



TransBioLine

Translational Safety Biomarker Pipeline

821283 – TransBioLine

Translational Safety Biomarker Pipeline

WP7 – Assay and Sample Management

D7.02 SOP for sample collection, processing, storage, and shipment

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Document History

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V1.0	20.05.2019	First Draft
V2.0	05.11.2019	Second Draft
V3.0	31.12.2019	Comments
V4.0	06.01.2020	Draft
V5.0	22.01.2020	Final Version

Definitions

Participants of the TransBioLine Consortium are referred to herein according to the following codes:

UZH. University of Zurich. Switzerland

UMA-IBIMA. Universidad de Málaga, Spain

ITTM. Information Technology for Translational Medicine, Luxembourg

Landspitali. Landspitali University Hospital. Iceland

KUM. Klinikum der Universität München. Germany

UNOTT. The University of Nottingham. United Kingdom

USAL. Universidad de Salamanca. Spain

IR-HSCSP-ICCC. Fundació Privada Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau. Spain

TAM. TAmirNA GmbH. Austria

SIGNATOPE. SIGNATOPE GmbH. Germany

ABX-CRO. ABX-CRO Advanced Pharmaceutical Services Forschungsgesellschaft mbH. Germany

MetaHeps. MetaHeps GmbH. Germany

APHP. Assistance Publique - Hopitaux de Paris. France

SYNAPSE. Synapse Research Management Partners S.L. Spain

Charité. Charité - Universitätsmedizin Berlin. Germany

UNEW. University of Newcastle Upon Tyne. United Kingdom

ULIV. The University of Liverpool. United Kingdom

MLM. MLM Medical Labs GmbH. Germany

UL. University of Leiden. Netherlands

SAS. Servicio Andaluz de Salud. Spain

PFIZER. LTD PFIZER UK

MSD. Merck Sharp & Dohme Corp. USA & France

LLY. Eli Lilly. USA & UK

NOVARTIS. NOVARTIS Pharma AG. Switzerland

ROCHE. F. Hoffmann-La Roche Ltd. Switzerland

Janssen. JANSSEN Pharmaceutica NV. Belgium; U.S.A.

SARD. SANOFI-AVENTIS RECHERCHE & DEVELOPPEMENT. France

Grant Agreement. The agreement signed between the beneficiaries and the IMI JU for the undertaking of the TransBioLine project (No 821283).

Project. The sum of all activities carried out in the framework of the Grant Agreement.

Consortium. The TransBioLine Consortium, comprising the above-mentioned legal entities.

Consortium Agreement. Agreement concluded amongst TransBioLine participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

Publishable Summary

The Translational Safety Biomarker Pipeline (TransBioLine) is an international project with 27 partners in 10 countries. The Central Biomaterial Bank Charité (ZeBanC) is responsible for the biobanking including coordination of sample-related processes, the provision of sample kits, storage and distribution of samples to the analysis laboratories. In addition, ZeBanC contributes significantly to the harmonization of data management and data flow.

Projects of this dimension suffer from a considerable heterogeneity of partners and contributors. As every recruitment site and analysis partner has their own standard procedures and workflows it is very important to harmonize and standardize the fundamental processes.

The first major deliverable for work package 7 is to harmonize standard operating procedures (SOPs) for sample collection, processing, shipment, aliquoting and shipment. This harmonization should lead to samples and related data of high quality and comparability.

1. Introduction

The aim of this project deliverable is to harmonize standard operating procedures (SOPs) for sampling, processing, interim storage and shipment. This step is of high importance due to the heterogeneity of the 27 project partners located in 10 different countries and to the variety of biomarkers to be analysed. Differences in the pre-analytical procedures can affect sample quality and might thus cause analytical data reflecting the source of the samples rather than biological variations. The standardization of the mentioned processes is intended to guarantee the consistent sample and data quality for biomarker analysis.

2. Methods

2.1 Retrieval of information

2.1.1 Request of information for analyses

In order to assess the requirements of the different TBL collections, a survey for collection of process and sample details was initiated. All information on the collection strategy (sample type, number) and sample handling such as centrifugation parameters etc. were compiled. In this context, questions were also asked about the biomarkers to be analyzed. For a better understanding, the biomarker companies were also involved in order to include their requirements (sample quantities and quality parameters, if applicable) into the survey.

2.1.2 Information study protocols/SOPs

Organ-related work packages (WP1 to WP 5) and EFPIA partners were asked to contribute with their own protocols/SOPs.

