Standard operating procedure for Sample Exchange on a pan-European level to be used in the HBM4EU initiative

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Entity	Name of person responsible	Short name of institution	
Work Package Leader	Ulrike Fiddicke	UBA	
Task leader	Dominik Lermen	IBMT	
Responsible author	Dominik Lermen	E-mail	Dominik.lermen@ibmt.fraunhofer.de
Short name of institution	IBMT	Phone	+49 6897 9071 251
Co-authors	Martina Bartel-Steinbach (IBMT), Frederik Gwinner (IBMT), Sabine Müller (IBMT), Agneta Åkesson (KI), Marika Berglund (KI), Anna Bergstrom (KI), Karin Leander (KI), Milena Horvat (IJS), Janja Tratnik (IJS), Argelia Castaño Calvo (ISCIII), Marta Esteban (ISCIII)		

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1 Purpose of the SOP

This SOP is developed to assist in the proper shipment of biological materials and in assuring the quality of shipped biological materials. It includes information about how to properly classify, package, mark and label your shipment and provide the required templates for a sample exchange. This manual also describes which legal and ethical documents the sample provider (here "provider") has to submit in advance to the HBM4EU Task 1.5 leader.

2 Scope

The SOP is intended for use in the project HBM4EU.

3 Change Control

Changes to the previous version are described in Chapter 16 Version History.

4 Abbreviations

ADN	Accord européen relatif au transport international des marchandises dangereuses par voie de navigation intérieure (European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways)
ADR	Accord européen relatif au transport international des marchandises Dangereuses par Route (The European Agreement concerning the International Carriage of Dangerous Goods by Road)
EU	European Union
HIV	Human immunodeficiency virus
IATA	International Air Transport Association
ICAO	International Civil Aviation Organization Technical Instructions for the Safe Transport of Dangerous Goods by Air
LTP	Linked Third Party
MTA	Material Transfer Agreement

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MDTA	Material and associated Data Transfer Agreement
MDTRF	Material and associated Data Transfer Record Form
RID	Reglement concernant le transport international ferroviaire de marchandises (Regulations concerning the International Carriage of Dangerous Goods by Rail)
SOLAS	International Convention for the Safety of Life at Sea
SOP	Standard Operating Procedure
TBC	Tuberculosis (Mycobacterium tuberculosis)
UNCETDG	United Nations Committee of Experts on the Transport of Dangerous Goods

5 Shipping Overview

Follow these steps when shipping biological materials and dry ice.

- Before shipment can be planned, **all necessary legal and ethical documents defined in Annex 1 to the HBM4EU Legal and Ethics Policy Paper** (ethical approval, informed consent template, data protection approval, biobank approval, the data transfer agreement, material and associated data transfer record form) **must be ready and - if required - signed by both parties** (see section 6.2).
- Send copies of all necessary **legal and ethical documents and information** to Task 1.5 leader (see Section 6)
- **Classify your materials** for shipment (see Section 7.3)
- **Schedule the process of shipment jointly with the receiver** of the biological materials (e.g., shipment date, expected delivery date, import permit if required)
- **Package, mark, and label your material**(s) appropriately (see Section 7.5)
- Fill out the **Sample Transfer Protocol** and complete the **Material and associated Data Transfer Record Form** (see Section 6.2 and 9.4)
- Fill out the **Sample Data Transfer Template** and send it to the recipient (see Section 12.2).
- If you plan on importing biological materials from **non-EU countries** or exporting biological materials to a non-EU country, specific permits may be required (see Section 9.4.2)

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6 Ethical and Legal Aspects

6.1 Required ethical documents

For any data/sample exchange process, partners responsible for studies in HBM4EU are obliged to provide all required ethics documents to the Task 1.5 leader as soon as the use of data/samples have been agreed between WP leader(s) and no later than 6 weeks before shipment and before the analyses of data/samples is planned to start. Table 6-1 shows in detail which documents and information should be provided to Task 1.5 leader. For reporting ethics task 1.5 developed an excel template as Annex 1 to the HBM4EU Legal and Ethics Policy Paper (https://www.hbm4eu.eu/deliverables/).

Send these documents and information as digital copy as attachment to the filled in excel template for reporting ethics to task 1.5 leader Lisbeth E. Knudsen, E-mail: liek@sund.ku.dk.

Table 6-1: Required information and ethics documents

		Recipient	Note
Study	Name of the Study in national language	**WP1.5**	No later than 6 weeks before the work on data/samples is planned to start
	Name of the Study in English		
	Used acronym		
	Country		
Owner of the study	Institute		
	Partner acronym in HBM4EU, and for LTPs who is the beneficiary		
	Contact Person(s): name(s)		
	Contact Person(s): e-mail-address(es)		
Informed consent	Copy of the informed consent(s) and related information material (information to participants) in national language		
	Copy of the informed consent(s) and related information material in English		
Ethical approval	Copy of the ethical approval in national language		
	Copy of the ethical approval in English, if available		
	Is secondary use of data/samples allowed		
	Name of the body/bodies issuing the ethical approval		
	Date of approval		
	Expiration of approval		
Data protection	Copy of data protection approval in national language, if available		
	Copy of data protection approval in English, if available		
	If English version not available, provide a short summary of the contents		
	Name of the body/bodies issuing the date of approval		
	Identification number for approval		
	Expiration date for approval		
Biobank	Copy of biobank approval in national language, if available		
	Copy of biobank approval in English		
	If English version not available, provide a short summary of the contents		
	Is secondary use of data/samples for HBMEU allowed		
	Name of the body/bodies providing approval		
	Identification number for approval		
	Expiration date for the approval		

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	Renewal of the approval(s) is required before use in HBM4EU		
	Which documents require renewal		
Material Transfer Agreement	Copy of Material Transfer Agreement (MTA)		

Human samples used by HBM4EU researchers must be in accordance with the informed consent signed by the subject and the Grant Agreement of HBM4EU. **Ethical approval and arrangements for data protection are mandatory.**

6.2 Material and associated Data Transfer Agreement (MDTA)

A material transfer agreement (MTA) or a similar type of agreement, that is based on the content of a respective prior informed consent (PIC) given from the material donor, has to be signed between provider and recipient to define the use of the material and its associated data and to govern the sample and data transfer.

The **HBM4EU Material and associated Data Transfer Agreement** (HBM4EU MDTA, Annex 6) is such a document and is based on good scientific practice and takes into account relevant regulations of the General Data Protection Regulation (GDPR).

