but also for research in other disciplines, e.g. in universities or research institutes. The establishment of these ethics committees, which usually have an advisory function, is not legally required but can be regarded as an instrument of self-regulation in research. Accordingly, the procedures for application and the requirement for documentation to be submitted with the application may vary from case to case. Besides these institutional ethics committees there are two national ethics committees in Germany: the German Ethics Council ("Deutscher Ethikrat"), which may give recommendations which are not binding, and the Central Ethics Committee for Observance of Ethical Principles in Medicine and its Adjacent Fields of the German Medical Association of the German Medical Association ("Zentrale Kommission zur Wahrung ethischer Grundsätze in der Medizin und ihren Grenzgebieten", ZEKO), which gives opinions on general ethical issues and which may give advice to other medical ethics committees.

The first time, when the pilot DBS study was carried out in Germany in SHARE wave 4, the German SHARE Country Team (as well as the central international SHARE coordination) was located at the University of Mannheim. Since SHARE is no clinical study, the Ethics Committee of the University of Mannheim was responsible for the approval of the DBS collection in SHARE wave 4. During the review of this first DBS pilot, several questions came up regarding the content and the exact wording of consent forms and information leaflets; the committee made several suggestions for improvement. Finally, all the concerns raised by the ethics committee could be solved. This initial critical reflection has proved very useful as to the preparation of the full-scale implementation of the DBS collection in SHARE, in particular with respect to the preparation of accurate (generic versions of the) consent documents and, not least, also with regard to all further ethics committee approval applications.

Between SHARE wave 4 and wave 5 the central SHARE coordination and the German Country Team moved to Munich and became part of the Max Planck Institute for Social Law

and Social Policy. Since then, the Ethics Council of the Max Planck Society was responsible for the SHARE DBS review for the German part of the study. Since the entire SHARE project also is centrally coordinated in Germany, the Ethics Council of the Max Planck Society also reviewed the entire survey (and not only the DBS part of the project).

Since, based on the experiences that have been made during the pilot projects in SHARE waves 4 and 5 in Germany, the German SHARE Country Team decided to slightly modify the procedure of the DBS collection for SHARE wave 6, a new application was submitted to Ethics Council prior to this wave of data collection. One condition of the former approval of the Ethics Committee of the University of Mannheim was that the German Country Team had to report back all 'out-of-the-norm' values of the DBS analyses back to the participants via their general practitioners. The procedure, which was required by the ethics committee prior to the DBS collection and analyses, however, due to several practical reasons, could not be implemented in a satisfactory way. This had raised certain ethical issues, due to which, the Country Team came to the conclusion that not reporting back the results of the DBS analyses to the participants would be the preferable option.

Regarding this application, the German Country Team and the Ethics Council agreed that the review covered the entire survey again and include the suggested modification. For this reason the following documents have been submitted: the DBS survey protocol, the information documents for the participants and the consent forms (in German and English), information on data protection in SHARE, information about interviewer trainings, other fieldwork documents (such as the SHARE data protection statement or the DBS interviewer manual and instructions), short CVs of investigators, the SHARE questionnaire, general information about the SHARE project, former ethical review statements and ethical considerations of the responsible researchers with regard to the suggested modification (i.e. the reasons for the modification). After the submission of all these documents the Ethics Council reviewed and approved the project, including the DBS collection and the suggested modification with regard to the procedure in Germany.

➔ *The entire project including the collection of DBS in Germany has been approved successfully. DNA analyses of DBS samples were excluded from the application in Germany from the very beginning.*

TABLE 5: OVERVIEW – DE

Type of ethics committee (EC)	Institutional REC (ECs are organised at an institutional level; amongst others there are 53 medical RECs, which are legally competent to assess biomedical research)
Number of ethics committees to be consulted	1
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS + Entire survey (international review, since SHARE is centrally coordinated in Germany)
Special requirements regarding ethics	DNA analyses of DBS samples were excluded

committee approval	(self-restriction)
Required form of consent	Informed written consent
Special requirements regarding consent	No
Special data privacy requirements	No
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	No
Feedback of blood (DBS) analyses results to the participants	Not required (may also be required by the responsible ethics committee depending on the concrete circumstances)
Relevant national legislation	Bundesdatenschutzgesetz, [de, en]
Relevant ethical guidance	Declaration of Helsinki; Belmont Report
Fees of ethics approval	No fees
Duration of ethics approval procedure	About 1-3 months (DBS only)
Other requirements	If feedback of blood analyses results to the participants is requested, it may be required that this has to be done via the general practitioners of the participants
Similarities to other countries	- As in BE, FR, IL, IT, LU, PL, PT, SE and SI DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

3.6 DK – Denmark

Legal Framework Conditions

Regarding the collection of DBS there are no special legal constraints in Denmark. In Denmark, DBS samples can be collected by trained laypersons (interviewers) or via 'self-pricking'. There are no legal restrictions concerning the shipment of DBS samples, i.e. DBS samples may be sent to other countries for analyses. With regard to the collection of DBS samples by trained interviewers (laypersons), the general liability insurance of the survey agency covers any possible harm to the participants.

However, in general, if sensitive personal data (which includes biological material such as blood and tissue samples, etc.) is processed in a research or statistics project, the project must be notified to the Danish Data Protection Agency (Datatilsynet) and must obtain the agency's authorisation. Furthermore, with regard to the storage of the samples in Denmark, any newly established research biobank has to be registered with the Danish Data Protection Agency.

➔ *The DBS collection in SHARE had to be notified to the Danish Data Protection Agency.*

The central relevant data protection law with regard to the processing of personal data in Denmark is the Act on Processing of Personal Data (compiled English version), which implements the European Data Protection Directive (95/46/EC). In order to conduct a collection of DBS in Denmark written informed consent of the participants is necessary.

The research ethics committee system in Denmark is regulated by the Act on Research Ethics Review of Health Research Projects. Health science research projects that involve living or deceased human beings or biological material from humans, foetuses, etc. have to be approved by an ethics committee.

Ethics Committee Approval System

Denmark has a health research ethics committee system, which consists of a national committee and 11 regional committees. Detailed information about the Danish system of health research ethics committee can be found on the website of the National Committee on Health Research Ethics ("Den Nationale Videnskabsetiske Komité").

According to the Act on Research Ethics Review of Health Research Projects, all research projects involving human subjects or any kind of human tissue, cells etc. need permission from one of the regional ethics committees. In the case of multinational or multicentre research, the investigator (i.e. the Danish SHARE Country Team located at the University of Southern Denmark) approval of one of the regional committees is sufficient. At this, the Danish investigator of the research project has to apply to the regional committee in the area, where the investigator is employed, which in the case of SHARE is the Research Ethics Committee of the Region of Southern Denmark ("Videnskabsetiske Komité for Region Syddanmark").

An electronic application form has to be filled out and submitted together with the study protocol, the subject information, the procedure for obtaining the informed consent of the participants (and all related documents such as consent forms and information leaflets) and a 'résumé' of the protocol.

The committee meets every month, and if all requirements are met the application process takes about one to two months. After submission, an answer by the ethics committee must be given within 60 days (in uncomplicated cases it may take less time to obtain ethics committee approval, about one month).

Before the pretest of SHARE wave 5, an application with regard to the DBS collection in Denmark was submitted for the first time. This first application (for the pilot project in the pretest of wave 5), however, has not been approved by the committee straight away, because it did not involve feedback to the participants about pathological values of HbA1c and CRP. As a result of several discussions with the ethics committee, the Danish SHARE Country Team changed the procedure in this regard and agreed to give feedback to participants about pathologically high HbA1c values, since these may reflect undiagnosed cases of diabetes. With regard to CRP values, however, the committee finally agreed that a feedback of this marker would not be necessary, since this would hardly be of value for the participants due to its rapid change and as it is non-specific disease marker. Subject to the condition that feedback is given to the participants about elevated HbA1c values, the Danish Country Team finally received approval of the DBS collection.

In general, the approval in Denmark does only cover pre-specified analyses. If other analyses are intended to be conducted with same DBS samples, an amendment protocol must be submitted to the ethics committee, which then will make a new evaluation. This has been done prior to the DBS collection of SHARE wave 6, since with regard to the collected blood samples of this wave some additional markers (e.g. Vitamin D) were planned to be analysed. The procedure, however, remained the same in comparison to the pilot project of SHARE wave 5 and ethics committee approval (of the amended protocol) could be obtained very quickly.

➔ *Final conditions of the approval of the DBS collection in SHARE wave 6 are that an advance letter has to be sent to survey participants, that elevated HbA1C and cholesterol levels as well as reduced Vitamin D levels have to be reported back to the participants and that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before such analyses may be carried out. Furthermore, the storage duration of the samples is limited until 31 December 2028.*

TABLE 6: OVERVIEW – DK

Type of ethics committee (EC)	Regional medical REC (there are 11 regional RECs and 1 national REC)
Number of ethics committees to be consulted	1
Other authorities to be consulted	Danish Data Protection Agency (Datatilsynet)
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee; An advance letter including the consent documents has to be sent to the participants; DBS samples storage is limited (destruction date: 31.12.2028)
Required form of consent	Written informed consent
Special requirements regarding consent	Advance letter to be sent to participants
Special data privacy requirements	Newly established research biobanks (storage of samples) have to be registered with the Danish Data Protection Agency (Datatilsynet)
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	No
Feedback of blood (DBS) analyses results to the participants	Required (for pathological blood levels)
Relevant national legislation	Act on Processing of Personal Data (compiled version) [en] Act on Research Ethics Review of Health Research Projects [en]
Relevant ethical guidance	Declaration of Helsinki
Fees of ethics approval	About 650-900 EUR (650 EUR per application and 250 EUR per possible amendment)
Duration of ethics approval procedure	About 1-2 months
Other requirements	None known

Similarities to other countries	- As in CH, IT and SE an advance letter has to be sent to the participants. - As in AT, HR, NL, PL (and maybe LU) the participants have to be informed about certain analyses results. - As in BE, CH, EE, ES, FR, IT, LU, PT, SE and SI additional ethics committee approval for further analyses of the DBS samples is needed. - As in FR, GR, IT, NL and PT and the storage duration of the DBS samples is limited.

3.7 EE – Estonia

Legal Framework Conditions

Regarding the collection of DBS there are no special legal constraints in Estonia. Neither are there legal restrictions with regard to the collection of DBS samples by trained laypersons nor concerning the shipment or storage of DBS samples. DBS samples may be sent to other countries and the storage duration is not limited in principle.

In order to conduct a collection of DBS in Estonia informed written consent has to be obtained from the participants. At this, all the measures taken to protect the privacy and anonymity of the participants and their data during all the stages of the study must be described in the written information that is given to the participants.

The central relevant data protection law with regard to the processing of personal data in Estonia is the Personal Data Protection Act, which implements the European Data Protection Directive (95/46/EC). According to this act, processing of sensitive personal data (as well as of personal data without the consent of the data subject) for scientific research purposes has to be registered at the Estonian Data Protection Inspectorate (DPI). Besides the SHARE survey (which has to be registered since as part of the sampling process certain personal data is processed without the consent of the data subject), the processing of data related to the DBS collection has to be registered at the DPI, since sensitive personal data is processed.

➔ *The entire SHARE study and, at this, particularly the DBS collection, which includes the processing of sensitive information, has to be registered with the Estonian Data Protection Inspectorate (DPI).*

Ethics Committee Approval System

In Estonia, there are two ethics committees which are responsible for the review of all kind of human studies involving human subjects, including psychological and behavioural studies, biomedical research and clinical trials: the Research Ethics Committee of the University of Tartu and the Tallinn Medical Research Ethics Committee ("Tallinna Meditsiiniuuringute

Eetikakomitee", TMEK) operating at the National Institute for Health Development. Even though there is no specific act regulating scientific human research in Estonia that provides a list of research projects that need to be approved by an ethics committee[11], it is advisable to contact one of those ethics committees in order to find out, if a specific research project needs ethics approval. To conduct medical or health-related research involving human subjects, usually approval by either of the two committees is needed. With regard to the DBS collection in Estonia (covering the entire country) it turned out that approval of TMEK was required.

➔ *Since SHARE besides socio-economic research also involves health-related research, not only the DBS collection but the entire SHARE study is subject to ethical review in Estonia.*

The ethics committee meets monthly and gives its evaluation on an application of a research study within 60 days after submission of the application at the latest (the process until a first opinion is given takes between 10 and 60 days): therefore, the application has to be submitted to the secretary of the TMREC no later than 60 days before the scheduled start of the investigation. In the event that changes are necessary, the revised application will be reviewed by the committee as soon as it has been submitted. The new decision regarding the application can be made in the period between the committee's meetings.

The application documents that have to be submitted to TMEK are specified in the Statutes of the TEMK, which can be found on the committee's website. In the case of SHARE, the following documents were prepared and submitted: a standard application form containing the main particulars about the research study, the DBS survey protocol (including a description of the SHARE survey as a whole), the consent documents (including the DBS information leaflet and consent form for the participants) and further DBS fieldwork materials and documents (CAPI module, interviewer manual, short instructions, training description, a description of the data protection measures).

As part of the evaluation, the question of whether feedback about DBS analyses results should be given to the participants has been discussed with the ethics committee. According to TMEK, reporting back 'out-of-the-norm' blood results to the participants is not necessary if the participants are explicitly informed that their blood results will not be announced to them and the reasons for that are given.

➔ *A final condition of the approval of the DBS collection in SHARE wave 6 is that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before such analyses may be carried out.*

[11] For further information please see: Parve, V. (2003). "National Regulations on Ethics and Research in Estonia." Brussels: European Commission.