2.2. Harmonization of SOPs

2.2.1 SOP for sample collection and processing

The ZeBanC elaborated common procedures and adapted similar workflows where possible. However, minor differences due to local settings and standards will not be avoidable.

After retrieving all information the ZeBanC created a harmonized protocol focusing primarily on the requirements of the partners for biomarker analyses to cover optimal sample conditions. The local staff will be trained according to this protocol in order to allow compliance to the agreed protocol.

3. Results

3.1 SOP for sampling, processing and intermediate storage

The finalised document KP-08_04.29a SD TransBioLine Processing Manual version 1 was uploaded to the TransBioLine SharePoint for availability of all TBL partners. Additionally, the document was send on request to the staff member without direct access to SharePoint. To facilitate implementation especially in daily practice, the ZeBanC produced movies with detailed explanation of all the important processes such as sampling, processing of samples and shipment and uploaded the movies to SharePoint. If desired, the ZeBanC will organise a video conference training the staff. This way, the staff members can follow a specific workflow to retrieve all required information.

Deviations from the protocol such as different centrifugation conditions, varying temperatures have to be documented in the eCRF and/or on the sample data sheet.

To allow easier identification of the different sample types at the recruitment sites, a color-coding system for the tubes is used. Different colours of the tube lid for different types of materials facilitate easier and safe aliquoting (e.g. orange for serum, green for EDTA-plasma, blue for the 2x centrifuged plasma (defined as liquid biopsy) and yellow for urine). The volume and number of aliquots to be collected need to be confirmed by each work package. For serum and urine measured at MLM 5 ml barcoded tubes are used which will be labelled accordingly.

Each sample kit that is provided is accompanied with sample data sheets. This document carries the respective barcodes and sample IDs and the general sample information should be collected e.g. TBL patient ID (provided by eCRF or ABX-CRO), date and time of sampling etc. This data sheet should assist in collecting the necessary data, which then can be entered into the respective eCRF.

3.2. SOP for storage

The ZeBanC already has standard procedures for sample storage. All samples from TransBioLine (TBL) will be stored at -80°C and documented in our laboratory information and management system (LIMS, here CentraXX). 2D barcoded tubes (containing 2D barcode, 1D barcode and human readable number) will be used for easier and unique identification. Samples will be stored in defined spaces, are tracked and easily detectable from freezer to rack and single tube. A standard procedure for the removal/destruction of samples and data in case of consent withdrawal has still to be defined. For this, all the informed consents from the organ work packages have to be available and the responsibilities and contacts have to be defined.

3.2.3 SOP for shipment

After sample collection, each organ work package and/or location, which is not using the eCRF has to send a data export to ABX-CRO. There the data will be checked and a TBL-patient-ID will be allocated to each patient. This ID is very important for patient

and sample identification within the TransBioLine project. For work packages using the eCRF, the patient ID will be generated automatically.

Prior to each sample shipment to the biobank, each partner has to upload the data of the samples to their specific ownCloud folder (contact ITTM) and inform the biobank and ABX-CRO. ABX-CRO will cleanse the data and clear for usage. The biobank will check the data and confirm shipment. Only after this confirmation, the samples can be transferred to the biobank.

The SOP for shipment is included into the document KP-08_04.29a SD TransBioLine Processing Manual version 1. Additionally, a video on packaging for shipment was uploaded to SharePoint. It describes the general handling and packaging of biological samples, which are assigned to UN3373 regulations. As every site is using their own transport service small deviations may apply.

4. Discussion

(Include if relevant deviations from DoA and contingency plans)

Biobanking in a heterogeneous research consortium requires harmonization in order to generate reliable and reproducible data. Different data structures, different local infrastructures, different qualification of staff members and diverse procedures must be brought to a comparable level.

The harmonization of SOPs depends not only on the different organ-specific work packages and their recruitment sites, but also on the respective partner for biomarker analyses. The harmonized SOP is based on a compilation of the various study protocols and the requirements of the partners for biomarker analyses. Deviations from these protocols have to be documented. Minor changes such as the use of different tubes due to their own vendors were tested and implemented.