The **HBM4EU MDTA is** the basis for controlled sample exchange between the partners in HBM4EU. As pseudonymised data will be exchange with any material transfer, the HBM4EU MDTA includes **also a data controller - data processor agreement** that governs the processing of the material associated pseudonymised data. The terms and conditions of the HBM4EU MDTA should be agreed to apply fundamental legal and ethical aspects. This is done by signing the **HBM4EU Material and Associated Data Transfer Record Form** (HBM4EU MDTRF, Attachment A of the HBM4EU MDTA). The HBM4EU MDTRF is an integrated part of the HBM4EU MDTA and cannot be used separately from it. **With signing this form the terms and conditions defined in the HBM4EU MDTA and the included data controller data – processor agreement are accepted.**

In addition, the HBM4EU MDTRF serves to specify the general conditions of the HBM4EU MDTA, e.g., to describe exactly which samples are concerned, for what purpose according to the Informed Consent the samples may be used (e.g., analysis plan), whether residual samples of the samples must be returned or destroyed, to describe the material associated personal data and to provide instructions regarding the processing of the material associated personal data by the data processor (for more details see HBM4EU MDTRF).

The HBM4EU MDTA is provided digitally for download as Annex 6 to the deliverable D7.2 (https://www.hbm4eu.eu/deliverables/). Before exchanging samples, please read the HBM4EU MDTA carefully and fill in the HBM4EU MDTRF (Attachment A of the HBM4EU MDTA) according to the required information. The HBM4EU MDTRF has to be signed by both parties, the sample provider and the sample recipient, prior to shipment.

A digital copy of the HBM4EU MDTRF (**Attachment A** of the HBM4EU MDTA) signed by both parties **has to be sent jointly with digital copies of the following legal and ethical documents** defined in the HBM4EU Legal

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and Ethics Policy Paper (D1.5) Annex 1 **to task leader 1.5** (Lisbeth Knudsen, E-mail: liek@sund.ku.dk) and **the HBMEU coordinator UBA** (HBM4EU@uba.de):

- the filled in Excel Template for Reporting Ethics (D1.5, Annex 1)
- the ethical approval (digital copy)
- the information sheet/material to the recruited participants (digital copy)
- the informed consent template (digital copy)
- the data protection approval (digital copy)
- the biobank approval (digital copy)

Documents in National language have to be explained in English in the Excel Template for Reporting Ethics additionally (Annex 1 to D1.5 HBM4EU Legal and Ethics Policy Paper; download D1.5 at: https://www.hbm4eu.eu/deliverables/).

Hardcopies of the HBMEU MDTRF shall be sent to the HBM4EU coordinator UBA (Umweltbundesamt, Marike Kolossa-Gehring, Project Coordinator HBM4EU, P.O. Box 33 00 22, 14191 Berlin, Germany) Send copies **not later than 6 weeks before shipment** and before the analyses of data/samples is planned to start.

7 Packaging

7.1 International Regulations and guidelines:

Packaging and shipping of human samples must conform to all applicable regulations and standards governing packing, marking and labelling (see Table 7-1). All personnel involved in shipping biological materials should be trained properly for both air and ground shipments. In addition, HBM4EU researchers should use practices, which are in line with applicable standards and regulations to protect samples from factors that could influence sample integrity (i.e. temperature) and to provide protection to workers, individuals involved in the transportation of the specimens, and the environment.

Table 7-1: Important International Regulations and guidelines

UN Recommendations on the Transport of Dangerous Goods (http://www.unece.org/trans/danger/publi/unrec/rev19/19files_e.html)	
	**ADR** **European Agreement concerning the International Carriage of Dangerous Goods by Road** https://www.unece.org/trans/danger/publi/adr/adr2017/17contentse0.html
	**RID** **Regulation concerning the International Carriage of Dangerous Goods by Rail** http://otif.org/en/?page_id=174
	SOLAS

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	**International Convention for the Safety of Life at Sea** http://www.imo.org/en/About/Conventions/ListOfConventions/Pages/International-Convention-for-the-Safety-of-Life-at-Sea-(SOLAS),-1974.aspx **ADN** **European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways** http://www.unece.org/trans/danger/publi/adn/adn2017/17files_e0.html
	**ICAO** **International Civil Aviation Organization Technical Instructions for the Safe Transport of Dangerous Goods by Air** https://www.icao.int/safety/DangerousGoods/Pages/technical-instructions.aspx **IATA** **International Air Transport Association Dangerous Goods Regulations (DGR)** http://www.iata.org/publications/dgr/Pages/index.aspx

Dangerous goods are assigned UN numbers and proper shipping names according to their hazard classification and their composition. Proper shipping names are used to clearly identify the dangerous article or substance.

Air transport regulations are the most restrictive and the packaging specifications are the most rigorous. Thus, providers who comply with the air transport regulations (of the International Air Transport Association (IATA)) also will meet the requirements of other transport modes (truck, rail, ship).

7.2 Training requirements

Dangerous goods are categorized according to nine classes. International regulations (IATA) require that staff responsible for shipping dangerous goods must be appropriately trained. Specific training is only required for the shipment of category A samples. This must be documented and is valid for two years for IATA. Federal regulations might require additional trainings. Their validity might be country specific.

7.3 Categories of Infectious Substances

7.3.1 Category A

An infectious substance, which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals.

- Infectious substances meeting these criteria, which cause disease in humans or both in humans and animals, shall be assigned to United Nations number **UN 2814**.
- Infectious substances, which cause disease only in animals, shall be assigned to **UN 2900**.
- The packaging requirements are set out as **Packing Instructions PI620**.

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7.3.2 Category B

An infectious substance, which does not meet the criteria for inclusion in Category A, is classified as Category B. Infectious substances in Category B shall be assigned to **UN 3373**.

- The packaging requirements are set out as **Packing Instructions PI650**.
- All fresh and frozen tissues and liquid specimens from human beings used in the HBM4EU initiative should be considered potentially infectious. For this reason, packaging instructions for Category B samples PI650 have to be applied (see below 7.5)

7.3.3 Exemptions

Substances that do not contain infectious substances or that are unlikely to cause disease in humans or animals are not subject to dangerous goods regulations, unless they meet the criteria for inclusion in another class.

Because of the differences in the hazards posed by Category A infectious substances (UN 2814 and UN 2900) and Category B infectious substances (UN 3373), there are variations in the packaging, labelling and documentation requirements for the two categories. The packaging requirements are determined by UNCETDG and are set out as Packing Instructions PI620 and PI650.