TABLE 7: OVERVIEW – EE

Type of ethics committee (EC)	Medical REC (there is 1 medical REC and 1 university REC on the national level)
Number of ethics committees to be consulted	1
Other authorities to be consulted	DPI
Type of approval needed (entire survey, health related data, DBS collection, etc.)	Entire survey + DBS
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee
Required form of consent	Written informed consent
Special requirements regarding consent	Written information for participants must contain information on data privacy
Special data privacy requirements	No
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	No
Feedback of blood (DBS) analyses results to the participants	Not required (if this fact is explicitly explained to the participants)
Relevant national legislation	Personal Data Protection Act [en]
Relevant ethical guidance	Declaration of Helsinki; Nuremberg Code; Oviedo Convention
Fees of ethics approval	No fees
Duration of ethics approval procedure	10-60 days (max. 60 days)
Other requirements	No
Similarities to other countries	- As in CH and SE the entire survey has to be approved. - As in BE, CH, DK, ES, FR, IT, LU, PT, SE and SI additional ethics committee approval for further analyses of the DBS samples is needed.

3.8 ES – Spain

Legal Framework Conditions

In Spain, there are no special legal constraints with regard to the collection of DBS. There are no legal restrictions with regard to the collection of DBS samples by trained laypersons (interviewers, in the case of SHARE). DBS samples may be sent to other countries and the storage duration of the samples is not limited in principle.

The main data protection legislation with regard to the processing of personal data in Spain is the Organic Act on the Protection of Personal Data 15/1999 ("Ley Orgánica de Protección de Datos de Carácter Personal" [es], LOPD), which formally implements the European Data Protection Directive (95/46/EC) and the ancillary Royal Decree 1720/2007, which, e.g., sets out security measures for personal data processing. In 1993 the Spanish Data protection Agency ("Agencia Española de Protección de Datos", AEPD) was created in order to control and enforce the data protection laws in Spain.

In order to conduct a collection of DBS in Spain informed written consent has to be obtained prior to their collection. Participants must be given detailed information about the objectives and procedures of the study.

Ethics Committee Approval System

In Spain, every health centre that carries out clinical trials has an ethics committee. There are more than 140 so-called Clinical Research Ethics Committees ("Comités de Ética en Investigación Clínica", CEICs) in Spain, which are accredited by the health authority of the respective community and have to be notified to the Spanish Agency of Medicines and the Coordinating Centre of Ethical Committees. They are organised at a local level.

In the province of Girona (where one of the two Spanish SHARE Country Teams is located) there are two CEICs that are competent to review research projects such as the DBS collection in SHARE. Approval of one of these two ethics committees covers all provinces in Spain.

In general, the Spanish ethics committee approval system can be described as highly decentralised, which makes it difficult for inexperienced researchers to maintain an overview and to identify the competent ethics committee/s to which an application should to be submitted. During the preparation phase for the DBS collection in the pretest of SHARE wave 5, it first seemed that permission from as many regional ethics committees as covered in the Spanish SHARE sample would have to be obtained. Since prior to this DBS pilot such a scenario has not been anticipated and therefore the timeframe for the preparation was set to narrow, the pilot DBS collection of the pretest of SHARE wave 5 could not be carried out in Spain.

Against the background of this experience in SHARE wave 6 much more time for preparation was allotted from the very beginning, so that this issue could be further investigated and clarified. Finally it turned out that one approval of a Spanish ethics committee would be sufficient.

The members of the CEIC-IAS (ethics committee of the Institut d'Assictència Sanitària), to which the Spanish SHARE Country Teams submitted their applications, meet monthly (between 1st and 5th of each month). It is possible that the principal investigator of the study attends the meeting of the ethics committee to present the study and to response to the committee's questions. The procedure takes one month or longer until a decision of the ethics committee is provided to the applicants. In the event that changes with regard to a specific application are required, the process will at least last one more month.

The following documents and fieldwork materials had to be prepared and submitted to the CEIC-IAS: a study protocol including the usual sections of rationale, objectives, hypothesis, methods and expected results and all consent documents, i.e. the DBS consent form and the DBS information leaflet in the case of SHARE.

➔ *A final condition of the approval of the DBS collection in SHARE wave 6 is that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before such analyses may be carried out.*

TABLE 8: OVERVIEW – ES

Type of ethics committee (EC)	Medical EC (there are 140+ medical ECs at regional, local and institutional levels)
Number of ethics committees to be consulted	1
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee
Required form of consent	Written informed consent
Special requirements regarding consent	No
Special data privacy requirements	No
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	No
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Ley Orgánica 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal [es] Royal Decree 1720/2007
Relevant ethical guidance	Declaration of Helsinki; Oviedo Convention
Fees of ethics approval	Each ethics committee: 350 EUR
Duration of ethics approval procedure	1 month and longer (+ minimum 1 more month if changes required)
Other requirements	No
Similarities to other countries	- As in BE, CH, DK, EE, FR, IT, LU, PT, SE and SI additional ethics committee approval for further analyses of the DBS samples is needed.

3.9 FR – France

Legal Framework Conditions

In France, regarding the collection of DBS several special legal requirements have to be met. According to French law, only medical staff are allowed to take blood samples. Participants, however, may prick their own fingers in order to collect blood samples in the context of a study such as SHARE. The DBS collection, in principle, is considered as medical research (since it includes the collection of DNA). For this reason, it is mandatory that the principal investigator of the research is a medical doctor. Furthermore, taking a specific participant insurance is required.

Besides, several authorities have to be consulted in order to be able to perform such a collection as part of a research project.

Since the DBS collection in SHARE (including pricking participants'' fingers with a lancet) in France is considered to be an 'interventional study', approval of the French National Agency for Medicines and Health Products Safety (Agence nationale de securité du médicament et des produits de santé, ANSM) has to be obtained.

Additionally, approval from the National Commission on Informatics and Liberty (Commission nationale de l'informatique et des libertés, CNIL), i.e. the French data protection authority, is needed.

According to CNIL, the study also needs approval from the Comité consultatif sur le traitement de l' information en matière de recherche dans le domaine de la santé (CCTIRS), which provides advice to CNIL and issues opinions with regard to the methodology of research projects, their (scientific) relevance and the need to use personal data in relation to the aims of the research.

The central relevant data protection law with regard to the processing of personal data in France is the Law No. 78-17 of 6 January 1978 on Information Technology, Data Files and Civil Liberty. This act was amended by the Law No. 2004-801 of 6 August 2004, which implements the European Data Protection Directive (95/46/EC).

In order to conduct a collection of DBS in France informed written consent is necessary. Participants must be fully informed about the aims and methods of the study as well as about the processing of their samples and personal data. There are no major legal restrictions concerning the shipment of DBS samples; they may be sent to other countries as long as the country guarantees to individuals a sufficient level of protection in terms of privacy and fundamental rights and liberties.

➔ *Therefore, DBS samples are to be collected in France via 'self-pricking'. In order to be able to conduct the collection a specific participant insurance was taken. Furthermore, approval of the DBS collection in SHARE wave 6 has been obtained from ANSM, CNIL and CCTIRS. According to CNIL, the DBS samples collected in SHARE can be sent to other countries participating in SHARE and the USA for analyses.*

Ethics Committee Approval System

In France, there are 40 research ethics committees (Comités de protection des personnes, CPPs). CPPs provide advice to biomedical research projects involving human subjects and assure the adequate protection of research participants in terms of ethics, data protection and medical safety. The 40 ethics committees (cf. Veerus et al. 2013) are divided up in seven regions[12]. 11 of them are located in the Ile de France region around Paris (where the home

[12] For more details see: http://www.recherche-biomedicale.sante.gouv.fr/pro/comites/coordonnees.htm.

institutions of the French SHARE Country Team are located). All of them are competent for the whole region and also can approve projects on a national level.

The CPP of the hospital Pitié-Salpêtrière was responsible for the review of the DBS collection in SHARE wave 6 in France. As described in the legal framework conditions section, besides the CPP several other authorities have to be consulted in France. At this, first the CPP has to be consulted, then ANSM has to be contacted and finally approval of CNIL and CCTRIS has to be obtained.

The CPP of the hospital Pitié-Salpêtrière meets once a month. The exact duration until approval of the ethics committee is granted may vary depending on the specific research project and on the question of whether documents have to be re-submitted or submission of additional documents are demanded by the CPP. In general, it can be said that in comparison to other countries, the entire process in France, considering the many authorities that have to be involved, is extremely complex and time consuming.

The following documents and fieldwork materials had to be prepared and submitted to the CPP: the survey protocol, a data protection leaflet, all consent-related documents such as information leaflets and consent forms and a detailed description of the training of the interviewers with regard to the DBS collection. All application documents for the ethics committee need to be submitted in French language.

➔ *Besides the various legal requirements (see legal framework conditions section above) a final condition of the ethics approval of the DBS collection in SHARE wave 6 is that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before such analyses may be carried out. Furthermore, the storage duration of the samples is limited until 31 December 2024. DNA analyses of DBS samples were excluded from the application in France from the very beginning.*

TABLE 9: OVERVIEW – FR

Type of ethics committee (EC)	Medical REC (40 CPPs in France; 11 CPPs in the region around Paris)
Number of ethics committees to be consulted	1
Other authorities to be consulted	ANSM, CCTRIS, CNIL
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee; DNA analyses of DBS samples were excluded (self-restriction); DBS samples storage is limited (destruction date: 31.12.2024)
Required form of consent	Written informed consent
Special requirements regarding consent	None
Special data privacy requirements	None known
Shipment of biological samples (DBS)	DBS samples can be sent to other countries (restricted to countries participating in SHARE

	and USA)
Medical risks related requirements	DBS collection only via 'self-pricking' of the participants; Specific study participant insurance required; PI of the DBS part of the study has to be a medical doctor
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Law No. 78 17 of 6 January 1978 on Information Technology, Data Files and Civil Liberty [en] Decree No 2005-1309 of 20 October 2005 enacted for the application of Act No 78-17 of 6 January 1978 on Data Processing, Files and Individual Liberties amended by Act No 2004-801 of 6 August 2004 [en]
Relevant ethical guidance	Declaration of Helsinki
Fees of ethics approval	No fees
Duration of ethics approval procedure	n/a (since many authorities have to be involved in FR, the entire process is extremely complex and time consuming)
Other requirements	Application documents for the ethics committee need to be in French
Similarities to other countries	- As in BE, CH, DK, EE, ES, IT, LU, PT, SE and SI additional ethics committee approval for further analyses of the DBS samples is needed. - As in CH, IL, LU and SI the principal investigator of the study has to be a medical doctor. - As in BE, CH, HU, IL, LU and NL a specific study participant insurance is required. - As in DK, GR, IT, NL and PT and the storage duration of the DBS samples is limited. - As in BE, DE, IL, IT, LU, PL, PT, SE and SI DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

3.10 GR – Greece

Legal Framework Conditions

There are no special legal constraints with regard to the collection of DBS samples in Greece. There are no restrictions with regard to the collection of the samples by trained laypersons. DBS samples may be shipped to other countries and the storage duration is not limited in principle.

The central relevant data protection law with regard to the processing of personal data in Greece is the Law 2472/1997 on the Protection of Individuals with regard to the Processing of Personal Data, as amended by several other laws (e.g. Law 3471/2006 on Protection of personal data and privacy in the electronic telecommunications sector). According to Law 2472/1997, the collection and processing of sensitive personal data is prohibited unless

permitted by the Hellenic Data Protection Authority (HDPA), subject to certain conditions, which are specified in Art. 7. Since in SHARE health related data is being collected and processed, permission of the HDPA has to be obtained. This also concerns the collection of the DBS samples as well as the processing of data related to the DBS collection.

In order to conduct a collection of DBS in Greece informed written consent has to be obtained from the participants. With regard to the analyses of the DBS samples, it is required, that all planned analyses are specified in the information provided to the participants. 'Broad consent' is not permitted by the HDPA. Any further analyses exceeding the ones explicitly covered by informed consent may only be carried out with prior (additional) consent of the participants.

Furthermore, according to the HDPA, the storage duration of human material for scientific research has to be limited. At this, the permitted storage duration depends on the specific research purpose(s).

➔ *Therefore, permission for the collection and procession of all health related data in SHARE, including the DBS collection, has been obtained from the Hellenic Data Protection Authority (HDPA). Further analyses of the DBS samples (not explicitly mentioned in the consent information) may only be carried out with prior additional consent of the participants. As a legal requirement, the permission of the HDPA regarding the storage duration of the samples has been limited. The SHARE DBS samples have to be destroyed by 31 December 2024 (expected end of the SHARE project).*

Ethics Committee Approval System

Greece has a National Bioethics Commission that advises the Government on broad ethics issues. The Hellenic National Bioethics Commission issues opinions and reports related to research ethics; it however, does not evaluate specific protocols of research projects. Besides, there are various local research ethics committees (RECs) in hospitals, in research institutions and in higher education institutions (e.g. medical faculties). Since there are no separate jurisdictions at a local level in Greece, approval of one of these ethics committees is sufficient in order to carry out research projects on a national level.

Since a member of the Greece SHARE Country Team is affiliated to the Faculty of Medicine of the University of Crete, an application was submitted to the Research Ethics Committee of the University of Crete, which has 'university-wide' responsibilities for the review and approval of research protocols.

The REC of the University of Crete has an established procedure for ethics review and approval of research projects: After the submission of an application to the REC one member of the committee gives feedback to the applicant. The member's report and the applicant's reply are discussed during the next meeting of the REC and if no (further) issues are raised, approval is granted. The committee meets three to four times a year (there are

no fixed dates) and applications have to be submitted a few weeks before the next scheduled meeting. From then on, the ethics approval procedure lasts about one month. If according to the ethics committee changes are necessary, it might, however, happen that applicants have to wait for the next meeting until final approval is granted.