5. Conclusion

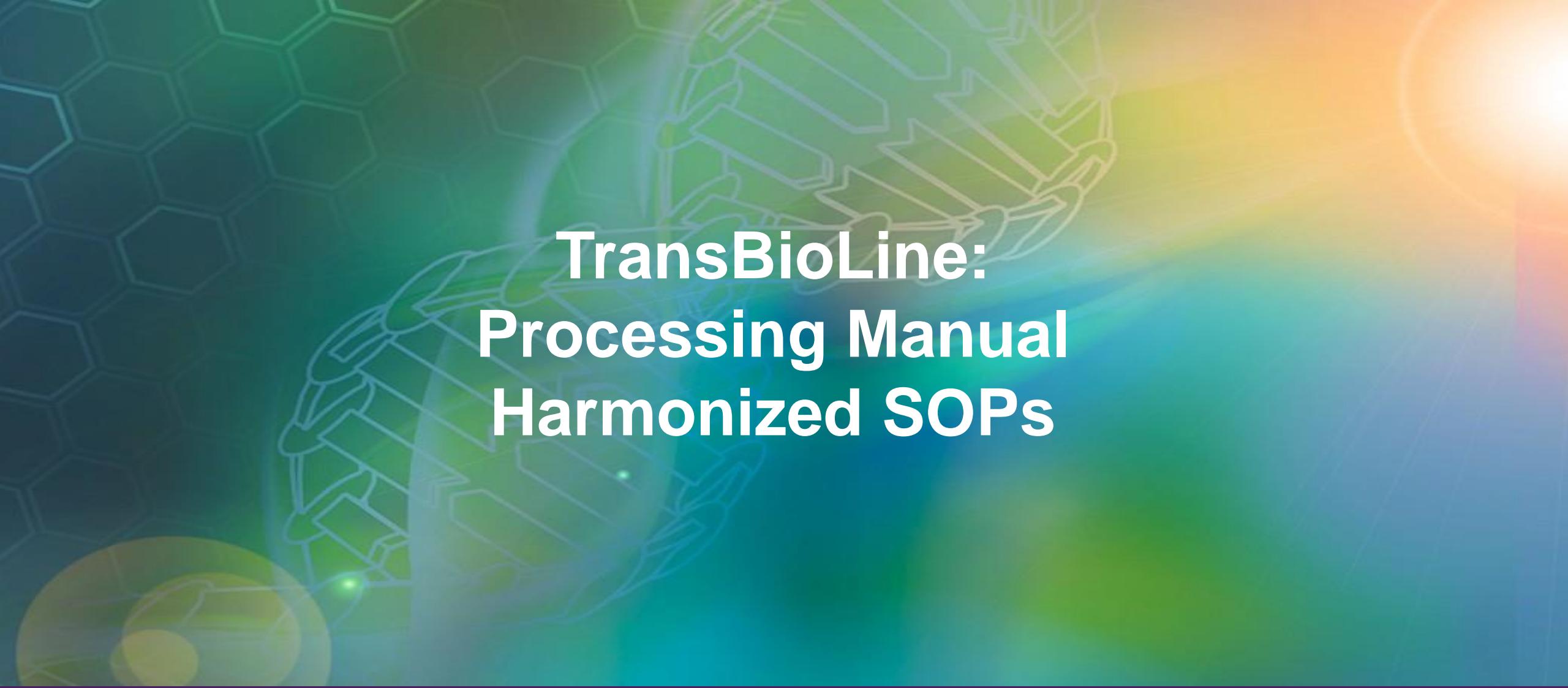
The respective documents and videos for sample collection, processing, storage and shipment have been created and accessible for everyone within the TransBioLine consortium. If desired, the ZeBanC will organise a video conference training the staff. Whenever questions occur, the ZeBanC staff is happy to support.

Annexes

Annex 1

KP-08_04.29a SD Transbioline Processing Manual

KP-08_04.30 VA TBL-Prozesse intern



TransBioLine: Processing Manual Harmonized SOPs

Contents

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- (7) Sample data sheet – general information
- (8) Sample data sheet – patient information
- (9) Sample data sheet – sample information
- (10) Sample data sheet - barcodes
- (11) Sample processing
- (12) Serum (SR)
- (13) EDTA-plasma (EP)
- (14) Liquid biopsy (LB)
- (15) EDTA-Plasma/Liquid biopsy
- (16) Urine (UR)
- (17) Shipping
- (18) Packing UN3373
- (19) Contact/ Shipping address

Request of sample kits

3

Order form TransBioLine sample kits

Please fill in the form and send via email to zebanc-labor@charite.de

Please send us the following sample kits:

1)