7.4 General preparation of shipments for transport

Providers of infectious substances shall ensure that packages are prepared in such a manner that they arrive at their destination in good condition and present no hazard to persons or animals during transport.

7.4.1 Universal safety precaution and training requirements

Prior hepatitis vaccinations of staff members are mandatory. Specific training according to IATA regulations is only required for shipment of category A samples. Handle all specimens as if capable of transmitting disease. Latex or Nitrile gloves and lab coat are required for the packing of any packages being shipped. Dry ice can cause 3rd degree burns when it contacts exposed skin. Wear cryo-protective gloves when handling.

7.4.2 Classifying shipping categories for human samples

Depending on whether specimens are known to contain infectious agents, biological specimen shipments may be regulated as infectious substances or as diagnostic specimens. Samples that are commonly used in Human Biomonitoring studies include human tissues and body fluids. In most cases, these specimens are not investigated with regard to their infection status. Therefore, **all fresh and frozen tissues and liquid specimens from human beings used in the HBM4EU initiative should be considered potentially infectious**. For this reason, **packaging instructions for Category B samples PI650 have to be applied for samples** that will be exchanged between HBM4EU partners. Specific details of the packing instruction PI650 are described below.

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Human specimen might be considered as patient specimens for which there is minimal likelihood that pathogens are present. In determining whether a patient specimen has a minimal likelihood that pathogens are present, an element of **professional judgment is required to determine if a substance is exempt**. That judgment should be based on the known medical history, symptoms and individual circumstances of the source, human or animal, and endemic local conditions. If there is any reason to suspect that the specimen contains a pathogen, it cannot be shipped as exempt.

7.5 Packing according to Category B requirements (PI650)

A triple packaging system has to be used for all infectious substances. It consists of three layers as follows:

1) A primary receptacle

2) A secondary packaging

3) A rigid outer packaging

7.5.1 Primary receptacle

The primary receptacle (e.g. test tube or other container) or the secondary packaging shall be capable of withstanding, without leakage, an internal pressure of 95 kPa (0.95 bar) between -40°C to 55°C.

The primary container holds the biological material and must be leak-proof for liquids or sift-proof for dried specimens. Primary receptacles may be made of glass, metal or plastic. Petri plates cannot be used as primary receptacles.

Limits:

For liquid specimens, the primary receptacle must not contain more than 1 L. For dried specimens, the primary receptacle must not exceed the outer packaging weight limit.

Figure 7-1: Examples of primary receptacles

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7.5.2 Secondary packaging

A second durable, watertight, leak-proof or sift-proof packaging to **enclose and protect the primary receptacle(s)**.

Choose only secondary containers certified by the manufacturer for Biological Substance, Category B (UN 3373) prior to use. For liquids, add enough adsorbent to the primary containers to absorb the entire contents of all primary receptacles.

Acceptable **absorbent materials** include cellulose wadding, cotton balls, super-absorbent packets and paper towels.

There are different absorbent materials available (bags or sheets made out of absorbent material). The absorbing capacity depends on the material and size.

As example, a high performance sheet from the company Alex Breuer (Item Number 91740000.02) absorbs more than 100 ml of liquid per square decimetre of sheet.

Several cushioned primary receptacles may be placed in one secondary packaging, but sufficient additional **absorbent material** shall be used to absorb all fluid in case of breakage or leakage. To prevent contact between multiple fragile primary receptacles, individually wrap or separate (e.g. Cryobox) them inside the secondary container.

Place primary receptacles into leak-proof secondary packaging such as container or sealed plastic bags which are compatible with dry ice (-80 ° C) in case of frozen shipments.

Figure 7-2: Examples of secondary receptacles: Certified plastic bag (left), leak-proof plastic container with waterproof cap (right)

7.5.3 Outer packaging

The outer packaging has to be rigid and must not contain more than 4 L (for liquids) / 4 kg (for solids). At least one surface of the outer packaging must have 100 mm x 100 mm, in order for required markings and labels to fit.

If frozen or refrigerated shipment, place your secondary receptacle in an appropriate styrofoam box, place dry ice/refrigerant packs outside of secondary packaging. If a shipment includes dry ice the outer packaging must allow for the release of carbon dioxide gas when the solid sublimates.

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Before sealing the outer packaging, you must make an **itemized list of the contents** of the package and enclose the list together with the **completed „HBM4EU_WP7.4_Sample_Transfer_Protocol _V1.0"** between the secondary packaging and outer packaging.

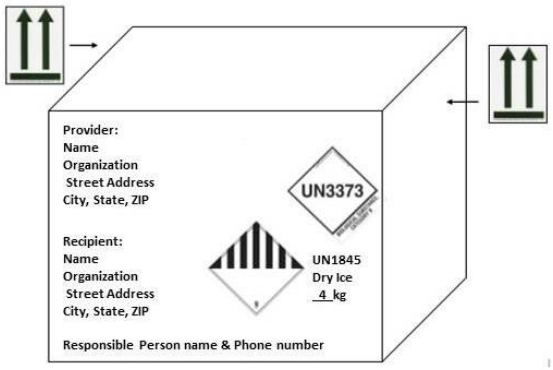

Figure 7-3: Examples of overpacks (left) (http://www.inmarkstp.com/assets/b2b/requests/services/main/18CB4CC294138FDC5687107CD5C2FA0E_src.jpg) **and with the respective labelling (right)**

7.6 Packing for Exempt Specimens

Human or animal specimens (patient specimens) for which there are minimal likelihood that pathogens are present may be shipped as **exempt specimen**.

Similar to Category B (UN3373) shipments, the specimen has to be transported in a packaging which will prevent any leakage and which is marked with the words "Exempt human specimen" or "Exempt animal specimen", as appropriate.

Likewise, the **triple packaging system** has to be used:

- a leak-proof primary receptacle(s)
- a leak-proof secondary packaging
- an outer packaging of adequate strength for its capacity, mass and intended use, and with at least one surface having minimum dimensions of 100 mm × 100 mm

For liquids, absorbent material in the secondary packing shall be used to absorb all fluid in case of breakage or leakage.

7.7 Packing within HBM4EU

An element of professional judgment is required to determine if a substance is exempt. That judgment should be based on the known medical history of the sample (see Section 7.4.2).

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Best practice: To secure all safety requirements, we suggest that fresh or frozen **samples shipped within HBM4EU should be classified as "BIOLOGICAL SUBSTANCE, CATEGORY B" (UN 3373)**. All samples, also infected blood samples (e.g. HIV- or TBC-infected), are correctly packed with the **Packaging Instruction PI650**.