Besides an application form (which includes details of the research protocol, the research team's CVs, the sampling method, recruitment of participants, sources of financing, consent procedures, potential benefit to the participants and other issues) that had to be filled in in Greek language, in the case of SHARE, the following documents and materials had to be prepared and submitted: consent documents in Greek language, a research protocol and general information about the research project.

➔ *With regard to the ethics committee approval the same conditions as those set out by the HDPA apply.*

TABLE 10: OVERVIEW – GR

Type of ethics committee (EC)	Local REC (besides the National Bioethics Commission there are several medical and institutional RECs)
Number of ethics committees to be consulted	1
Other authorities to be consulted	HDPA (all health related data)
Type of approval needed (entire survey, health related data, DBS collection, etc.)	All health related data (including DBS)
Special requirements regarding ethics committee approval	No (the same conditions as those set out by the HDPA apply)
Required form of consent	Informed written consent
Special requirements regarding consent	Further analyses may only be carried out with prior (additional) consent of the participants
Special data privacy requirements	DBS samples storage is limited (destruction date: 31.12.2024)
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	No
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Law 2472/1997 on the Protection of Individuals with regard to the Processing of Personal Data [en]
Relevant ethical guidance	Declaration of Helsinki; Oviedo Convention
Fees of ethics approval	No fees
Duration of ethics approval procedure	Minimum 1 month (committee, meets only 3-4 times a year, applications are discussed during these meetings)
Other requirements	Consent documents to be submitted in Greek
Similarities to other countries	- While in BE, CH, DK, EE, ES, FR, IT, LU, PT and SE additional approval of the responsible ethics committee/s is needed for further analyses of the DBS samples, in GR (similarly) prior permission of the HDPA has to be obtained.

	- As in DK, FR, IT, NL and PT and the storage duration of the DBS samples is limited. - In GR no further analyses are permitted. Thus DNA analyses are excluded as in BE, DE, FR, IL, IT, LU, PL, PT, SE and SI.

3.11 HR – Croatia

Legal Framework Conditions

In Croatia, there are no special legal constraints with regard to the collection of DBS. There are no legal restrictions with regard to the collection of DBS samples by trained laypersons (i.e. interviewers, in the case of SHARE). The storage duration of the samples is not limited in principle and DBS samples may be sent to other countries. In general, personal information may be sent to another country if that country has adequate level of personal data protection. Otherwise, approval from Croatian Personal Data Protection Agency ("Agencija za zaštitu osobnih podataka", AZOP) has to be obtained.

The central relevant data protection law with regard to the processing of personal data in Croatia is the Act on Personal Data Protection (including its amendments), which implements the European Data Protection Directive (95/46/EC).

In order to conduct a DBS collection in Croatia informed written consent has to be obtained from the participants prior to the collection of the samples.

Ethics Committee Approval System

In Croatia, ethics committees are organised at a local/institutional level (e.g. at medical research institutes, hospitals, schools of medicine). Besides these various committees, there is a Central Ethics Committee (CEC) at the Ministry of Health, which is the only one competent to review and approve clinical trials protocols for the investigation of drugs and medical devices (pharmaceutical studies). All other research (lying outside the scope of the CEC) are reviewed and approved by the local ethics committees.

The Ethics Committee of the Institute for Medical Research and Occupational Health (IMROH, to which a member of the Croatian SHARE Country Team is affiliated) in Zagreb is competent to approve DBS collection in the context of SHARE for the entire country. In 2011 the Scientific Council of IMROH passed a Code of Ethics, which amongst other things lays down the responsibilities of the ethics committee and includes procedural provisions.

After submission of an application for ethics approval, the ethics committee examines all relevant documentation and the members of the ethics committee discuss the request in question at a meeting of the ethics committee (usually, no specific dates have to be taken into account). Finally, the ethics committee renders its opinion in writing and delivers it to the person who submitted the request. The committee has an obligation to give its

evaluation on an application of a research study within 60 days after submission of the application at the latest; usually the approval procedure is finished within one month after submission of a request.

Further information on the application documents that have to be submitted to TMEK is provided in the IMROH Code of Ethics. With regard to the DBS collection in SHARE the following documents and fieldwork materials were prepared and submitted: a short description of the SHARE project (e.g. goals, methodology, source of financing, name and affiliation of the coordinator); names of the Croatian Country Team Members, a justification of the necessity of conducting the research involving humans subjects and a statement of how ethical issues are dealt with (concerning the anonymity of participants, data protection, voluntary nature of participation, health protection of study participants, interviewers and household members, biological waste management, etc.), the DBS information leaflet and consent form (in Croatian language), the DBS interviewer manual, a description of the data protection measures in place and a statement concerning approvals of other ethics committees.

The committee may ask the person who submitted the request to produce additional explanations, notifications and relevant documentation, if necessary. If this is the case, the procedure may take up to 90 days longer.

With regard to the DBS collection in SHARE, the ethics committee demanded that pathological values should be reported back to the participants since, according to the committee, there is a considerable possibility that older people in poor and in rural areas in Croatia do not often see a doctor. Considering this situation, in a case of chronic diseases such as diabetes, the ethics committee therefore considered it to be better to inform participants, even if this only would be possible with a delay of 2 years, than not informing them at all.

➔ *A final condition of the approval of the DBS collection in SHARE wave 6 is that elevated HbA1C and cholesterol levels have to be reported back to the participants.*

TABLE 11: OVERVIEW – HR

Type of ethics committee (EC)	Local medical EC (ECs are organised at an institutional level)
Number of ethics committees to be consulted	1
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	No (apart from requirement to report back analyses results to participants)
Required form of consent	Informed written consent
Special requirements regarding consent	No
Special data privacy requirements	No
Shipment of biological samples (DBS)	DBS samples can be sent to other countries

Medical risks related requirements	No
Feedback of blood (DBS) analyses results to the participants	Required (for pathological blood levels)
Relevant national legislation	Act on Personal Data Protection [en]
Relevant ethical guidance	Declaration of Helsinki; IMROH Code of Ethics
Fees of ethics approval	No fees
Duration of ethics approval procedure	About 1 month (max. 60 days after receipt of the application; + max. 90 days after submission of additional documentation, if requested)
Other requirements	No
Similarities to other countries	- As in AT, DK, NL, PL (and maybe LU) the participants have to be informed about certain analyses results.

3.12 HU – Hungary

Legal Framework Conditions

Since Hungary did not participate in the SHARE wave 6 data collection, the legal conditions under which DBS can be collected in Hungary have not been completely clarified so far. This in particular is the case with regard to the question of whether interviewers (i.e. trained laypersons) may collect the DBS samples or if the DBS collection may only be carried out by medical professionals.

Furthermore, it still has to be clarified if blood samples can be sent to another country for storage and analyses and (if this would be possible) whether sending the samples via postal mail would be allowed.

The central relevant data protection law with regard to the processing of personal data in Hungary is Act CXII of 2011 on Informational Self Determination and Freedom of Information, which came into force on 1 January 2012 and implements the European Data Protection Directive (95/46/EC). Besides, Act XLVII of 1997 on Processing and Protection of Medical and Other Related Personal Data (Medical Data Act) regulates the conditions and purposes of the processing of sensitive data concerning an individual's state of health and related personal data. Research on human beings is regulated on different levels in Hungary. Basic provisions concerning research are incorporated in the Act CLIV of 1997 on Health (Health Care Act) and in Act XXV of 1998 on Medicinal Products for Human Use.

In order to conduct a collection of DBS in Hungary informed written consent has to be obtained from the participants prior to their collection. Participants must be given detailed information about the objectives and procedures of the study. At this, all measures taken to protect the privacy and anonymity of the participants and their data during all the stages of the study must be described in the written information that is given to the participants. Furthermore, participants have to be informed about the voluntary nature of the research and about their right to withdraw their consent at any time without any explanation.

Each research protocol intending to involve human beings usually has to be reviewed by two ethics committees[13]: One ethics committee at the institutional level, i.e. the institutional research ethics board (IRB) of the health care institution where the research is intended to be carried out, and the competent regional/national ethics committee (see ethics committee approval system section below).

Since collecting DBS in Hungary is defined as a 'clinical trial with intervention' (since biological material is removed from the body of the participants), it is also required that the reviewing IRB is named and that contact details of an independent medical practitioner are given in the consent documents. Moreover, due to this definition, a specific participant insurance, i.e. a liability insurance covering clinical research, has to be taken. Furthermore, it may be required that one copy of the consent documents (information leaflet and signed consent form) have to be included to the medical file of the respective participant (this, however, has not been completely clarified).

➔ *There may be special legal constraints in Hungary regarding the collection of DBS; to clarify possible issues further investigation is needed concerning the legal framework conditions. Since the collection of DBS is defined as clinical research, all legal requirements that apply to clinical trials have to be fulfilled, such as taking a specific liability insurance.*

Ethics Committee Approval System

In Hungary, there is a national research ethics committee, which is the competent authority for clinical trials with medical devices as well as epidemiological and non-interventional medical studies: the Scientific and Research Ethics Committee ("Tudományos és Kutatásetikai Bizottsága", TUKEB) of the Medical Research Council. TUKEB does not directly provide ethics approval but issues opinion statements. Based on the opinion of TUKEB legal authorisation is given by the relevant regional and sub-regional offices of the National Public Health Service (ÁNTSZ). There are about 150 regional offices in Hungary. If a regional office does not authorise the research, an appeal to appeal can be made to the central Office of the Chief Medical Officer at ÁNTSZ against its decision.

Additionally in the case of the DBS collection, it might be necessary (since Hungary did not participate in the SHARE wave 6 data collection, this was never fully clarified) to send an application to the Office of Health Authorization and Administrative Procedures (EEKH). If this is necessary depends on whether there is a medical device involved in the research.

Therefore, if the lancet used to prick the participant's fingers (in order to collect the DBS in SHARE) would be defined as a medical device, the lancet would have to be registered at EEKH in a first step. If this would be the case, EEKH would provide its opinion regarding the medical device to TUKEB. In a second step, an application has to be submitted to TUKEB,

[13] For further information please see: Sándor, J., Dósa, Á. and Bártfai, Z. (2003). "National Regulations on Ethics and Research in Hungary." Brussels: European Commission.

which finally has to be forwarded to ÁNTSZ in order to receive a final legal authorisation for the DBS collection in SHARE. Besides (as described above in the legal framework conditions section), an ethics approval of the IRB of the health care institution where the research is intended to be carried out has to be obtained. In order to be able to apply for the opinion of TUKEB a health care institution has to be involved in the research project.

The review at TUKEB, which meets once a month, takes about one month (max. 45 days). The committee may ask for additional explanations and documents or request the implementation of changes. If this is deemed necessary by the committee, the procedure may take up to 45 days longer (following the second submission).

The following documents and fieldwork materials have to be prepared and submitted to TUKEB: An official proposal of the principal investigator, a detailed research plan (including a detailed budget, a list of contributors and a description of the scope of activities), the consent documents used (in Hungarian), CVs of the principal investigator and a medical doctor involved in the study, a certificate about the liability insurance covering the risks of the DBS collection, a statement from the principal investigator on the compliance with the Helsinki Declaration, the Oviedo Convention and Hungarian laws as well as general information about the research project and about the data handling procedures and data protection measures of the project. In the case of an international study ethics approvals from other countries may be requested.

➔ *Ethics approval of the DBS collection in SHARE may be subject to special conditions in Hungary (e.g. feedback of the DBS analyses results to the participants may be requested); since Hungary, however, did not participate in the SHARE wave 6 data collection, no application has been made to the responsible committees (IRB and TUKEB).*

TABLE 12: OVERVIEW – HU

Type of ethics committee (EC)	Medical REC (besides TUKEB there are several regional ECs and many local IRBs)
Number of ethics committees to be consulted	2 (TUKEB and IRB)
Other authorities to be consulted	ÁNTSZ (about 150 regional offices), maybe EEKH
Type of approval needed (entire survey, health related data, DBS collection, etc.)	n/a
Special requirements regarding ethics committee approval	A medical doctor has to be involved in the study (affiliation to health care institution required)
Required form of consent	Informed written consent
Special requirements regarding consent	Detailed information has to be provided to the participants
Special data privacy requirements	None known
Shipment of biological samples (DBS)	No restrictions known
Medical risks related requirements	Specific study participant insurance required (hospital liability insurance); A physician has to be involved in the study; Info n/a: if DBS collection only by medical professionals

Feedback of blood (DBS) analyses results to the participants	n/a
Relevant national legislation	Act CXII on Informational Self Determination and Freedom of Information [en] Act XLVII on Processing and Protection of Medical and Other Related Personal Data (Medical Data Act) Act CLIV on Health (Health Care Act) [en]
Relevant ethical guidance	Declaration of Helsinki; Oviedo Convention
Fees of ethics approval	Approval procedure: About 1.500 EUR (including fee for ethics committee: 1.100 EUR)
Duration of ethics approval procedure	About 2-4 months
Other requirements	Medical partner institution in the research project is needed
Similarities to other countries	- As in BE, CH, FR, IL, LU and NL a specific study participant insurance is required. - As in NL a medical doctor has to be involved in the study.

3.13 IL – Israel

Legal Framework Conditions

Regarding the collection of DBS there are no special legal constraints in Israel, as far as data protection legislation is concerned. Furthermore, there are no legal restrictions with regard to the collection of DBS samples by trained laypersons or the shipment and storage of DBS samples (as far as it concerns European countries or the USA).