Work package	<input type="checkbox"/> WP1 – DIKI	<input type="checkbox"/> WP3 – DIP1	<input type="checkbox"/> Healthy volunteers (HV)
	<input type="checkbox"/> WP2 – DILI	<input type="checkbox"/> WP4 – DVI	
Location	<input type="checkbox"/> CDG	<input type="checkbox"/> MUC	<input type="checkbox"/> SLM
	<input type="checkbox"/> TXL	<input type="checkbox"/> KEF	<input type="checkbox"/> LID
	<input type="checkbox"/> EFP	<input type="checkbox"/> LPL	<input type="checkbox"/> NCL
	<input type="checkbox"/> PST	<input type="checkbox"/> NQT	<input type="checkbox"/> ZRH
	<input type="checkbox"/> BCN	<input type="checkbox"/> AGP	<input type="checkbox"/>

2)

Number of kits
(patients)

3)

Contact person for further enquiry: _____
Telephone number/ e-mail: _____
Date of order : _____
Signature: _____
.....

Delivery sent (via courier service)

5)

Date : _____
ZeBanC signature: _____
.....

Receipt (please e-mail document to zebanc-labor@charite.de)
Date of receipt sample kits: _____
Signature : _____
Note : _____

Please request sample kits via the provided order form and send to zebanc-labor@charite.de

- 1) **Work package** - please, tick respective workpackage
- 2) **Location** - please, tick location code, list will be provided
- 3) **Number of kits** – number of racks and sets (patients) in brackets (will differ between work packages)
- 4) **Contact** – please, fill in contact details in case of questions
- 5) **Receipt** – The request sheet will be enclosed in the package. Please fill in date of sample reception.

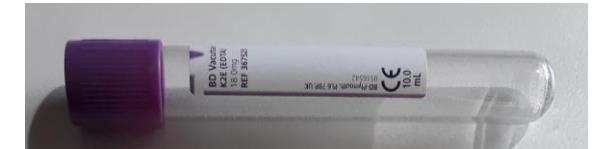
Note: Please order at least 1 week in advance!

Sample collection containers

- Master samples

Plasma

- BD Vacutainer™ Hemogard Closure Plastic K2-Edta Tube, 10 ml (Brand: BD 367525)
- VACUETTE® TUBE 6 ml K3E K3EDTA 13x100 lavender cap-black ring, PREMIUM (Brand: Greiner 456036)



Serum

- BD Vacutainer® Plastic Serum Tube with Red BD Hemogard™ Closure, 10ml (Brand: BD 367896)
- VACUETTE® TUBE 9 ml CAT Serum Separator Clot Activator, gold cap-gold ring (Brand: Greiner 455034)



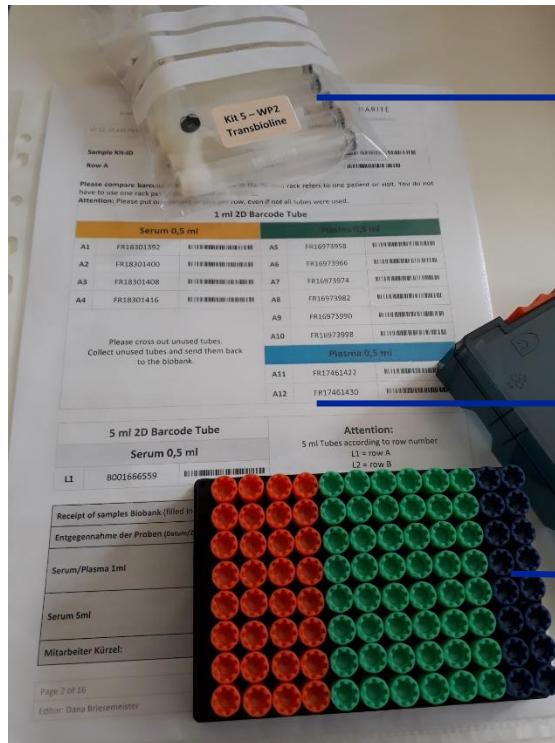
Urine

- BD Vacutainer™ Plastic Urinalysis Tubes (Brand: BD 364915)



If other, please specify on data sheet

Sample kits - I



Bag with 5 ml barcoded tubes (MLM)

Box for 5 ml barcoded tubes

Sample data sheet

Rack with 0.8 ml barcoded tubes



- One sample kit usually contains tubes for several samplings (several sets)

Example WP2

- 1 Rack 0.8 ml barcoded tubes (8 patients, one patient per row)
- 1 bag with 5 ml barcoded tubes (8, one per patient)
- Several empty racks (0.8 ml) and boxes (5ml) for storage in freezer