If more than one specimen will be shipped, place samples in suitable boxes (see Figure 7-4) and place boxes and enough adsorbent into the secondary packaging.

Figure 7-4: Example of a cryobox (picture: ratiolab)

If sample volumes of more than 4 L / 4 kg have to be sent, the volume has to be distributed to two or more outer packages. If desired, these can be included into an overpack.

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8 Cooling

Samples can be shipped under different temperature conditions:

- Unchilled at ambient temperature
- Chilled between 2° and 8° C (using cool packs)
- Frozen with dry ice (-79°C)
- Frozen with liquid nitrogen (-196°C using a dry shipper)

Best practice: To secure a high quality of samples by constantly low temperatures while shipping, all frozen samples should be shipped on dry ice within HBM4EU.

Dry ice is available in several shapes and forms such as pellets, sticks or plates. It is offered by several companies. Likewise, many shipping companies provide dry ice for the shipment.

8.1 Packaging with dry ice

For shipments with dry ice, a thermo packaging is required. Usually, the outer package (overpack) consists of a fiberboard box with a Styrofoam inset. These packages are available from several companies. Likewise, the shipping companies provide the packages for a frozen shipment.

The samples (packed in primary and secondary package) are put in the outer package and covered by dry ice. Dry ice sublimates and at the same time displaces oxygen. Boxes therefore should never be hermetically sealed when they contain dry ice.

8.2 Temperature monitoring

As minimum requirement, the temperature of the samples should be measured and documented in the **Sample Transfer Protocol** (Annex 4 to D7.2) immediately before shipping and directly after sample receipt.

Best practice: The optimum is to monitor the temperature in the package using a data logger (the price for a commercially available temperature data logger ranges from 100 – 200 €): This allows to control that the samples have constantly been cooled during the shipment.

Some shipping companies provide a temperature data logger upon request.

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Figure 8-1: Example of a temperature logger (Source: http://www.messbar.de)

9 Labelling and documentation

9.1 Labelling for Category B shipment (UN3373)

Each completed package is required to be correctly marked, labelled and accompanied with appropriate shipping documents (as applicable).

The requirements for these aspects are

1) Name and address of the provider (sender, consignor) must be provided on the package
2) Name and address of the receiver (consignee) must be provided on the package
3) Name and telephone number of a responsible person must be provided on the air waybill or on the package
4) A diamond-shaped UN 3373 label and the proper shipping name ("BIOLOGICAL SUBSTANCE, CATEGORY B")

For transport, the mark illustrated left shall be displayed on the external surface of the outer packaging on a background of a contrasting colour and shall be clearly visible and legible. The mark must be in the form of a square set at an angle of 45° (diamond-shaped) with **each side having a length of at least 50 mm**; the width of the line shall be at least 2 mm and the letters and numbers shall be at least 6 mm high. The proper shipping name "BIOLOGICAL SUBSTANCE, CATEGORY B" in letters at least 6 mm high must be marked on the outer package adjacent to the diamond-shaped mark.

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9.2 Additional labelling of shipments with dry ice

Dry ice is regulated and considered a dangerous good. Therefore, the following packaging marking is required:

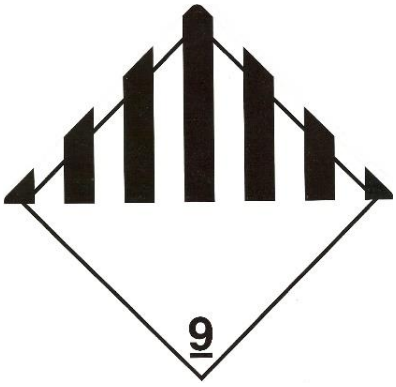
- Class 9 label
- The Proper Shipping Name ("Dry Ice" or "Carbon Dioxide Solid") and identifier "UN 1845"
- The net quantity of dry ice in the package

This label includes all information:

- Class 9 label
- the Proper Shipping Name
- the UN 1845 identifier
- the information about the quantity

Minimum dimensions of label: 100 × 100 mm

Colour: Black and white



The Proper Shipping Name, the UN 1845 identifier and the information about the quantity are given on an external label.

Minimum dimensions of Class 9 label: 100 × 100 mm

Colour: Black and white

Figure 9-1: Examples of Class 9 labels

Dry ice must always be mentioned in the air waybill.

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9.3 Additional labelling for multi-part shipments

Since the size of the packages is limited, multi-part shipments might be required when large numbers of samples have to be transferred. If you send samples in more than one package, please indicate the total number of packages on the external surface of the outer packaging of each single package as indicated in the example below:

Example: Four packages

Package 1	Package 2	Package 3	Package 4
1/4	2/4	3/4	4/4

9.4 Customs requirements, sample information and shipping documents

9.4.1 Sample exchange within the European Union

For shipments within the EU, there are only two documents required:

1) The **air waybill** (house waybill) for air transport or equivalent documents for road, rail and sea journeys. Each courier service provides its own waybill (see Figure 9-2).