In order to conduct a collection of DBS in Israel informed written consent is necessary.

There are no major legal restrictions concerning the shipment or storage of DBS samples. They may be sent to other countries and the storage duration is not limited in principle.

The central relevant data protection law with regard to the processing of personal data in Israel is the Protection of Privacy Law 5741-1981. In order to conduct a collection of DBS in Israel informed written consent is necessary. Participants must be fully informed about the aims and methods of the study as well as about the processing of their samples and personal data.

However, with regard to the shipment of equipment to Israel, e.g. the DBS kits including the lancets needed to prick participant's fingers, issues may occur. This has to be considered when planning a collection of DBS in Israel since solving such issues related to special import requirements may be quite time consuming.

Moreover, taking a specific study participant insurance, which covers any damage that may arise from the DBS collection, is required. Standard liability insurance will allow a collection of DBS only when the blood drops are collected via 'self-pricking' of the participants; to

allow interviewers to perform the pricking of participants' fingers a specific clinical insurance is required.

Ethics Committee Approval System

In Israel, research ethics committees are organised on an institutional level in medical centres. The applicant – and therefore the principal investigator of the DBS part of the study – is required to be a medical doctor.

In the case of SHARE, the Institutional Helsinki Committee at the Hadassah University Medical Center Jerusalem was responsible for the approval of the DBS collection in Israel. While the Israeli SHARE Country Team is located at in Jerusalem, the actual fieldwork in SHARE Israel is conducted by a survey agency located at the Tel Aviv University. Therefore, in addition, the research project was presented to the ethics committee of the Tel Aviv University (Tel Aviv Sourasky Medical Center Institutional Review Board (Helsinki Committee)).

For the ethics review an electronic application form has to be filled out and submitted together with comprehensive information about the project and its procedures. With regard to the DBS collection in SHARE, the following documents had to be prepared and submitted to the Institutional Helsinki Committee at the Hadassah University Medical Center Jerusalem: a protocol of the study as well as a summary of this protocol, a data protection description, training descriptions and interviewer manuals, the consent forms and information documents for the participants and an approval letter of the principal investigator of the study. These documents had to be submitted three to four months before the planned starting date of the study.

The application has to be submitted three weeks before one of the scheduled ethics committee meetings, which take place once a month. A decision of the committee can usually be expected within ten days after the meeting; the ethics review process takes up to two month. In the event that changes with regard to a specific application are required, the process will last one to two additional months.

For the DBS collection, the ethics committee may require that specific study participant insurance is taken to cover the specific risks of the research project. In the case of the SHARE study this requirement was stipulated by the ethics committee of the Tel Aviv University.

➔ *One important finding with regard to the ethics review is that the principal investigator (PI) of the DBS part of the study has to be a medical doctor. Moreover, a specific study participant insurance was required by the ethics committee; otherwise interviewers would not have been allowed to prick the participant's fingers but only 'self-pricking' would have been possible. DNA analyses of DBS samples were excluded from the application in Israel from the very beginning.*

TABLE 13: OVERVIEW – IL

Type of ethics committee (EC)	Institutional medical EC (ECs are organised at an institutional level in medical centres)
Number of ethics committees to be consulted	1 (in the case of SHARE 2 committees were consulted since two universities are involved)
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	DNA analyses of DBS samples were excluded (self-restriction)
Required form of consent	Written informed consent
Special requirements regarding consent	No
Special data privacy requirements	No
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	Specific study participant insurance required (if the interviewer pricks the participant a clinical insurance is required); PI of the DBS part of the study has to be a medical doctor
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Protection of Privacy Law 5741-1981 [en]
Relevant ethical guidance	Declaration of Helsinki; ICH Guidelines GCP
Fees of ethics approval	No fees
Duration of ethics approval procedure	2 month (+ 1-2 months if changes required)
Other requirements	Shipment of Lancets etc. to Israel has to be well prepared (and may be time consuming)
Similarities to other countries	- As in CH, FR, LU and SI the principal investigator of the study has to be a medical doctor. - As in BE, CH, FR, HU, LU and NL a specific study participant insurance is required. - As in BE, DE, FR, IT, LU, PL, PT, SE and SI DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

3.14 IT – Italy

Legal Framework Conditions

Regarding the collection of DBS there are no special legal constraints in Italy. Neither are there legal restrictions with regard to the collection of DBS samples by trained laypersons nor concerning the shipment or storage of DBS samples. DBS samples may be sent to other countries and the storage duration is not limited in principle.

In order to conduct a collection of DBS in Italy informed written consent has to be obtained prior to their collection. Participants must be fully informed about the objectives and procedures of the study.

The main data protection legislation with regard to the processing of personal data in Italy is the Legislative Decree no. 196 of 30 June 2003 ("Codice in materia di protezione dei dati personali" [it], the so-called "Data Protection Code"), which formally implements the European Data Protection Directive (95/46/EC). In 1997 the Italian Data protection Agency (Garante per la protezione dei dati personali) was created in order to protect fundamental rights and freedoms in connection with the processing of personal data, to ensure respect for individuals' dignity and to enforce the data protection laws in Italy.

Furthermore, when conducting research the "Code of conduct and professional practice applying to processing of personal data for statistical and scientific purposes" applies.

Ethics Committee Approval System

The ethics committee system in Italy appears to be quite complex. Almost 300 ethics committees are organised in a decentralised manner on regional, local and institutional levels.[14] Most of them are located at the municipality level, e.g. in hospitals and health care units, but there are also some established at scientific research institutions (universities, etc.). The committees are independent, i.e. each committee has its own rules, procedures and time schedule. Even though there is a National Bioethics Committee (NBC) in Italy, at first sight no single ethics committee clearly is solely responsible for an ethics review of research at the national level, since the NBC's task is to express opinions and to address ethical and legal issues that may arise as a result of the progress in scientific research and technological developments.

As regards experiments, trials and other research carried out by health care personnel, applications have to be made to the ethics committee of the respective hospital/health care unit. These ethics committees can in principle also be approached by external bodies in the case that a research project involving human subjects is planned to be conducted in the catchment area of the hospital/health care unit[15]; this however may imply that if the research project is conducted in more than one municipality applications need to be made to several ethics committee separately.[16] With regard to the ethics review of scientific research projects (in which no health care personnel and patients are involved), however,

[14] While Veerus et al. (2013) counted 264 ethics committees in Italy in the year 2010, according to an unofficial list available at http://www.comitatietici.it/elenco/default.html currently there are 271 ethics committees in Italy. With regard to the implications of a reform of the ethics approval system regarding clinical research in Italy 2012/2013, it is noted that according to Minacory et al. (2015) since then the number of ethics committees in Italy has been drastically reduced. This, however, could not be verified during the online research conducted for this SERISS deliverable. Nonetheless, it is acknowledged that since the DBS collections in SHARE in particular in Italy many legal and organisational changes have taken place, and therefore some of the information included in this chapter may not reflect the current situation anymore.

[15] In the DBS collection pilot in the pretest of SHARE wave 5, a test run which also was carried out in Italy, only participants from the municipality of Padua were recruited. Therefore, an application was made to the hospital ethics committee in Padua, which reviewed and finally approved the project for the region.

[16] It is noted that according to Minacory et al. (2015) in consequence of the Law n. 189 of 8 November 2012 and the Ministry of Health Decree of 8 February 2013 research ethics committees are not serving a single hospital or research institution but regions.

also a research ethics committee of an affiliated research institution (e.g. a university) can be approached, which are not bound by catchment areas with respect to their reviving competences.

Therefore, with regard to ethics review of the DBS collection in SHARE wave 6 the Milano-Bicocca University Research Ethics Committee (Comitato Etico dell'Università degli Studi di Milano-Bicocca) has been approached by the Italian SHARE Country Team. The committee meets every month, and if all requirements are met the application process takes about one to two months. At this, a medical doctor affiliated to the Milano-Bicocca University has to be involved in the study that is subject to the review.

For the ethics review, an application has to be submitted together with comprehensive information about the project and its procedures to the ethics committee. Detailed information about how and by whom the DBS collection in SHARE was conducted had to be submitted, including information about the involved institutions and the CVs of the responsible persons. Furthermore, besides several statements of the responsible persons, information of the following documents were compiled: the DBS survey protocol, a description of the SHARE survey as a whole (including its objectives) and the questionnaire of the study, proof of sufficient insurance coverage, information on data processing and on the data protection measures taken, the consent documents (including the DBS information leaflet and consent form for the participants) and further DBS fieldwork materials and documents (such as the interviewer manual, interviewer short instructions, interviewer training description).

Before the pretest of SHARE wave 6, an application based on these documents and information was submitted to the Milano-Bicocca University Research Ethics Committee. This application, however, has not been approved by the committee straight away, because the ethics committee demanded some changes with regard to the consent documents.[17] At this the committee placed particular importance on the respondents being given the option to explicitly express their opinion to the use of the samples for other purposes than the ones indicated in the consent form and to be contacted in the event that such use would be planned. After the requested changes have been implemented in the consent form, the Ethics Committee of the University of Milano-Bicocca finally approved the DBS collection in the context of SHARE for the entire country.

➔ *Final conditions of the approval of the DBS collection in SHARE wave 6 are that an advance letter has to be sent to survey participants (informing them about the project and providing them with the consent documents) and that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed*

[17] Regarding this, it is noted that ethics committees in Italy use to have their own specific consent forms and if other documents are used (as this was the case in SHARE, in which for reasons of cross-country harmonisation, generic English templates are used in all participating countries) it is likely that these are compared to the committee's documents and may have to be adapted to them.

consent) have to be approved by the ethics committee before such analyses may be carried out. Furthermore, the storage duration of the samples is limited until 31 December 2024. DNA analyses of DBS samples were excluded from the application in Italy from the very beginning.

TABLE 14: OVERVIEW – IT

Type of ethics committee (EC)	University REC (besides there are about 264 regional, local and institutional medical ECs, which are organised in a decentralised manner)
Number of ethics committees to be consulted	1 university REC if affiliated to respective university (or many hospital RECs if medical personnel involved and not within the scope of responsibility of a university REC)
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee; An advance letter including the consent documents has to be sent to the participants; A medical doctor has to be involved in the study; DNA analyses of DBS samples were excluded (self-restriction); DBS samples storage is limited (destruction date: 31.12.2024)
Required form of consent	Informed written consent
Special requirements regarding consent	Advance letter to be sent to participants; Participants must be given the option to explicitly express their opinion to the use of the samples for other purposes and to be re-contacted in such an event
Special data privacy requirements	No
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	No
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Data Protection Code - Legislative Decree no. 196/2003 [en, it] Code of conduct and professional practice applying to processing of personal data for statistical and scientific purposes [en]
Relevant ethical guidance	Declaration of Helsinki
Fees of ethics approval	University REC: no fees / Or each local ethics committee (medical EC): 2.000-3.500 EUR
Duration of ethics approval procedure	1-2 months
Other requirements	No
Similarities to other countries	- As in CH, DK and SE an advance letter has to be sent to the participants. - As in BE, CH, DK, EE, ES, FR, LU, PT, SE and SI additional ethics committee approval for further analyses of the DBS samples is needed.

	- As in DK, FR, GR, NL and PT and the storage duration of the DBS samples is limited. - As in BE, DE, FR, IL, LU, PL, PT, SE and SI DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

3.15 LU – Luxembourg

Legal Framework Conditions

In Luxembourg, due to occupational restrictions it is forbidden for laypersons to collect blood samples. According to Article 6 of the Law on Blood Transfusion of 15 March 1979 ("Loi du 15 mars 1979 portant réglementation de la transfusion sanguine" [fr]; cf. Mémorial A No 30 of 17 April 1979, p. 590ff [fr]), the collection of human blood or plasma can only be carried out by a medical doctor or under his supervision (i.e., the principal investigator of a study has to be a medical doctor). Even though, when analysing the legal situation and discussing this with experts, there were some indications that the collection of DBS samples via a finger-prick might not be covered by this law this issue could never be entirely clarified.

Therefore – as regards the DBS part of the SHARE study – the legal framework had to be interpreted restrictively, i.e. assuming that only certified medical personnel (such as medical doctors and nurses) are allowed to collect DBS samples as this would also be the case for a standard blood collection. This restrictive interpretation also implies that participants may not be instructed to prick their own fingers by trained laypersons in order to collect blood samples in the context of a study such as SHARE.

Furthermore, according to Articles 4 and 5 of the Law on Blood Transfusion of 15 March 1979 only specific institutions with medical personnel are granted a special authorisation to export human blood or its derivatives for medical reasons. In the light of the necessary restrictive legal interpretation it had to be assumed that the Luxembourgian SHARE Country Team would not have been allowed to send blood samples abroad for storage and analyses.

➔ *Therefore (due to severe legal uncertainties), in Luxembourg a DBS collection cannot be carried out in the context of SHARE.*

In order to conduct a collection of DBS in Luxembourg informed written consent would be required. As part of this participants must be fully informed about the objectives, methods, duration, place, risks and possible inconveniences of the study as well as well as about the data privacy measures that are taken to ensure the protection of their private life.

The main legal source of data protection in Luxembourg is the Act of 2002 relating to the protection of individuals in relation to the processing of personal data (2002 Data Protection Act, as amended from time to time), which implements the European Data Protection Directive (95/46/EC). The Act aims to protect the freedom and fundamental rights of

individuals, and notably their private life, in relation to the processing of their personal data. The National Commission for the Protection of Data (Commission Nationale pour la Protection des Données, CNPD) is responsible for enforcing these rules.