Sample kits - II

6

- The ZeBanC will provide sample kits with 2D barcoded tubes and sample data sheets for each WP. The number of tubes will differ, but the layout will be the same:

- Serum**

0.8 ml tubes



5 ml tubes



- EDTA-Plasma**
(1x centrifuged)

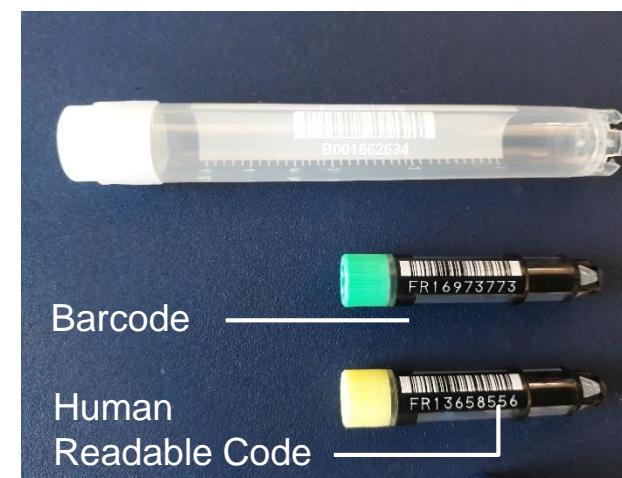
- Liquid Biopsy**
(2x centrifuged, cell free plasma)

- Urine**



Infobox Barcodes

5 ml



0.8 ml

Sample data sheet – general information

1)

Sample Kit-ID	<<<(1)>>>	<<<(d1)>>>	
Rack ID	<<<(r1)>>>	<<<(s1)>>>	
TBL Patient ID*	_____		
Pro Euro DILI ID	_____		
Site name**	<input type="checkbox"/> NQT <input type="checkbox"/> AGP <input type="checkbox"/> BRN <input type="checkbox"/> LIS <input type="checkbox"/>		
Patient population**	_____		
Visit	<input type="checkbox"/> V1 <input type="checkbox"/> V1b <input type="checkbox"/> V1c <input type="checkbox"/> V2 <input type="checkbox"/> V3 <input type="checkbox"/> V4 <input type="checkbox"/> V5		
Sample type	Serum [SR]	EDTA-Plasma [EP]	Liquid Biopsy [LB]
Sampling date	20 _ _ / _ _ / _ _		
Sampling time	_ _ : _ _	_ _ : _ _	_ _ : _ _
Master sample ID*	_____		
Volume master sample	____ ml	____ ml	____ ml
Start 1. Centrifugation	_ _ : _ _	_ _ : _ _	_ _ : _ _
Time of freezing	_ _ : _ _	_ _ : _ _	_ _ : _ _
Storage location 0.8 ml tubes	Rack ID: _____ / Freezer: _____		
Storage location 5.0 ml tubes	Rack ID: _____ / Freezer: _____		
Sampling by***	Processing by***		

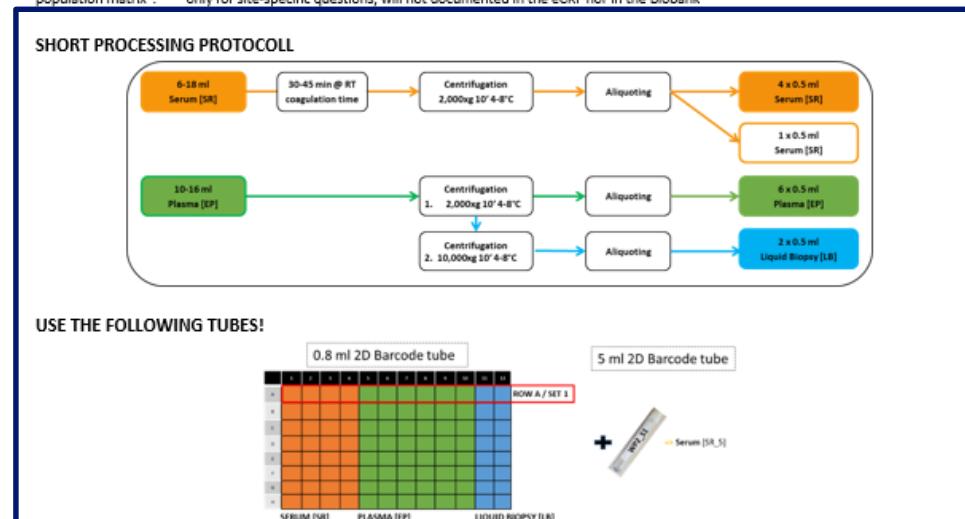
* Generated in the eCRF mask or will be provided by the Biobank, ** Code can be found in the document "WP2 recruitment site and patient population matrix", *** only for site-specific questions, will not documented in the eCRF nor in the Biobank