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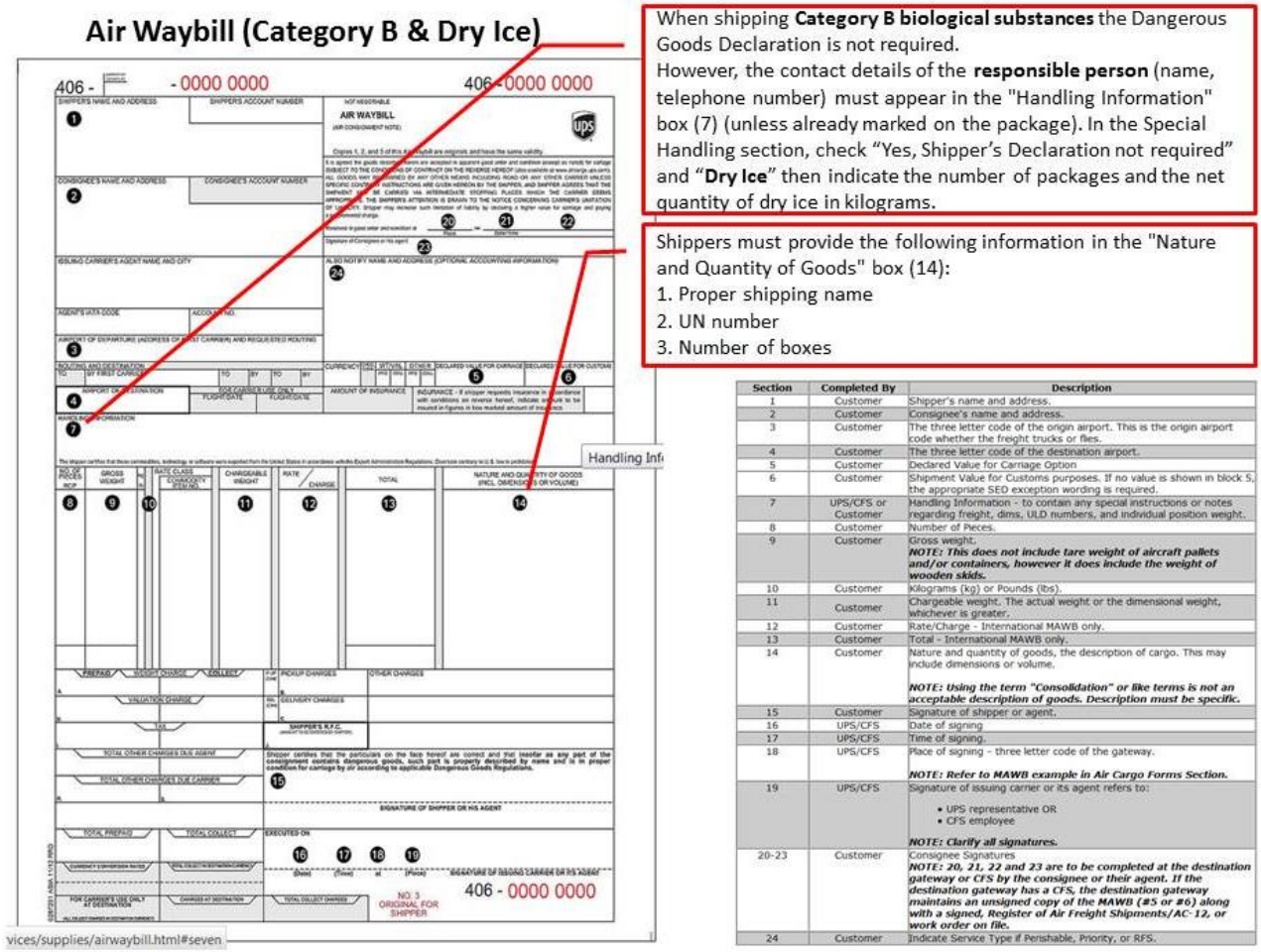

Section	Completed By	Description
1	Customer	Shipper's name and address.
2	Customer	Consignee's name and address.
3	Customer	The three letter code of the origin airport. This is the origin airport code whether the freight trucks or flies.
4	Customer	The three letter code of the destination airport.
5	Customer	Declared Value for Carriage Option
6	Customer	Shipment Value for Customs purposes. If no value is shown in block 5, the appropriate SED exception wording is required.
7	UPS/CFS or Customer	Handling Information - to contain any special instructions or notes regarding freight, dims, ULD numbers, and individual position weight.
8	Customer	Number of Pieces.
9	Customer	Gross weight. ***NOTE: This does not include tare weight of aircraft pallets and/or containers, however it does include the weight of wooden skids.***
10	Customer	Kilograms (kg) or Pounds (lbs).
11	Customer	Chargeable weight. The actual weight or the dimensional weight, whichever is greater.
12	Customer	Rate/Charge - International MAWB only.
13	Customer	Total - International MAWB only.
14	Customer	Nature and quantity of goods, the description of cargo. This may include dimensions or volume. ***NOTE: Using the term "Consolidation" or like terms is not an acceptable description of goods. Description must be specific.***
15	Customer	Signature of shipper or agent.
16	UPS/CFS	Date of signing
17	UPS/CFS	Time of signing.
18	UPS/CFS	Place of signing - three letter code of the gateway. ***NOTE: Refer to MAWB example in Air Cargo Forms Section.***
19	UPS/CFS	Signature of issuing carrier or its agent refers to: • UPS representative OR • CFS employee ***NOTE: Clarify all signatures.***
20-23	Customer	Consignee Signatures ***NOTE: 20, 21, 22 and 23 are to be completed at the destination gateway or CFS by the consignee or their agent. If the destination gateway has a CFS, the destination gateway maintains an unsigned copy of the MAWB (#5 or #6) along with a signed, Register of Air Freight Shipments/AC-12, or work order on file.***
24	Customer	Indicate Service Type if Perishable, Priority, or RFS.

Figure 9-2: Example of an air waybill

2) The **Sample Transfer Protocol** (Manifest) that includes the provider's and the receiver's address and the details of content. **The Sample Transfer Protocol should include emergency contact details (name and telephone number) at both ends.** This document has to be placed into the package (outside of the secondary packaging).

The documents have to be prepared by the provider or the provider's agent. A Provider's Declaration on Dangerous Goods is <u>not</u> required for Category B substances.

9.4.2 Sample shipment from EU countries to non-EU countries

Currently, four countries, which are not member states of the European Union, participate in the HBM4EU initiative: Iceland, Israel, Norway and Switzerland.

To ship human samples from the EU to one of these countries, the following specific regulations and procedures have to be considered:

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- Additionally to the air waybill a **pro-forma invoice** is required (see Appendix A). Please fill out the pro-forma invoice as described in Appendix A. **Sign pro-forma invoice with a blue pen**. For customs clearance, **attach the original of the pro-forma invoice and two copies in a protective bag to the outside of the overpack**.
- Further country-specific import permits might be required. The person receiving the materials is generally regarded as the importer, and thus responsible for obtaining, where necessary, all appropriate permits or licences. Ensure that the receiver has arranged for any import a permit required by the respective national authorities. **The receiver has to provide the permit to the provider**. It should be placed jointly with the pro-forma invoice in the protective bag outside the box.

Best practice: In order to guarantee a safe transportation of your samples, **a courier service should be ordered to conduct the actual transportation**. Most courier services will take care of customs clearance and the required documents. Appendix B provides a compilation of selected courier services in Europe, their contact details for each of the partner countries and information on additional services (e.g., dry ice service, temperature data logger supply).