In Luxembourg, in general, research projects involving human subjects have to be notified to or authorised by CNPD. This also applies with regard to the collection of DBS (for further information regarding the procedure in SHARE please see the following section on "Ethics Committee Approval System").

➔ *Approval of the DBS collection in SHARE has been obtained from the national Data Protection Authority (CNPD).*

Ethics Committee Approval System

Luxembourg has a national ethics committee which is responsible for all investigational sites within the country: the Comité National d'Ethique de Recherche (CNER). CNER closely cooperates with CNPD (one member also attends the national ethics committee meetings as an observer) and other authorities such as the Ministry of Health, from which e.g. investigators of clinical trials also have to obtain approval before the clinical trial may be conducted. CNER also sends copies of its opinions to CNPD as well as to the competent authority (in the case of SHARE: the Ministry of Health).

After submission of an application for ethics approval, the members of CNER examine all relevant documents and discuss the request at a meeting of the ethics committee.

The following application documents have to be submitted to CNER: a standard application form containing the main particulars about the research study (the descriptive summary sheet can be downloaded from the committee's website), a study protocol and all amendments, the written consent form and information sheets for the participants in French and German (and, if applicable, English original) language versions, information about the subject recruiting procedure and sample design, information regarding the financial aspects of the study (including the financial contract signed by the sponsor and the principal investigator), a copy of the insurance policy covering the study, the curriculum vitae of the (national) coordinator, questionnaires given to participants (if applicable) and any other available project-specific materials and documents (e.g. in the case of SHARE: CAPI module, interviewer manual, short instructions, training description, a description of the data protection measures).

The documents must be submitted in several (13) copies three weeks before a meeting of the ethics committee, which takes place once every two months. In general, CNER provides an opinion one week after the ethics committee meeting; it, however, can take up to 60 days (max.) until an opinion is provided. If additional information is requested by CNER after the meeting, the review process will continue as soon as the additional information has been submitted.

In the case of SHARE, after the national data protection authority CNPD approved the DBS collection, an application has been submitted to CNER, which only gave its conditional approval. CNER demanded the legal uncertainties (see above) to be clarified before the DBS collection (carried out by trained laypersons and including the shipping of the samples to another European Country for storage and analyses) could be conducted in Luxembourg. Based on this opinion the legal issues that needed clarification were submitted to the legal department of the Ministry of Health – these, however, were not entirely clarified (see section on "Legal Framework Conditions" above).

As part of the evaluation of CNER, the question of whether feedback about DBS analyses results should be given to the participants has been discussed with the ethics committee, which – depending on a final legal clarification – has been considered to be likely. Furthermore, it would be likely that further analyses have to be approved by the ethics committee

➔ *Since there were several legal uncertainties left in Luxembourg the DBS collection in SHARE wave 6 was only approved conditional upon the clarification of all remaining legal issues. Conditions that according to the conditional approval are likely to apply are that the results of the DBS analyses have to be reported back to the participants and that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before such analyses may be carried out. DNA analyses of DBS samples were excluded from the application in Luxembourg from the very beginning.*

TABLE 15: OVERVIEW – LU

Type of ethics committee (EC)	National REC
Number of ethics committees to be consulted	1
Other authorities to be consulted	CNPD , (Ministry of Health)
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	It is likely that further analyses have to be approved by the ethics committee; DNA analyses of DBS samples were excluded (self-restriction)
Required form of consent	Informed written consent
Special requirements regarding consent	No
Special data privacy requirements	None known
Shipment of biological samples (DBS)	Association to an institution which has a specific authorisation to export blood for medical reasons needed; DBS samples can be sent to those member states of the EU with similar data protection rules
Medical risks related requirements	Probably DBS collection only by medical professionals; PI of the DBS part of the study has to be a medical doctor; Specific study participant insurance required
Feedback of blood (DBS) analyses results to the	Likely to be required

participants	
Relevant national legislation	Loi du 15 mars 1979 portant réglementation de la transfusion sanguine [fr] 2002 Data Protection Act [en, de, fr]
Relevant ethical guidance	Declaration of Helsinki; EU-ICH Guidelines GCP
Fees of ethics approval	Approval procedure: 500-1.000 EUR
Duration of ethics approval procedure	2-3 months (max. 60 days after the meeting of the EC, which meets every 2 months)
Other requirements	Consent documents have to be submitted in French and Dutch to the ethics committee; Several copies of all documents have to be submitted
Similarities to other countries	- It is likely that as in the AT, CZ and PL only medical personnel are allowed to take blood samples and participants are not allowed to prick their own fingers. - As in BE, CH, FR, HU, IL and NL a specific study participant insurance is required. - As in CH, FR, IL and SI the principal investigator of the study has to be a medical doctor. - It is likely that as in BE, CH, DK, EE, ES, FR, IT, PT and SE additional ethics committee approval for further analyses of the DBS samples is needed. - It is likely that as in AT, DK, HR, NL and PL the participants have to be informed about certain analyses results. - As in BE, DE, FR, IL, IT, PL, PT, SE and SI DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

3.16 NL – The Netherlands

Legal Framework Conditions

In the Netherlands all research involving human subjects is mainly regulated by the Medical Research Involving Human Subjects Act (unofficial English translation of the "Wet medisch-wetenschappelijk onderzoek met mensen", WMO).[18] All research that falls under the WMO has to be submitted to an accredited medical research ethics committee for ethics approval (for more details, please see the following section on the "Ethics Committee Approval System" in the Netherlands).

Regarding the collection of DBS the WMO does not imply legal constraints with regard to the collection of DBS samples by trained laypersons or concerning the shipment or storage

[18] An overview of relevant Dutch legislation can be found on the website of the Central Committee on Research Involving Human Subjects (CCMO): http://www.ccmo.nl/en/national-legislation-dutch.

of DBS samples. DBS samples can be collected by trained interviewers (or alternatively via 'self-pricking') and may be sent to other countries for storage and analyses.

The central relevant data protection law with regard to the processing of personal data in the Netherlands is the Personal Data Protection Act (unofficial English translation), which implements the European Data Protection Directive (95/46/EC).

In order to conduct a collection of DBS in the Netherlands written informed consent of the participants is necessary. Participants must be given written information about the study, which provides the basis for their consent. The information has to be written in a form that is comprehensible to all potential research subjects and must in all cases cover the following aspects of the study: the purpose, nature and duration of the study, risks and inconvenience to which the research subject could be exposed, information about the participants' right to withdraw from the study at any time, information about insurance for the research subjects and contact information of an independent medical doctor or other independent expert.

At this, the last requirement regarding the informed consent documents listed above implies the requirement that a medical doctor who is not involved in the study – or another independent expert – must be available to provide research subjects with (independent) information.

Furthermore, a specific study participant insurance is required that covers any possible damage suffered by research subjects as a result of the participation I the study (i.e. a liability insurance regarding research project).

Ethics Committee Approval System

The ethics committee approval system in the Netherlands is regulated by the WMO. According to this law, with regard to the assessment of research involving human subjects there are two types of committees: accredited Medical Research Ethics Committees (MRECs) on a regional level and the Central Committee on Research Involving Human Subjects (CCMO). The MRECs and the CCMO are independent governmental bodies which have legal jurisdiction to make decisions on the basis of the WMO that are binding to citizens of the Netherlands.

As indicated in the "Legal Framework Conditions" section above, all research that falls under the WMO must first be submitted to an accredited medical research ethics committee or the Central Committee on Research Involving Human Subjects (CCMO). The law determines whether a research project must be reviewed by the CCMO or an accredited MREC. Only in certain cases the CCMO acts as the reviewing committee; i.e. in practice the accredited MRECs review the majority of research projects. There are 23 accredited MRECs[19] which

[19] An overview of all accredited MRECs in the Netherlands can be found on the website of the CCMO: http://www.ccmo.nl/en/accredited-mrecs

usually are linked to an institution such as an academic medical centre or a hospital. The majority of MRECs review research projects for the entire country.

In the case of SHARE, the METC Brabant located at the Elisabeth Hospital in Tilburg was responsible for the review of the DBS part of the study in SHARE wave 6 since the Dutch part of the survey is coordinated at Tilburg University.

Regarding the ethics review, the procedure for application and the requirement for documentation to be submitted with the application is standardised amongst the CCMO and all MRECs. An application has to be submitted together with comprehensive information about the project and its procedures. At this, a so-called "Standard Research File" has to be filled out and compiled, which has to be composed of a number of basic documents[20] for many of which the ethics committee provides templates.

In the case of SHARE, the following main documents were prepared and submitted: a covering letter to the reviewing committee, a general assessment and registration form (ABR-form), including a summary (which has to be submitted online, including date and signature), the DBS study protocol (research protocol, including a description of the SHARE survey as a whole), the consent documents (including the DBS information leaflet and consent form for the participants), further DBS fieldwork materials and documents (CAPI module, interviewer manual, short instructions, training description, a description of the data protection measures), the questionnaires accompanying the DBS collection, insurance information, CVs of the coordinating investigator and the independent medical expert and a compiled so-called "Research Declaration Form".

When preparing the documents for the application it turned out that the DBS collection in SHARE had to be described as a multicentre study[21] in the application. Furthermore, in particular with regard to the review in the Netherlands, it became clear that the ethics committee system is rather geared towards the review of bio-medical research, giving precedence to bio-medical ethics over social sciences ethics requirements. While claiming to be responsible to review cross-disciplinary studies such as SHARE, from the perspective of the SHARE team, the committee tended to overlook certain intrinsic differences in substance and methodology between clinical and social science research. This lead to lengthy discussions and resulted in several time-consuming submissions of documents before the final ethics approval was given by the MREC.

In general the timeframe for the review of 'ordinary' medical-scientific research (not including research on medical products) is determined by the General Administrative Law

[20] All details regarding the various documents that need to be submitted for a specific research project can be found on the website of the CCMO: http://www.ccmo.nl/en/standard-research-file. At this the list of documents (also available here: http://www.ccmo.nl/attachments/files/toelichting-bij-standaardonderzoeksdossier-nieuwe-website-dd-1-7-2015-engels.pdf) can be extended or amended by the MREC if deemed appropriate.

[21] For more details see: http://www.ccmo.nl/en/multicenter-research.

Act (Algemene wet bestuursrecht [nl]). It applies a so-called 'reasonable time period' of 8 weeks (which can be extended by another 8 weeks if announced by the MREC during the first 8 weeks), meaning that MREC has a maximum of 8-16 weeks to come to a decision regarding a submitted application. The committee meets once per month and the review time period starts on the day after the MREC has received the complete application including all relevant documentation in accordance with the Standard Research File. If there are any requests for changes and additional information or suggestions of the MREC, the timeline is stopped by the MREC and continues as soon as the new documents have been submitted or another appropriate reaction of the applicant has been received by the MREC (depending on the time needed to answer the request of the MREC, this may lead to a prolonged overall duration of the review process). Finally, the MREC will send its opinion to the submitting party within 7 workdays after the final decision has been reached.

➔ *A final condition of the approval of the DBS collection in SHARE wave 6 is that certain blood analyses results have to be reported back to the participants if this is the express wish of a participant and that this option has to be offered to the participants. Besides, an independent medical doctor – or another independent expert – has to be involved in the study and a specific study participant insurance has to be taken, which both are also legal requirements. Furthermore, the storage duration of the samples is limited until 31 December 2024.*

TABLE 16: OVERVIEW – NL

Type of ethics committee (EC)	Medical EC (23 on a regional level and 1 central)
Number of ethics committees to be consulted	1 (even if classified as a multicentre study)
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	An independent medical doctor (or another independent expert) has to be involved in the study; DBS samples storage is limited (destruction date: 31.12.2024)
Required form of consent	Informed written consent
Special requirements regarding consent	Participants must be given the option to indicate whether they want to be informed about pathological blood levels
Special data privacy requirements	No
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	Specific study participant insurance required (i.e. liability insurance regarding research projects); Independent medical doctor required to provide information to participants
Feedback of blood (DBS) analyses results to the participants	Required (for pathological blood levels)
Relevant national legislation	Medical Research Involving Human Subjects Act (WMO) [en, nl] Personal Data Protection Act [en] General Administrative Law Act [nl]

Relevant ethical guidance	Declaration of Helsinki; CCMO Manual for the Review of Medical Research Involving Human Subjects 2002; EU-ICH Guidelines GCP
Fees of ethics approval	Ethics committee: 1.000 EUR (excl. 21% VAT)
Duration of ethics approval procedure	8-16 weeks (may take longer if requests are made by the ethics committee)
Other requirements	n/a
Similarities to other countries	- As in BE, CH and SI SHARE is considered as a multicentre study. - As in AT, DK, HR, PL (and maybe LU) the participants have to be informed about certain analyses results. - As in BE, CH, FR, HU, IL and LU a specific study participant insurance is required. - As in HU a medical doctor has to be involved in the study. - As in DK, FR, GR, IT and PT and the storage duration of the DBS samples is limited.

3.17 PL – Poland

Legal Framework Conditions

In Poland, due to occupational restrictions it is forbidden for laypersons to perform any medical procedure involving the collection of human blood, including the DBS related procedure of pricking participant's fingers. Only medical doctors and nurses under supervision are allowed to take blood from the capillary system. Consequently, the collection of DBS by laypersons such as trained interviewers is not possible in Poland. It is also not allowed that participants take blood drops themselves via 'self-pricking' as this would be considered as an attempt of bypassing the professional requirements of the Polish legal system.

The main legal source regarding medical studies and experiments on human subjects is the Medical Profession Act of 1996 ("Ustawa z dnia 5 grudnia 1996 r. o zawodzie lekarza" [pl], amended from time to time). The Medical Act e.g. specifies that only medical doctors can conduct such experiments, including clinical trials. The Medical Profession Act also established a new network of ethics committees, so-called Bioethics Committees (see following section on the "Ethics Committee Approval System" in Poland).