1) General information for Biobank

2) Processing

- a) Overview processing
- b) Aliquoting scheme

- Each sample kit will include tubes for several patients/visits (here one patient per row = row A comprises 4 orange, 6 green and 2 blue tubes, next row, row B =next patient)
- Please check, which row(s) you will need for your patient!



Sample data sheet – patient information

Please fill in the following information for each patient/visit:

1) TBL Patient ID*	_____		
2) Pro Euro DILI ID	_____		
3) Site name**	<input type="checkbox"/> NQT <input type="checkbox"/> AGP <input type="checkbox"/> BRN <input type="checkbox"/> LIS <input type="checkbox"/> _____		
4) Patient population**	_____ _____		
5) Visit	<input type="checkbox"/> V1 <input type="checkbox"/> V1b <input type="checkbox"/> V1c <input type="checkbox"/> V2 <input type="checkbox"/> V3 <input type="checkbox"/> V4 <input type="checkbox"/> V5		
Sample type	Serum [SR]	EDTA-Plasma [EP]	Liquid Biopsy [LB]
Sampling date	20 ____ / ____ / ____		
Sampling time	____ : ____	____ : ____	____ : ____
Master sample ID*	_____		
Volume master sample	____ ml	____ ml	____ ml
Start 1. Centrifugation	____ : ____	____ : ____	____ : ____
Time of freezing	____ : ____	____ : ____	____ : ____
Storage location 0.8 ml tubes	Rack ID: _____ / Freezer: _____		
Storage location 5.0 ml tubes	Rack ID: _____ / Freezer: _____		
Sampling by***	Processing by***		

* Generated in the eCRF mask or will be provided by the Biobank, ** Code can be found in the document " WP2 recruitment site and patient population matrix". *** only for site-specific questions, will not documented in the eCRF nor in the Biobank

- 1) **TBL (Transbioline) Patient ID** – will be created by eCRF or if data transfer by ABX-CRO
- 2) Study specific ID – only if applicable e.g. DILI
- 3) **Site name** - specific TBL site code, a list for each WP will be provided
- 4) **Patient population**- specific population code for each WP, a list for each WP will be provided
- 5) **Visit** – Visit number

Sample data sheet – sample information

Please fill in the following information for each patient/visit:

TBL Patient ID*	_____		
Pro Euro DILI ID	_____		
Site name**	<input type="checkbox"/> NQT <input type="checkbox"/> AGP <input type="checkbox"/> BRN <input type="checkbox"/> LIS <input type="checkbox"/> _____		
Patient population**	_____ _____ _____		
Visit	<input type="checkbox"/> V1 <input type="checkbox"/> V1b <input type="checkbox"/> V1c <input type="checkbox"/> V2 <input type="checkbox"/> V3 <input type="checkbox"/> V4 <input type="checkbox"/> V5		
Sample type	Serum [SR]	EDTA-Plasma [EP]	Liquid Biopsy [LB]
Sampling date	20 ____ / ____ / ____		
Sampling time	____ : ____	____ : ____	____ : ____
Master sample ID*	_____		
Volume master sample	____ ml	____ ml	____ ml
Start 1. Centrifugation	____ : ____	____ : ____	____ : ____
Time of freezing	____ : ____	____ : ____	____ : ____
Storage location 0.8 ml tubes	Rack ID: _____ / Freezer: _____		
Storage location 5.0 ml tubes	Rack ID: _____ / Freezer: _____		
Sampling by***	Processing by***		

* Generated in the eCRF mask or will be provided by the Biobank, ** Code can be found in the document " WP2 recruitment site and patient population matrix". *** only for site-specific questions, will not documented in the eCRF nor in the Biobank

- 6) **Sampling Date** – format yyyy/mm/dd
- 7) **Sampling time** – time point when sample was taken
- 8) **Master sample ID** – automatically generated by eCRF mask or provided by the Biobank
- 9) **Volume master sample** – volume in millilitre (ml) in original sampling device before centrifugation
- 10) **Start 1. Centrifugation** – time point 1st centrifugation (important for data about sample quality)
- 11) **Time of Freezing** – time point of freezing at -80°C
- 12) **Storage location** – temporary freezer location of rack at recruitment site
- 13) **Sampling by/ Processing by** – name of person, who sampled the biospecimens and name of person who performed centrifugation, aliquoting