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10 Shipping Information Summary

Shipment Type	Proper Shipping Name	UN Number	Hazard Class	Packing Group (PG)	Packing Instruction (PI)	Hazard Label(s)	Max. Net qty/pkg. for Passenger Aircraft	Max. Net qty./pkg. for Cargo Aircraft	Special Provisions
Category A infectious substance	Infectious substance, affecting humans (*1)	UN 2814	6.2	-	620	UN 2814 Infectious substance	50 mL / 50 g	4 L / 4 kg	A81, A140
Category B infectious substance	**Biological substance, category B**	**UN 3373**	**6.2**	**-**	**650**	**UN3373**	**4 L / 4 kg**	**4 L / 4 kg**	**-**
Dry Ice	Dry Ice	UN 1845	9	III	954	UN 1845 Dry Ice	200 kg	200 kg	A48
Exempt Human Specimens (minimal likelihood that pathogens are present)	N/A (*2)	N/A	N/A	N/A	See Section 7.6	N/A	N/A	N/A	N/A

*1 Identify technical name of agent in parenthesis

*2 not applicable

11 Technical procedure of Shipment

See form “HBM4EU_WP7.4_Shipping_Flowchart_V1.0” and fill in the “HBM4EU_WP7.4_Sample_Transfer_Protocol_V1.0” and the “HBM4EU_WP7.4_Pro-Forma_Invoice_V1.0”.

12 Data exchange

Sample quality and sustainability are key factors in human biomonitoring. To allow long-term tracking of sample quality based on a complete sample history, a sophisticated documentation system is required. In consequence, sample related data as well as data related to sample exchanges should be documented in a sample data management system.

12.1 Data management system for sample and sample-linked data

In HBM4EU currently no software solution is available to document and track the sample and sample-linked data exchange. Sample exchange protocols, however, are to be tested in 2018/2019 for DINCH in DEMOCOPHES samples (Task 8.2). In consequence, we recommend a temporary solution based on a straightforward file exchange between sample provider and receiver to ensure the minimum of required documentation.

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12.2 Data exchange

The file **"HBM4EU_WP7.4_Sample_Data_Transfer_Template_V2.0.xlsx"** (Annex 5 to D7.2) contains a template excel/csv file to be used in the sample data exchange between provider and receiver, and includes a minimum of required documentation. The following table lists the variables defined in the template file. In case abbreviations (marked in bold) are available, please use these where possible. If none of the permissible values apply, please use the prefix "O:" (for other) followed by a clear text description. The table below also marks whether provided information is optional or mandatory.

Table 12-1: Description of the sample data transfer template

Variable	Note / Permissible values	Mandatory/Optional
Shipment number	Shipment number of the courier or another unique number (same number as on the sample transfer protocol)	Mandatory
Name of the study	In national language	Mandatory
Name of the study	In English	Optional
Owner of the study	In national language	Mandatory
Country of the institution	In English	Mandatory
Partner acronym	in HBM4EU, and for LTPs who is the beneficiary	Mandatory
Contact person: name	First name, Family name	Mandatory
Contact person: e-mail address		Mandatory
Sample identification number	unique identifier	Mandatory
Label type	**HW** (handwritten) **1D** (one-dimensional barcode) **2D** (two-dimensional barcode) **QR** (Quick Response code) **RN** (Registration number) **O:** (Other: _____)	Mandatory
Sampling year	YYYY	Mandatory
Sampling month	MM	Mandatory
Sample type	**WB** (Whole Blood) **PL** (Plasma) **SE** (Serum) **UCB** (Umbilical Cord Blood) **U24** (Urine (24 h)) **USR** (Urine spot sample – random) **USF** (Urine spot sample – first morning) **O:** (Other: _____)	Mandatory
Type of sample container	primary receptacle: manufacturer and order/catalogue number separated with a semicolon	Mandatory
Container volume	in mL	Mandatory
Sample volume	in mL	Mandatory
Supplement	**NS** (No supplement) **EDTA** (EthyleneDiamineTetraacetic Acid) **NAH** (Sodium-Heparin) **LIH** (Lithium-Heparin) **CIT** (Citrate) **FHG** (Fluoride-Heparin/Glucose) **FEG** (Fluoride-EDTA/Glucose) **CPDA1** (Citrate Phosphate Dextrose-Adenine 1) **CITF** (Citrate-Fluoride) **CTAD** (Citrate, Theophylline, Adenosine and Dipyridamole) **NH4H** (NH4-Heparin) **HA** (Hydrochloric acid) **BA** (Boric acid) **O:** (Other: _____)	Mandatory
Cleaning of new tubes	**NC** (Not cleaned)	Mandatory

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	RW (Rinsed with de-ionized water) **RM** (Rinsed with methanol) **RN** (Rinsed with nitric acid) **Rall** (Rinsed with nitric acid + methanol + de-ionized water) **O:** (Other: _____)	
Biological safety level	**BSL-1** (Biosafety Level 1)* **BSL-2** (Biosafety Level 2) **O:** (Other: _____)	Mandatory
Storage temperature before shipping	**EF20** (Electrical Freezer -20°C) **EF80** (Electrical Freezer -80°C) **LIN** (< -130°C) **O:** (Other: _____)	Mandatory
Shipping category	**A** (Packaging instruction PI620) **B** (Packaging instruction PI650)	Mandatory
Shipping temperature	**CP** (Cool packs -20°C) **DI** (Dry Ice) **LIN** (< -130°C) **O:** (Other: _____)	Mandatory
Information on sample history available	**y** (yes) **n** (no)	Mandatory
Prior informed consent (PIC) available	**y** (yes) **n** (no)	Mandatory
Material transfer agreement (MTA) available	**y** (yes) **n** (no)	Mandatory
Data protection form available	**y** (yes) **n** (no)	Mandatory
Ethical approval available	**y** (yes) **n** (no)	Mandatory
Availability of sample linked data	**y** (yes) **n** (no)	Mandatory

* According to *EU-Directive 2000/54/EC*

Material (Sample) associated data transfer between HBM4EU consortium members has to be in line with the General Data Protection Regulation (GDPR) that is in force since May 2018. Note that even pseudonymised data like a unique identifier is personal data as long as code or encryption key is left as defined in the GDPR, Article 4(1). Hence, transfer of sample associated data (including the unique identifier) is only granted when it corresponds with the prior informed consent information to which the material donor has given his consent.

Sample associated data transfer has to be in line with the HBM4EU data management policy (c.f. Deliverable 10.1: Data management plan; https://www.hbm4eu.eu/deliverables/) and hence has to follow the terms and conditions defined in the data controller – data processor agreement included in the HBM4EU Material and associated Data Transfer Agreement. Sample provider (data controller) and recipient (Data processor) have to document the sample and associated data exchange by signing the HBM4EU Material and associated Data Transfer Record Form (see chapter 6.2) that is used to specify the terms and conditions for a material associated data exchange and to provide instructions for the processing of pseudonymised data by the data processor (for details see 6.2).