Regarding medical studies, in general, a specific study participant insurance is required. Since the insurance of the Jagiellonian University (SHARE Country Team's home institution) already covers any damage that may arise from the DBS collection no action had to be taken.

➔ *Therefore, the DBS collection could not be fully implemented in Poland in the context of the regular SHARE wave 6 data collection. As part of the pretest of SHARE wave 6,*

however, a small biomarker validation experiment with regard to the method of DBS analyses was carried out: For this purpose, nurses visited a small group of participants and collected DBS samples as well as venous blood samples.

The central relevant data protection law with regard to the processing of personal data in Poland is the Act of August 29, 1997 on the Protection of Personal Data (Personal Data Protection Act [en]), which implements the European Data Protection Directive (95/46/EC).

In order to conduct a collection of DBS in Poland informed written consent has to be obtained (in the case of inability to express written consent verbal consent in the presence of two witnesses is sufficient). Participants must be informed in detail about the objectives, methods, conditions and risks of the study as well as about the processing of their samples and personal data and related rights. There are no special legal restrictions with regard to shipment and storage of DBS samples abroad.

Ethics Committee Approval System

In Poland, local ethics committees are established at regional chambers of physicians, at medical colleges or universities with a medical department and at medical research and development units. These so-called Bioethics Committees have been established under the Medical Profession Act of 1996. Detailed information about the Polish system of local research ethics committees (Bioethics Committees) can be found on the website of the EURECNET project of the "European Network of Research Ethics Committees" (EUREC)[22].

According to the law only medical experiments (i.e. experiments carried out by medical doctors or dentists) require notification of the Bioethics Committees.[23] Since the conduction DBS part of the SHARE study, under the Polish law, only would have been possible in a setting that is considered as a medical study (cf. section on "Legal Framework Conditions" in Poland above), in any case it would have required prior approval of the responsible Bioethics Committee. As due to this restriction instead a small biomarker validation experiment with regard to the method of DBS analyses was set up, ethics approval was required undoubtedly.

In the case of SHARE, the Medical Ethics Committee of the Jagiellonian University Medical College was responsible for the review of the project. It – as all Bioethics Committees – is competent to approve the research project for the entire country.

For the ethics review regarding the biomarker validation experiment in SHARE wave 6, the following documents had to be prepared and submitted to the Bioethics Committee: a

[22] The website of EUREC provides an overview of Research Ethics Committees in Europe from a bio-medical point of view: http://www.eurecnet.org/ index.html.

[23] Please note that in Poland interventional studies involving human subjects which are not classified as medical experiments (e.g. experimental psychology), research on human biological material and observational studies involving human subjects (including analyses of records containing biomedical information) are not subject to legal regulations.

medical research protocol of the study, the consent forms (two separate consent forms: one regarding the participation in the study and one regarding the processing of personal data of the participants), information documents for the participants (including information on purposes and principles of the study, expected medical and other benefits as well as associated risks), a CV of the scientific investigator, a list of the relevant scientific literature (if possible, accompanied by copies of the literature) and any further documents necessary to evaluate the application such as a data protection description, training descriptions and interviewer manuals.

Besides, information and proof has to be provided on whether the project is part of the research of the Jagiellonian University or the Jagiellonian University Medical College (which is the case for SHARE) or whether it is classified as 'sponsored research' (in which case additional information and documents regarding project partners and the availability of appropriate insurance coverage have to be provided).

All application documents have to be submitted two weeks before one of the scheduled ethics committee meetings, which usually take place once a month. Furthermore, the applicant's presence is required at the meeting since the applicant has to present the application at the meeting and will have to answer questions of the members of the committee. A decision of the committee can usually be expected within one week after the meeting. In the event that further documents or information is demanded by the committee or changes with regard to a specific application are required, requested amendments have to be provided after the meeting and will be reviewed at the committee's next meeting. A final decision of the committee can usually be expected three months after the submission of the application documents.

➔ *Final conditions of the approval of the DBS collection in SHARE wave 6 are that certain blood analyses results have to be reported back to the participants and that two separate consent forms have to be issued to the participants (for study participation and personal data processing). It is noted that in the specific context of the validation study in SHARE in Poland in which also venous blood samples are collected, reporting back the results of the analyses of the venous blood samples was considered as sufficient by the ethics committee. DNA analyses of the samples were excluded from the application in Poland from the very beginning (in this context, please note that DNA analyses also require special informed consent in Poland).*

TABLE 17: OVERVIEW – PL

Type of ethics committee (EC)	Local Medical REC (53 Bioethics Committees organised at an institutional level, including 1 central Committee at the Ministry of Health)
Number of ethics committees to be consulted	1
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS + additional venous blood collection (if medical research: entire study)

Special requirements regarding ethics committee approval	DNA analyses of the samples were excluded (self-restriction, but DNA analyses also require special informed consent in Poland)
Required form of consent	Informed written consent
Special requirements regarding consent	In the case of inability to express written consent verbal consent in the presence of two witnesses is sufficient; Separate consent forms for study participation and data processing are required; Detailed information has to be provided to participants
Special data privacy requirements	No
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	DBS collection only by medical professionals
Feedback of blood (DBS) analyses results to the participants	Required (depending on concrete circumstances: since in SHARE also venous blood samples are collected in PL, reporting back the results of the analyses of these samples is sufficient)
Relevant national legislation	Medical Profession Act of 1996 [pl] Personal Data Protection Act 1997 [en]
Relevant ethical guidance	Declaration of Helsinki; EU-ICH Guidelines GCP
Fees of ethics approval	Approx. 1.375 EUR
Duration of ethics approval procedure	About 1-3 months
Other requirements	No
Similarities to other countries	- As in AT, CZ (and probably LU) only medical personnel are allowed to take blood samples and participants are not allowed to prick their own fingers. - As in AT, DK, HR, NL (and maybe LU) the participants have to be informed about certain analyses results. - As in BE, DE, FR, IL, IT, LU, PT, SE and SI DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

3.18 PT – Portugal

Legal Framework Conditions

For performing clinical trials in Portugal, approval of the Portuguese Data Protection Authority (Comissão Nacional de Proteção de Dados, CNPD) has to be obtained. The same applies with regard to the collection of DBS. Apart from this requirement there are no special legal constraints in Portugal regarding the collection of DBS.

Detailed information about the legal framework in relation to medical research in Portugal can be found on the website of the EURECNET project of the "European Network of Research Ethics Committees" (EUREC).

In order to conduct a collection of DBS in Portugal informed consent is necessary.

There are no legal restrictions concerning the shipment or storage of DBS samples. DBS samples may be sent to other countries and the storage duration is not limited in principle.

The central relevant data protection law with regard to the processing of personal data in Portugal is the Act on the Protection of Personal Data, which implements the European Data Protection Directive (95/46/EC).

➔ *Approval of the DBS collection in SHARE has been obtained from the national Data Protection Authority (CNPD) in compliance with national requirements.*

Ethics Committee Approval System

In Portugal, ethics committees are organised on different levels: there are about 100 public and private ethics committees based in medical and academic institutions. By law all health care institutions must have an internal ethics committee, which is responsible for the evaluation of all clinical research that involves human subjects. Other studies need ethical approval from local or institutional ethics committees.

When first implementing the DBS collection in the pretest of SHARE wave 5 in Portugal, there was some uncertainty with regard to the question of which ethics committee would be responsible for ethics approval. Therefore, the Portuguese SHARE Country Team decided to first contact the National Ethics Council ("Conselho Nacional de Ética para as Ciências da Vida", CNECV) and ask for advice. This first step already turned out to be quite time consuming, since the Council does not meet often. At this, the Portuguese SHARE Country Team was told by the CNPD that an application should also be submitted to the Portuguese Blood Institute ("Instituto Português do Sangue"), which in turn told them that the application would not be within their competence and that the application should be submitted to the ethics committee of the respective university. Finally, the CNPD also told the Portuguese Country Team that they did not consider DBS collection to be within their area of competence and that the application should be submitted to the University's ethics committee.

In the case of SHARE, the Ethics Committee of the University of Minho (UMinho Ethics Commission, CEUM) was responsible for the approval of the DBS collection in SHARE in Portugal. The following documents had to be prepared and submitted to the CEUM: the SHARE survey protocol (including information regarding the sampling process of the study), a data protection description, training descriptions, the consent forms and information documents for the participants, CVs of the Portuguese Country Team members, a statement concerning the use of data and a letter from the director of the university's social sciences institute (approving the study).

➔ *Final conditions of the approval of the DBS collection in SHARE wave 6 are that the storage duration of the samples is limited until 31 December 2023 and that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before such*

analyses may be carried out. DNA analyses of DBS samples were excluded from the application in Portugal from the very beginning.

TABLE 18: OVERVIEW – PT

Type of ethics committee (EC)	University-based REC (in PT there are almost 100 local, institutional and medical ECs)
Number of ethics committees to be consulted	1
Other authorities to be consulted	CNPD
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee; DNA analyses of DBS samples were excluded (self-restriction); DBS samples storage is limited (destruction date: 31.12.2023)
Required form of consent	Informed consent
Special requirements regarding consent	None
Special data privacy requirements	None known
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	No
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Act No. 67/98, Act on the Protection of Personal Data [en]
Relevant ethical guidance	n/a
Fees of ethics approval	No fees
Duration of ethics approval procedure	n/a
Other requirements	No
Similarities to other countries	- As in BE, CH, DK, EE, ES, FR, IT, LU, SE and SI additional ethics committee approval for further analyses of the DBS samples is needed. - As in DK, FR, GR, IT and NL and the storage duration of the DBS samples is limited. - As in BE, DE, FR, IL, IT, LU, PL, SE and SI DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

3.19 SE – Sweden

Legal Framework Conditions

In Sweden, with regard to a collection of DBS several legal sources have to be taken into account: Swedish data protection law, ethics review related legislation and legislation regulating the collection and storage of biological samples in biobanks.[24]

[24] An overview of relevant Swedish legislation can be found on the CODEX website of the Swedish Research Council and Uppsala University.

The central relevant data protection law with regard to the processing of personal data in Sweden is the Personal Data Act ("Personuppgiftslagen", SFS 1998:204 [se], further information can be found on the website of the Swedish Data Protection Authority), which came into force on the 24 of October 1998. With this act Sweden implemented the European Data Protection Directive (95/46/EC).

Besides, the Act concerning the Ethical Review of Research Involving Humans (The Ethical Review Act, SFS 2003:460) and the Statute concerning the Ethical Review of Research Involving Humans (The Ethical Review Statute, SFS 2003:615) apply to all research fields and regulates the review of research that involves physical encroachment on human subjects, research using methods that aim to affect the subject physically or psychologically and studies on biological material traceable to specific individuals. Since the SHARE study from the very beginning included the measurement of physical functions such as grip strength, lung force/peak flow, walking speed, the entire study is subject to ethics review in Sweden.

In order to conduct a collection of DBS in Sweden written informed consent of the participants has to be obtained prior to the collection. At this, personal information on biobank donors falls also under the regulations in the Personal Data Act as well as other legislation regarding personal information, since this information is not considered a part of the biobank itself. Further details regarding the concrete information to be provided to participants in order to enable them to give their informed consent are laid down in the Ethical Review Act as well. According to the Ethical Review Act shall study participants be informed about the overall plan for the research, the purpose of the research, the methods that will be used, the consequences and risks that may be related to participation, the identity of the responsible research body, the fact that participation in the research is voluntary and their right to withdraw their participation at any time.

Finally, the Biobanks in Medical Care Act (SFS 2002:297, later complemented with Regulation SFS 2002:746) sets out regulations regarding biobanks in areas such as health and medical services. The law applies to biobanks that consist of tissue samples taken and collected for a specific purpose from patients or other donors within healthcare. According to Swedish legal advisors and a medical ethics committee this law also has to be complied with as regards the DBS part of the SHARE study and therefore, in particular, its restrictions regarding the shipment and storage of human biological samples have to be taken into account. According to the law it is not allowed to store blood samples collected in Sweden abroad for a longer period of time. Therefore, a competent partner institution running a biobank in Sweden had to be found before this part of the project could be continued with in the country.

Regarding the collection of DBS samples by trained laypersons (interviewers) or via 'self-pricking' of the participants there are no special legal constraints in Sweden.

➔ *Therefore, not only the DBS collection but the entire SHARE study is subject to ethical review in Sweden. Furthermore, since blood samples collected in Sweden may not be stored outside the country, the samples are to be stored in Sweden and may only be sent abroad for the very concrete purpose of conducting analyses (for a short period of time).*

Ethics Committee Approval System

In Sweden, research ethics committees are organised on a regional level. The research ethics committees are independent bodies and are responsible to the ministry of education. Each of the six large Swedish universities has a regional research ethics board, which may involve one to four different units for the review of medical research and (always) one separate unit for the review of non-medical research involving human subjects. Besides the six regional committees there also is a Central Ethical Review Board, which makes decisions on controversial issues (if submitted by a regional committee) and functions as appeal body for researchers with regard to decisions made by the regional committees.

In the case of SHARE, the regional Research Ethics Board in Umeå was responsible for the approval of the DBS collection. In Umeå there are two ethics committees units, one being responsible for the review of medical research and one for the review of research projects of other disciplines. As SHARE in principle is a non-medical study the application for ethics review had to be divided in two parts: while the 'usual' application regarding the study was filed to the non-medical research ethics committee unit the application for the DBS part of the study was filed to the medical research ethics committee unit.