Sample data sheet - barcodes

10

96 well ROW A / SET 1 0.8 ml 2D Barcode Tube			Single Tube No. WP2_S1 5 ml 2D Barcode Tube		
Serum [SR] 0.5 ml			Serum [SR] 0.5 ml		
SR_1	FR18305527		SR_5	B001666455	
SR_2	FR18305549				
SR_3	FR18305534				
SR_4	FR18305542				
Plasma [EP] 0.5 ml					
EP_1	FR16971733				
EP_2	FR16971729				
EP_3	FR16971731				
EP_4	FR16971728				
EP_5	FR16971792				
EP_6	FR16971706				
Liquid Biopsie [LB] 0.5 ml					
LB_1	FR22461488				
LB_2	FR18305528				

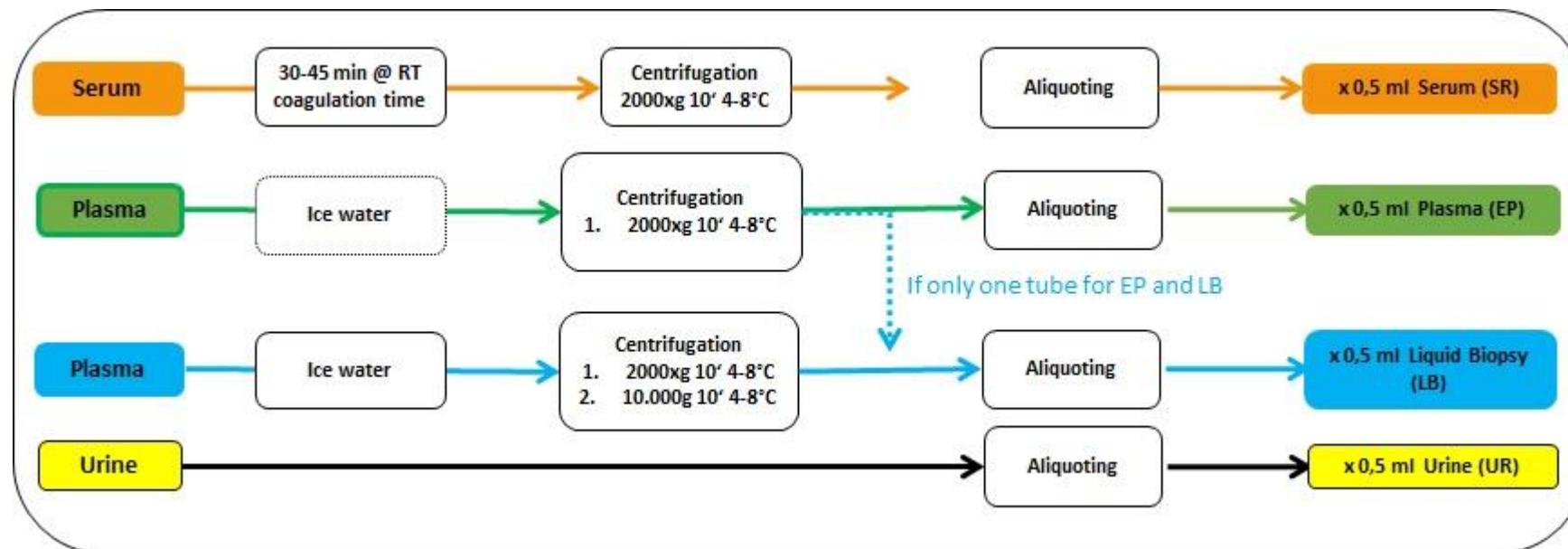
Please cross out unused tubes.
Collect unused tubes and send them back to the biobank.

- Overview about individual tubes with human readable number and barcode
- Please cross out all the tubes you don't use, collect them and send them back to biobank.
- Usage of 5 ml tubes depend on WP, but are labeled according to sample data sheet (here SR_5)
- Always compare numbers with barcodes on tubes!