Before shipment, the provider has to complete the corresponding sample data transfer template file "HBM4EU_WP7.4_Sample_Data_Transfer_Template_V1.2" (Annex 5 to D7.2) with the required information. The filled in data transfer template has to be sent to the receiver as encrypted e-mail. The subject line should

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start with “HBM4EU: Sample data transfer” and should furthermore contain the shipment number and the current date in the format “YYYY-MM-DD”.

Example:

HBM4EU: Sample data transfer_123456789012_2017-10-10

In order to document the sample exchange by an independent party, HBM4EU should be informed by copying the respective e-mail address “hbm4eu@uba.de” in Cc.

The electronic exchange of sample associated data between provider and recipient shall only be granted when the following good practices are followed:

- Do not allow to process/access data on mobile devices
- Require strong authentication, such as 2-factor authentication
- Information at rest must be encrypted using state of the art encryption algorithms
- Request adequate protection against malware
- Request logging of read & write access
- Only use a pre-approved set of applications under specific conditions as to guarantee confidentiality and integrity for transfer of information.

Hence, the filled in HBM4EU Sample Data Transfer Template file has to be encoded. Encoding must be cryptographic and state of the art (e.g., GNU privacy guard using WinPT). The tool that is used for data encoding and decoding must be documented in the HBM4EU Material and associated Data Transfer Record Form signed by both parties. The subject line of the electronic exchange should start with “HBM4EU: Sample data transfer” and should furthermore contain the shipment number and the current date in the format “YYYY-MM-DD”.

The following table provides an example of how to complete the sample data transfer template**. Please provide the requested information for each single tube.** To present all of the contained information in a legible manner, the table is divided into four parts.

Table 12-2: Example of a completed sample data transfer template

Shipment number	Name of the study (national language)	Name of the study (english)	Owner of the study	Country of the institution	Partner acronym	Contact person: name	Contact person: e-mail-address	…
123456789012	Umweltprobenbank des Bundes	Environmental Specimen Bank	Umweltbundesamt	Germany	UBA	Marike Kolossa-Gehring	marike.kolossa@uba.de	
123456789012	Umweltprobenbank des Bundes	Environmental Specimen Bank	Umweltbundesamt	Germany	UBA	Marike Kolossa-Gehring	marike.kolossa@uba.de	
123456789012	Umweltprobenbank des Bundes	Environmental Specimen Bank	Umweltbundesamt	Germany	UBA	Marike Kolossa-Gehring	marike.kolossa@uba.de	

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123456789012	Umweltproben-bank des Bundes	Environmen-tal Specimen Bank	Umweltbundes-amt	Germany	UBA	Marike Kolossa-Gehring	marike.ko-lossa@uba.de	

…	Sample identification number	Label type	Sampling year	Sampling month	Sample type	Type of sample container	Container volume	Sample volume	…
	8031/1/01-2011/80101/0/110-2	1D	2011	1	U24	Sarstedt; 60.541.500	13 mL	10 mL	
	A031/1/01-2017/80001/0/120-2	1D	2017	1	U24	Sarstedt; 60.541.501	13 mL	10 mL	
	8031/1/01-2011/80101/0/63-1	1D	2011	1	U24	Sarstedt; 60.541.502	13 mL	10 mL	
	8031/1/01-2014/80101/0/55-2	1D	2014	1	U24	Sarstedt; 60.541.503	13 mL	10 mL	

	Supplement	Cleaning of new tubes	Biological safety level	Storage temperature before shipping	Shipping category	Shipping temperature	…
	NS	Rall	BSL-2	LIN	B	DI	
	NS	Rall	BSL-2	LIN	B	DI	
	NS	Rall	BSL-2	LIN	B	DI	
	NS	Rall	BSL-2	O: -10°C	B	DI	

…	Information on sample history available	Prior informed consent (PIC) available	Material transfer agreement (MTA) available	Data protection form available	Ethical approval available	Availability of sample linked data
	Y	y	y	y	y	y
	Y	y	y	y	y	y
	Y	y	y	y	y	y
	Y	y	y	y	y	y

13 Receipt of Samples

The receiver of the samples should conduct a reception control to ensure that the requirements on a sample exchange and the quality criteria defined in this SOP are met.

To document this reception control, the receiver should complete the specific “HBM4EU_WP7.4_Sample_Transfer_Protocol_V1.0” for the corresponding shipment.

Table 13-1 summarizes the aspects, which should be checked and completed:

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Table 13-1: Details of reception control

Details of reception control	Format/required information
Date of receipt	YYYY-MM-DD
Time of receipt	HH:MM h
Person in charge	Please provide first and last name
Packaging in sound condition?	Please indicate “yes” or “no”
If no: Please specify!	Please describe the conditions of the packaging and provide pictures if possible.
Shipping temperature maintained during transport?	Please check temperature data logger in the parcel or, if no data logger is included, measure the temperature directly on the sample container immediately after you open the packaging. If the temperature is in line with the shipping temperature as documented by the provider in the sample transfer protocol, please indicate with yes.
If no: Please specify!	Please provide the measured temperature in “°C” or a printout of the temperature curve recorded by the temperature data logger.

Subsequently, the completed sample transfer protocol “HBM4EU_WP7.4_Sample_Transfer_Protocol_V1.0” should be sent to the provider via e-mail as confirmation of a successful sample transfer. The subject line should start with “HBM4EU: Sample transfer completed” and should furthermore contain the shipment number and the current date in the format “YYYY-MM-DD”.

Example:
HBM4EU: Sample transfer completed_123456789012_2017-10-14

In order to document the sample exchange by an independent party, HBM4EU should be informed by copying the respective e-mail address “hbm4eu@uba.de” in Cc.