While ethics approval for the SHARE study could be obtained without any major complications, the medical ethics committee unit first rejected the application regarding the DBS collection without deciding on its content. At this, the unit argued that the initial application did not refer to a concrete research project but rather to a research infrastructure and that the application missed the legally required element of a Swedish biobank for the storage of the DBS samples (cf. section on "Legal Framework Conditions" above). Therefore the committee argued that the application would not lie within their responsibility (to review applications for research projects).

Therefore, after a competent partner institution running a biobank in Sweden has been found, a corrected and more detailed application was submitted to the medical research ethics committee unit again, which also was accepted by the committee and finally resulted in an approval of the DBS part of the SHARE study.

For the ethics review, an application form has to be submitted together with comprehensive information about the project and its procedures to the medical research ethics committee unit. Regarding this, detailed information about how and by whom the DBS collection in SHARE was conducted had to be submitted. For this purpose, information of the following documents were compiled: the DBS survey protocol (including a description of the SHARE

survey as a whole and its objectives and information about how the participants are informed about their legal rights in Sweden and the EU), the consent documents (including the DBS information leaflet and consent form for the participants) and all further DBS fieldwork materials and documents (CAPI module, interviewer manual, short instructions, training description, a description of the data protection measures). In addition information demonstrating the scientific value of the study, including a specific description of research questions to be answered on the basis of the collected material/data had to be provided, since the ethics committee follows a research project based approach.

When submitting the application all relevant information and documents are required to be provided to the medical ethics committee unit at once. The committee meets every second month and gives its evaluation on an application of a research study within 1 month after submission of the application. In the event that changes or additional information are required by the committee, the amended application resp. the additional information will be reviewed by the committee as soon as it has been submitted. In this case it may take several months until final approval is granted.

➔ *An important precondition in order to be able to apply for ethics review of a project that involves the collection of human biological samples is the availability of a biobank in Sweden in which the samples can be stored (i.e. compliance with the related legal requirement). Final conditions of the approval of the DBS collection in SHARE wave 6 are that an advance letter has to be sent to survey participants (informing them about the project and providing them with the consent documents) and that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before such analyses may be carried out. DNA analyses of DBS samples were excluded from the application in Sweden from the very beginning.*

TABLE 19: OVERVIEW – SE

Type of ethics committee (EC)	Medical and non-medical RECs (6 RECs organised on a regional level, which include separate medical and non-medical units; besides there is one Central Ethical Review Board)
Number of ethics committees to be consulted	2: due to different scopes of responsibility different RECs had to be consulted for the SHARE survey and the DBS part of the study
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	Entire survey + DBS
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee; A SHARE advance letter mentioning the DBS collection has to be sent to the participants; DNA analyses of DBS samples were excluded (self-restriction)
Required form of consent	Informed written consent
Special requirements regarding consent	No

Special data privacy requirements	No (apart from storage restrictions, see below)
Shipment of biological samples (DBS)	DBS samples may only be stored in Sweden; The samples, however, may be sent to other countries for analyses (for a short period of time)
Medical risks related requirements	No
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Personal Data Act [en, se]; information in English Ethical Review Act [en] Ethical Review Statute [en] Biobanks in Medical Care Act [en]
Relevant ethical guidance	Declaration of Helsinki; Nuremberg Code; Oviedo Convention
Fees of ethics approval	Each ethics committee review: about 550 EUR
Duration of ethics approval procedure	About 1 month (committee meets every two months), if changes required: several months
Other requirements	Specific research questions to be answered on the basis of the collected material/data have to be formulated in order to obtain ethics approval of the medical REC (research project based approach)
Similarities to other countries	- As in CH and EE the entire survey has to be approved. - As in CH, DK and IT an advance letter has to be sent to the participants. - As in BE, CH, DK, EE, ES, FR, IT, LU, PT and SI additional ethics committee approval for further analyses of the DBS samples is needed. - As in BE, DE, FR, IL, IT, LU, PL, PT and SI DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

3.20 SI – Slovenia

Legal Framework Conditions

Regarding the collection of DBS there are no special legal constraints in Slovenia. Neither are there legal restrictions with regard to the collection of DBS samples by trained laypersons nor concerning the shipment or storage of DBS samples (unless the samples would be used for DNA analyses, which is not the case in SHARE). DBS samples as well as related consent forms may be sent to other countries and the storage duration is not limited in principle.

In order to conduct a collection of DBS in Slovenia obtaining written informed consent of the participants is necessary. As part of the informed consent procedure, in particular, participants have to be informed about the risks, burdens and benefits of the research as well as be informed about their right such as the right to withdraw consent at any time. The

information has to be provided in Slovene language and must be written in an easy to understand manner.

The central relevant data protection law with regard to the processing of personal data in Slovenia is the Personal Data Protection Act (of the Republic of Slovenia), which implements the European Data Protection Directive (95/46/EC).

Ethics Committee Approval System

In Slovenia, a formal ethics committee review system for medical research has been established since the 1960s which currently encompasses one central and several local ethics committees. At this, the central National Medical Ethics Committee (Komsija Republike Slovenije za Medicinsko Etiko, NMEC/ KME) takes care of the large majority of all ethical review of research in the country. As an independent authorised body the NMEC reviews proposals for biomedical research on human subjects for their 'ethical acceptability'. Ethics review is required for all medical research involving intervention on or interaction with human beings as well as all research on personal medical data and biological material of human origin.

In the case of an international multicentre research, as which (the DBS part of) the SHARE study is classified in Slovenia, all international ethics principles set out in the in the Helsinki Declaration and Oviedo Convention have to be considered. Additionally, since SHARE is an international study and the DBS collection is considered to be research in the medical field approval from the NMEC is required.

In order to obtain ethics approval, the application must be submitted to this committee and has to include the following documents and information: a protocol of the study (including a description of the design, methods, aim and scientific rationale of the study), a summary of the protocol in Slovene language, information on the participants of the study as well as the sampling, details about safety arrangements, insurance coverage and arrangements to ensure the confidentiality of personal data in the context of the study and a reflection of the applicant's own perception of ethical issues in relation to the study. In this connection, any previous ethical review regarding the same or related research should also be referred to and it also has to be stated whether the participants will have access to results regarding the health information collected and to the general outcome of the study.

Regarding these requirements, it is important to note that the "leader of the research" (i.e. in the case of SHARE: of the DBS part of the study) must be a medical doctor – otherwise no approval for the research is granted by the NMEC. Central aspects regarding the responsibility of this medical doctor are to ensure the safety of human subjects in the study and to provide participants (who must be provided the possibility to contact this person) with information in a form that is comprehensible to them. Therefore, besides the CV of the principal investigator, also information about the medical doctor, including details about the professional qualifications, has to be included in the application.

Additionally, a statement that the study be conducted in compliance with the principles of the Declaration of Helsinki, the Oviedo Convention and the Slovene Code of Medical Deontology as well as a declaration of the responsible investigator on existing or potential conflicts of interests have to be submitted. Furthermore, all information given to the participants has to be provided to the NMEC, which includes a short explanation of the study, any consent related information (e.g. risks, burdens and benefits have to be explained) and the informed written consent form (which must include information about the participants' rights to refuse participation and withdraw consent).

The NMEC holds meetings on a monthly basis. To be put on the agenda, applications must be received by regular mail at least one week prior to the next meeting of the ethics committee. Usually the response time of the committee is less than 4 weeks. It however may take 1-2 month until the final approval is given by the NMEC. As an exception, a preliminary opinion can be issued "by chairman's action" if there is a need to gain time for other official procedures.

➔ *One important finding with regard to the ethics review in Slovenia is that the principal investigator (PI) of the DBS part of the study has to be a medical doctor. A final condition of the approval of the DBS collection in SHARE wave 6 is that any further analyses of the DBS samples (exceeding the ones explicitly covered by informed consent) have to be approved by the ethics committee before such analyses may be carried out. DNA analyses of DBS samples were excluded from the application in Slovenia from the very beginning.*

TABLE 20: OVERVIEW – SI

Type of ethics committee (EC)	Medical EC (1 central and several local that may review local studies)
Number of ethics committees to be consulted	1 (even if classified as a multicentre study)
Other authorities to be consulted	None
Type of approval needed (entire survey, health related data, DBS collection, etc.)	DBS
Special requirements regarding ethics committee approval	Further analyses have to be approved by the ethics committee; DNA analyses of DBS samples were excluded (self-restriction)
Required form of consent	Informed written consent
Special requirements regarding consent	No
Special data privacy requirements	No
Shipment of biological samples (DBS)	DBS samples can be sent to other countries
Medical risks related requirements	PI of the DBS part of the study has to be a medical doctor
Feedback of blood (DBS) analyses results to the participants	Not required
Relevant national legislation	Personal Data Protection Act [en]
Relevant ethical guidance	Declaration of Helsinki; Oviedo Convention; EU-ICH Guidelines GCP; Slovene Code of Medical Deontology

Fees of ethics approval	No fees
Duration of ethics approval procedure	1-2 months
Other requirements	n/a
Similarities to other countries	- As in CH, FR, IL and LU the principal investigator of the study has to be a medical doctor. - As in BE, CH and NL SHARE is considered as a multicentre study. - As in BE, CH, DK, EE, ES, FR, IT, LU, PT and SE additional ethics committee approval for further analyses of the DBS samples is needed. - As in BE, DE, FR, IL, IT, LU, PL, PT and SE DNA analyses of DBS samples are excluded. In GR no further analyses are permitted.

4 Summary and Concluding Remarks

When collecting biomarkers in social surveys, using the method of dried blood spot (DBS) sampling, policy-rules on different levels have to be acknowledged: firstly the collection has to be conducted in accordance with legal provisions, secondly ethics requirements as requested by research ethics committees have to be met and thirdly the administrative formalities have to be complied with. If a collection of biomarker/DBS is to be implemented across several EU Member States – as it is the case for SHARE – the complexity of such an endeavour multiplies very quickly, since the relevant policy-rules vary a lot between countries, and sometimes even across regions and institutions. This constitutes a major challenge for researchers who try to implement such a collection in the context of a population-based survey.

Regarding the national legal requirements and restrictions, in particular the provisions set out in data protection laws and medicine laws have to be observed and complied with. They substantially differ between the different EU Member States. Here, one of the main issues – which had a massive impact in the case of SHARE, since in its result it prevented the DBS part of the study to be carried out in several countries – are legal and occupational restrictions not allowing unauthorised persons to collect capillary blood, which is what is done when DBS are collected. In Austria, Poland and the Czech Republic only medical doctors and nurses under supervision of a medical doctor are allowed to perform such tasks, and it is even not allowed that participants performs the finger-prick themselves, since the instruction would be given by laypersons (interviewers). These restrictions would have imposed a completely new setting to the DBS collection (employing nurses at least) which is neither practically nor financially feasible in the context of a large-scale survey project (cf. Chapter 2.1). In France, at least self-pricking of the participants is possible, even though only medical staff are allowed to actively take blood samples.

Another important legal requirement in some of the countries is the obligation to consult certain authorities. In most of the cases in which this is required the national data protection authority has to be consulted. Sometimes – as for example in France – several authorities have to be involved in order to be able to perform a collection of DBS as part of a research project, which imposes a high administrative burden upon the researchers. In some countries there is a clear legal obligation to obtain ethics approval from research ethics committees. In these cases the scope of the work of the committees, which generally operate at the interface between the legal system and ethical frameworks, is governed by law. Other committees' work takes place within the wider framework of research governance only.

In all countries obtaining informed consent in a written form is obligatory before a collection of DBS can be carried out. Regarding this issue, in principle the requirements have been observed to be similar across the countries in which the DBS collection in SHARE has been

carried out. When it comes to the very concrete question of how the participants' consent to collect their blood should be obtained, however, there are also differences, mainly due to ethics committees' requirements. Such differences could be observed regarding the information that has to be provided to the participants and regarding the content and form of the consent documents. In some cases information material and the consent forms had to be sent to the participants in the form of an advance letter; in other cases it was regarded to be sufficient to inform the participants during the interview prior to the DBS part of the study.

The organisation of national research ethics committee systems also differs a lot between different EU Member States. In accordance with the present fragmentation of the national ethics committee systems in Europe, the requirements with regard to the review of research projects vary a lot in the different countries. This becomes particularly apparent when conducting transnational cross-disciplinary research that includes the collection of biological samples and when bio-medical research ethics committees become involved.

In some countries even identifying the ethics committee/s responsible for the approval procedure regarding the DBS collection in SHARE turned out to be a real challenge. Some countries have one single ethics committee responsible for the review of national and international research projects easy to identify (e.g. Luxembourg and Slovenia); in other countries there are many research ethics committees – in some cases even hundreds of committees (cf. Italy) – and it is left to the researchers to find out which of them is the competent committee for the review of the research project. In Spain, for instance, during the period before the pretest of SHARE wave 5, it first seemed that approval from as many regional ethics committees as regions covered in the Spanish SHARE sample would be needed. Prior to this DBS pilot such a scenario has not been anticipated and finally this, together with time constraints, was the major reason why Spain was not able to participate in the SHARE DBS pilot of the pretest of SHARE wave 5 (even though it finally turned out that one approval of a Spanish committee would have been sufficient). Due to similar problems, the Swiss SHARE Country Team was only able to perform the DBS collection in one of the cantons in the pretest of SHARE wave 5.

In some of the countries participating in the DBS collection in SHARE it was also not sufficient to obtain ethics approval from a single ethics committee, but involving several ethics committees was mandatory (e.g. in Belgium, Switzerland and Sweden).

In this connection, it even could be observed that the requirements of different ethics committees within one and the same country may vary substantially. In the context of SHARE this experience was made in Belgium when the first application that was submitted prior to the DBS pilot in the pretest of SHARE wave 5. Although the content of the applications that were submitted to both committees was identical the project was approved by one ethics committee while it was not approved by another committee. Even though this fundamental contradiction could be solved finally and approval of both

committees was given, from the point of view of a researcher this finding is certainly irritating.

Since the collection of biological material in the context of surveys in the social sciences is relatively new and innovative, the review of the DBS collection in SHARE also seemed to be a new experience for some of the responsible ethics committees as well. Some of the remarks that were made by the ethics committees regarding the DBS collection in SHARE may probably be explained by fact that these committees are medical ethics committees that mainly review clinical or medical epidemiological studies.

In that sense, different requirements also might be connected to a different alignment and composition of the different ethics committees. While in some countries there is a differentiated ethics committee system, in which different ethics committees exist for different research purposes (e.g. social sciences and clinical trials), in other countries bio-medical research ethics committees are predominant, which mainly review clinical or medical epidemiological studies. In the latter case, bio-medical research ethics committees (which might give precedence to bio-medical ethics over social sciences ethics requirements and sometimes might overlook the intrinsic differences in substance and methodology between clinical and social science research) also claim to be responsible to review cross-disciplinary studies such as SHARE (cf. Schmidutz et al. 2013).

In summary, regarding the inclusion of DBS in cross-national population-based surveys, there are many legal, ethical and administrative issues that have to be taken into account on national, regional and institutional levels during and prior to the sample collection phase.

As described above and illustrated in the country-by-country documentation of the experiences in SHARE in Chapter 3, the attempt of an implementation of such a project in 20 countries is an extremely challenging task. The practical outcomes with regard to the DBS collection in SHARE are illustrated in Table 21.

In a few countries even legal and occupational restrictions exist, which eventually prevent a realisation of a biomarker collection in the context of a social survey (that relies on trained interviewers and not on medical personnel). Due to such restrictions, in Austria, the Czech Republic and Poland – and Luxembourg, where legal issues regarding this matter could not be entirely clarified – the DBS collection could not be implemented in the context of the regular SHARE wave 6 data collection.

Besides this, the process of obtaining ethics committee approval and (if applicable) permissions of other authorities in the remaining countries presents a real challenge for researchers. In particular, if the research is intended to be harmonised across different countries (not least in order to enable cross-national comparative analyses), meticulous preparations of the applications for ethics committee reviews have to be carried out (cf.

Chapter 2.3). In the context of the intended full-scale implementation of the DBS collection in SHARE wave 6, these challenges finally could be tackled successfully as can be seen in Table 21 below. In all countries in which the DBS collection has been carried out, all necessary ethics committee approvals as well as permissions of other authorities have been obtained prior to the sample collection.

TABLE 21: PARTICIPATING COUNTRIES IN THE DBS COLLECTION IN SHARE WAVES 4 TO 6

SHARE-country	DBS collection in SHARE			
	Wave 4 pilot project	Wave 5 pretest pilot	Wave 6 pretest	Wave 6 main data collection
Austria (AT)	-	-	-	-
Belgium French (BE-FR)	-	X	X	X
Belgium Dutch (BE-NL)	-	X	X	X
Croatia (HR)	-	-	X	-*
Czech Republic (CZ)	-	-	-	-
Denmark (DK)	-	X	X	X
Estonia (EE)	-	-	X	X
France (FR)	-	-	X	X
Germany (DE)	X	X	X	X
Greece (GR)	-	-	X	X
Hungary (HU)	-	-	-*	-*
Israel (IL)	-	-	X	X
Italy (IT)	-	X	X	X
Luxembourg (LU)	-	-	-	-
Poland (PL)	-	-	X**	-
Portugal (PT)	-	X	X	-*
Slovenia (SI)	-	-	X	X
Spain (ES)	-	-	X	X
Spain Girona (ES-G)	-	-	X	-*
Sweden (SE)	-	-	X	X
Switzerland (CH)	-	X	X	X
The Netherlands (NL)	-	-	X	-*

* *Non-participation of these countries (resp. SHARE Country Teams) in the DBS collection of the main data collection of SHARE wave 6 is not due to legal or ethical restrictions or requirements but other external restrictions of the survey (e.g. in Hungary: overall non-participation in wave 6 of the SHARE data collection).*

** *As an exception a small validation experiment was carried out in Poland, in which venous blood and DBS were collected by nurses.*

5 References

Christensen, K., Bathum, L. and Christiansen, L. (2007): "Biological indicators and genetic information in Danish twin and oldest-old Surveys." In: Weinstein, M., Vaupel, J.W. and Wachter, K.W. (Eds.): Biosocial Surveys. The National Academies Press, pp. 15-41.

Li, W. and Lee, M.S. (Eds.) (2014): "Dried Blood Spots: Applications and Techniques." John Wiley & Sons, Hoboken, New Jersey.

McDade, T.W., Williams, S., Snodgrass, J.J. (2007): "What a drop can do: dried blood spots as a minimally invasive method for integrating biomarkers into population-based research." In: Demography 44(4), pp. 899-925.

Minacori, R., Refold, P., Sacchini, D., Spagnolo, A.G. (2015): "Research Ethics Committees and clinical research in Italy: where are we going?" European Review of Medical and Pharmacological Sciences, 19, pp. 481-485. Retrieved June 30, 2016, from http://www.europeanreview.org/wp/wp-content/uploads/481-485.pdf.

Parve, V. (2003): "National Regulations on Ethics and Research in Estonia." Brussels: European Commission. Retrieved June 30, 2016, from http://ftp.infoeuropa.eurocid.pt/files/database/000036001-000037000/000036849.pdf.

Schmidutz, D., Ryan, L., Gjesdal, A. and De Smedt, K. (2013): "Report about New IPR Challenges: Identifying Ethics and Legal Challenges of SSH Research." DASISH, Work Package 6, Deliverable 6.1. Retrieved June 30, 2016, from http://dasish.eu/publications/projectreports/D6.1_final.pdf.

Sándor, J., Dósa, Á. and Bártfai, Z. (2003). "National Regulations on Ethics and Research in Hungary." Brussels: European Commission. Retrieved June 30, 2016, from http://www.aaalac.org/intlRefs/IntRegs/Hungary/Natl%20Regs%20on%20Ethics%20and%20Research.pdf

Singer, E. (2008). "Ethical Issues in Surveys." In: De Leeuw, Edith D. / Hox, Joop J. / Dillman, Don A. (Eds.). International Handbook of Survey Methodology. Psychology Press, Taylor & Francis, New York, pp. 78-96.

Veerus, P., Lexchin, J., Hemminiki, E. (2013): "Legislative regulation and ethical governance of medical research in different European Union countries." J Med Ethics, May 10, 2013, Epub ahead of print. Retrieved June 30, 2016, from https://www.researchgate.net/profile/Piret_Veerus/publication/236691692_Legislative_regulation_and_ethical_governance_of_medical_research_in_different_European_Union_countries/links/0c96051adb179bc8e4000000.pdf.

*<u>Links:</u> Whenever available online, links to **relevant legal documents, codes of ethics and general information portals** as well as to **websites of authorities and ethics committees** have been included directly in the text and the tables above. These links have been retrieved and checked in June 2016. Please note that a permanent availability cannot be guaranteed. The documents and institutions have been referred to with the official names, translated into English if a translation (official as well as unofficial) was found on the internet.*

6 Annex

6.1 Acronyms and Abbreviations

BS_module – Dried blood spots collection module in the SHARE questionnaire

CAPI – Computer-assisted personal interviewing

CRP – C-reactive protein

DASISH – Data Service Infrastructure for the Social Sciences and Humanities

DBS – Dried blood spots

EC/s – Ethics committee/s (in overview tables in Chapter 3 only)

EC – European Commission (elsewhere, e.g.: Data Protection Directive 95/46/EC)

EU – European Union

EUR – Euro (currency)

GDPR – General Data Protection Regulation

HbA1c – Glycated haemoglobin

HRS – Health and Retirement Study (United States)

ICH-GCP – International Conference on Harmonization Guidelines for Good Clinical Practice

MEA – Munich Center for the Economics of Aging

MPG – Max Planck Institute for Social Law and Social Policy, Max Planck Society for the Advancement of Science

REC/s – Research Ethics Committee/s

SERISS – Synergies for Europe's Research Infrastructures in the Social Sciences

SHARE – The Survey of Health, Ageing and Retirement in Europe

SHARE Central – Central coordination team of SHARE

SSH – Social Sciences and Humanities

WP(#) – Work Package(number) of the SERISS project

[en] – Reference document in English language

[…] – Reference document in … language

6.2 List of Tables

Table 1: Overview – AT 12
Table 2: Overview – BE 14
Table 3: Overview – CH 18
Table 4: Overview – CZ 20
Table 5: Overview – DE 22
Table 6: Overview – DK 25
Table 7: Overview – EE 28
Table 8: Overview – ES 30
Table 9: Overview – FR 32
Table 10: Overview – GR 35
Table 11: Overview – HR 37
Table 12: Overview – HU 40
Table 13: Overview – IL 43
Table 14: Overview – IT 46
Table 15: Overview – LU 49
Table 16: Overview – NL 53
Table 17: Overview – PL 56
Table 18: Overview – PT 59
Table 19: Overview – SE 62
Table 20: Overview – SI 65
Table 21: Participating countries in the DBS collection in SHARE waves 4 to 6 70

6.3 Transnational Inquiry on Ethics Committee Approvals

As part of the preparation for the full-scale implementation of the DBS collection in SHARE a transnational systematic inquiry regarding national legal requirements and ethics committee approval procedures with regard to the collection of biomarkers (derived from dried blood spots/DBS) has been carried out by. This preparatory work has been part of Work Package 6 of the DASISH project. MEA (MPG) collected the information by making use of the SHARE research network. The following set of questions was sent to the persons responsible for the application for ethics committee approval in the SHARE Countries (i.e. the SHARE Country Teams):

A. Ethics committee approval procedure

I. Responsibility and contact

- How does the ethics committee system of your country work in terms of scopes? Is it organised on an institutional or on a regional or local level?
- Which ethics committee or IRB (Institutional Review Board) is responsible for the approval procedure for the DBS collection in your country?
- Is a single ethics committee responsible for the approval of the DBS collection for the whole country or are there several ethics committees that have to be consulted?
- Who is/are the contact person/s of the ethics committee/s within your country?

II. Steps

- Which steps have to be taken in order to 'get the DBS through' the ethics committee?
- How will our (resp. your) request/application be processed by the ethics committee/s internally (from the submission of the request via the review by the committee/s to the delivery of an approval certificate)?

III. Documents and materials

- What materials and documents are needed by the ethics committee/s in order to be able to review the DBS collection?
- At what stage (of A.II.) must the DBS materials/documents be handed in?
- Are there any other requirements to be met? Is further information requested (e.g. about the SHARE survey as a whole)?

IV. Duration

- How often (and when) does/do the responsible ethics committee/s meet?
- Are there any specific dates that have to be taken into account?
- Approximately, how long does an approval procedure take?
- If we are asked by your ethics committee/s to implement changes, will the procedure take considerably more time in this case?

V. Costs

- Are there any fees or other foreseeable costs connected to the approval procedure of your ethics committee/s?
- Approximately, how much costs can be expected to 'get the DBS through' the approval procedure necessary in your country?

VI. Other important issues

- Are there any other important issues that should be considered when applying for an ethics committee approval within your country?

B. Legal framework

I. Collection of the DBS

- Are there any important legal constraints that have to be taken into account when collection DBS (DBS specific or regarding biological material in general) in your country? E.g.:
  - Are (trained) laypersons allowed to prick the fingers of the participants in order to collect the DBS?

II. Type of consent

- Depending on contemporary national legislation, (informed) consent sometimes has to be given in a written form, sometimes verbal consent is sufficient. What type of consent has to be given in your country?
- Are there any special requirements regarding the 'amount' of information which has to be given to the participants prior to their consent and the way in which they have to be informed?

III. Data privacy and consent forms

- May the DBS samples be sent to another country for analyses (i.e. to Denmark in our case)?
- May consent forms (containing personal information) be sent to another country in general? In other words, would we be allowed to send the consent forms to the laboratory?
- May both, the DBS consent form and the blood sample be stored (separately) at the laboratory at the same time in general?

IV. Liabilities

- Is it necessary to take out a specific "study participant insurance" for all persons participating in the DBS collection or will the "public liability insurance" of your institution cover harm (which is unlikely to occur, by the way) that might result from the DBS collection?

V. Other requirements/restrictions

- Are there any other important legal requirements or restrictions that should be taken into account when planning to collect DBS in your country?

C. Ethics committee/s – probable requirements/restrictions

I. Collection of the DBS

- Do we have to expect any specific or general reservations about the intended collection of DBS of (one of) "your" ethics committee/s? E.g.:
  - Might the ethics committee/s demand – extending beyond "your" country-specific legal constraints – that only medical staff will prick the fingers of the participants in order to collect the DBS?
  - Might the ethics committee/s demand that you take out a "study participant insurance" (see B.III.)?

II. Transmission of DBS analyses results

- Is it rather likely that the ethics committee/s of your country will commit us to inform the participants or their general practitioners about the blood results in case a value lies outside the normal range – or is it maybe even more likely that they advise us not to do so?

III. Other foreseeable requirements/restrictions

- Are there any other requirements or restrictions (which go beyond legal constraints) that can be expected to be considered to be important by "your" ethics committee/s that might make adaptions of our DBS procedures and/or materials necessary?