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14 Appendix A: Example of a pro-forma Invoice

Pro-Forma Invoice

Sent by/Provider		**Sent to/Receiver**	
TAX ID/VAT no.	DE129515865	TAX ID/VAT no.	SE202100297301
Contact name	Dr. Dominik Lermen	Contact name	Dr. Marika Berglund
Company name	Fraunhofer IBMT	Company name	Karolinska Institute
Street Address	Josef-von-Fraunhofer-Weg 1	Street Address	Nobels väg 13
City, Zip Code	Sulzbach, 66280	City, Zip Code	Stockholm, 171 77
Country	Germany	Country	Sweden
Phone	+49 6897 9071 251	Phone	+46 8 524 875 36
Fax	+49 6897 9071 490	Fax	+46 8 33 69 81
Email	dominik.lermen@ibmt.fraunhofer.de	Email	marika.berglund@ki.se
Invoice Number	HBM4EU/IBMT2017-001		
Terms of Delivery			
Reason for Export	**Research Purposes- Sample exchange between partners of the HBM4EU research initiative** (www.hbm4eu.eu)		

ID	**Detailed Description of Goods**	**Quantity**	**Country of Origin**	**Value and Currency**
1	Biological Substance Category B (UN3373) in accordance with PI650, human urine samples for research purposes. Dry Ice (UN 1845) used as a refrigerant in accordance with PI 954	300 x 2 ml	Germany	10,00 € *(For research samples a clearly defined value does not exist. Do not exceed 50,- €)*

Responsible Person	Name	Dr. Dominik Lermen
	Telephone number	+49 6897 9071 251
	Email	Dominik.lermen@ibmt.fraunhofer.de

I declare that the above information is true and correct to the best of my knowledge.

Date:	Name:	Signature:
Company Stamp		

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15 Appendix B: Information on selected couriers

		FedEX	TNT	UPS	World Courier
		http://www.fedex.com/	https://www.tnt.com	https://www.ups.com	http://www.worldcou-rier.com/
Temperature monitoring		On demand	yes	yes	yes
Temperature	2 °C - 8 °C	yes	yes	yes	yes
	-20 °C	yes	yes	yes	yes
	-80 °C	yes	yes	no	yes
	<-130 °C	no	yes	no	yes
Dry ice supply at customs		yes (external company)	yes	no	yes
International phone numbers					
Austria		(0043) 800 123 800	(0043) 5 77 00 77	(0043) 1 599 14 20 30	(0043) 5244 200 20
Belgien		(0032) 27527575	(0032) 70 233 633	(0032) 78 250 877	(0032) 2 712 50 60
Croatia		(00385)1 6057 440	(00385) 88 393 9390	(00385) 1 3454555	(00385) 1 637 05 20
Czech Republic		(00420) 233053200	(00420) 848 000 868	(00420) 841 11 11 44	(00420) 2 3311 3611
Denmark		(0045) 70 233 332	(0045) 7010 1180	(0045) 35 25 80 80	(0045) 32 46 06 80
Finland		(00358) 10 800 515	(00358) 300 188 800	(00358) 9 2311 3406	(00358) 9 8700 3300
France		(0033) 825 886 887	(0033) 825 033 033	(0033) 821 233 877	(0033) 1 48 63 48 63
Germany		(0049) 1806 111 800	(0049) 1806 900 800	(0049) 1806 882 663	(0049) 30 2431420
Greece		(0030) 210 6686600	(0030) 210 89 05 868	(0030)210 99 84 000	(0030) 210 675 6517
Hungary		(0036) 640 980 980	(0036) 640 31 31 31	(0036) 1 877 0000	(0036) 1 431 0550
Iceland		(00354) 4120 120	(00354) 580 1010	(00354) 4200900	(0045) 32460680
Ireland		(00353) 1800 535 800	(00353) 818 400 600	(00353) 1 890 99 55 00	(00353) 1 862 4001
Israel		(00972) 772206850	(00972) 8688070071	(00972) 1700 700877	(00972) 3 688 8811
Italy		(0039) 199151119	(0039) 199803868	(0039) 2 30 30 30 39	(0039) 02 3800 3900
Latvia		(00371) 80005300	(00371) 67668000	(00371) 67 805650	(00358) 9 8700 3300
Lithuania		(00370) 8 800 20200	(00370) 616 35937	(00370) 37 350505	(00358) 9 8700 3300
Luxembourg		(00352) 8002 35 55	(00352) 352 395 220	(00352) 8002 2510	(0032) 2 712 50 60
Netherlands		(0031) 800 0222 333	(0031) (0)800 1234	(0031) (0)900 2255 877	(0031) 20 653 4141
Norway		(0047) 63 94 03 00	(0047) 810 00 810	(0047) 800 33 470	(0047) 6394 6200
Poland		(0048) 801 002 800	(0048) 801 31 00 00	(0048) 22 489 48 77	(0048) 22 575 36 00
Portugal		(00351) 707 244 144	(00351) 707 100 868	(00351) 707 23 23 23	(00351) 218 411 120
Slovakia		(00421) 850111911	(00421) 800 100 868	(00421) 2 16877	(00421) 2 4341 5477
Slovenia		(00386) 80 21 91	(00368) 1 58 78 333	(00386) 4 281 1200	(00386) 4 27 91 93 1
Spain		(0034) 915209060	(0034) 902 111 868	(0034) 902 88 88 20	(0034) 917 461 010
Sweden		(0046) 200 252 252	(0046) 20 960 960	(0046) 8 627 42 00	(0046) 8 594 414 80
Switzerland		(0041) 848 1 33339	(0041) 800 55 55 55	(0041) 44 200 41 00	(0041) 61 486 85 00
United Kingdom		(0044) (0)3456 00 00 68	(0044) (0)800 100 600	(0044) (0)3457 877 877	(0044) (0)800 289 839

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16 Version History

Version	Valid since	Changes compared to the previous version
3.0	April 2019	Chapter 12: Adaptation of the text due to an update of Annex 5 to D7.2: HBM4EU_WP7.4_Sample_Data_Transfer_Template_V2.0
2.0	October 2018	Chapter 6.2: The Material and associated Data transfer Agreement is added; Chapter 12.2: Data transfer is adapted to the regulations described in the HBM4EU Data Policy; Chapter 17: Annex 6 to D7.2: HBM4EU_WP7.4_Material_and_associated_Data Transfer Agree-ment_V1.0
1.0	October 2017	First version

17 Further Applicable Documents

This SOP is annex 1 to the deliverable D7.2. The below listed further applicable documents are hence further annexes to D7.2 and can be found on the HBM4EU homepage (https://www.hbm4eu.eu/deliverables/) or in the HBM4EU document library (https://www.hbm4eu.eu/online-library/?mdocs-cat=mdocs-cat-20&mdocs-att=null).

Annex 2: HBM4EU_WP7.4_Shipping_Flowchart_V1.0

Annex 3: HBM4EU_WP7.4_Pro-Forma_Invoice_V1.0

Annex 4: HBM4EU_WP7.4_Sample_Transfer_Protocol_V1.0

Annex 5: HBM4EU_WP7.4_Sample_Data_Transfer_Template_V.2.0

Annex 6: HBM4EU_WP7.4_Material_and_associated_Data_Transfer_Agreement_V1.0

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