Sample processing

11

- Invert tubes according to manufacturer's instruction



Serum (SR)

12

- (1) Collect blood for serum
- (2) Invert tube **4-6 times**
- (3) Allow to coagulate for 30-60 min at room temperature
- (4) Centrifuge (within 2 hours) at **2000xg, 10 min, 4-8 °C (or RT)**
- (5) Carefully aliquot 0.5 ml supernatant (serum) into each 2D barcoded tube (**0.8ml orange cap, 5ml white cap**)
- (6) Freeze immediately and store at -80°C



supernatant (serum)

clot



- (1) Collect whole blood in EDTA-tubes
- (2) Invert tube 8-10 times
- (3) Store on wet ice in upright position
- (4) Centrifuge (within 2 hours) at **2.000xg, 10 min, 4-8 °C**
 - a) Aliquot 0.5 ml into 2D barcoded tubes (**EP, 0.8ml green cap**)
- (5) Freeze immediately and store at -80°C



- (1) Collect whole blood in EDTA-tubes
- (2) Invert tube 8-10 times
- (3) Store on wet ice in upright position
- (4) Centrifuge (within 2 hours) at **2.000xg, 10 min, 4-8 °C**
- (5) Carefully collect supernatant without disturbing the cell pellet and transfer to **new tube**
- (6) Centrifuge **new tube** at **10.000xg, 10 min, 4-8 °C**
 - a) Aliquot 0.5 ml into 2D barcoded tubes (**LB, 0.8 ml blue cap**)
- (7) Freeze immediately and store at -80°C



Only if using one master sample (collection tube) for EDTA-plasma and LB, you should continue here:

- (1) Collect whole blood in EDTA-tubes
 - (2) Invert tube 8-10 times
 - (3) Store on wet ice in upright position
 - (4) Centrifuge (within 2 hours) at **2.000xg, 10 min, 4-8 °C**
 - (5) Carefully collect **1.2 ml** of supernatant without disturbing the cell pellet and transfer to **new tube**
 - (6) Aliquot 0.5 ml into 2D barcoded tubes (**EP, 0.8 ml green cap**)
-
- (7) Centrifuge **new tube** at **10.000xg, 10 min, 4-8 °C**
 - a) Aliquot 0.5 ml into 2D barcoded tubes (**LB, 0.8 ml blue cap**)
 - (8) Freeze immediately and store at -80°C



- (1) Collect urine
- (2) Allow to cool down
- (3) Aliquot 0.5 ml into 2D barcoded tubes (**UR,0.8 ml yellow cap**)
- (4) Freeze immediately and store at -80°C



- The ZeBanC in Berlin has to be informed about the date of sample shipment in advance.
- The Biobank has to confirm its acceptance to receive a shipment of samples before the sample transfer.
- Samples have to be transferred frozen to the ZeBanC
- For transfer of frozen samples to the ZeBanC in Berlin make sure that the samples will be under dry ice all the time.
- For shipment use a carrier or shipping agent that guarantees delivery of samples in frozen status to the ZeBanC
- **Please note that delivery of samples to the ZeBanc should be from Monday to Thursday (9:00 to 16:00).**

Blood and its components have to be packed according to **UN3373** – biological substance category B

1. Wrap rack with aliquots (2D barcoded tubes) in fleece (A)
2. Put this into bag (B) and seal
3. Put racks on dry ice in styrofoam box (C)
4. Label box with address (always include name and phone number of sender and recipient) and UN 3373 sticker (D)
5. **Attention:** if air cargo, additional label for dry ice (E) and arrows (F) are needed

Usually, all provided by courier service!



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- Anton Behnke (IT), anton.behnke@charite.de, tel.: +49 (0)30 450 536170
- Laboratory: zebanc-labor@charite.de

Shipping address:

Charité - Universitätsmedizin Berlin,
Campus Virchow-Klinikum
Zentrale Biomaterialbank der Charité (ZeBanC)
Augustenburger Platz 1, intern: Südring 7
13353 Berlin

Germany

Contact: Dana Briesemeister +49 (0)30 450 636386

KP-08_04.30 VA TBL-Prozesse intern**1 Zweck**

Diese Verfahrensanweisung beschreibt die Prozesse und Verantwortlichkeiten der ZeBanC im Rahmen des Translational Safety Biomarker Pipeline Projektes (kurz TransBioLine). Die ZeBanC ist für die Herstellung der Probenkits, sowie für die Einlagerung, Dokumentation und den Weiterversand der Biomaterialien, welche im Rahmen des Projektes entnommen werden, verantwortlich.

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Geltungsbereich: ZeBanC, Transbioline	Campus: CVK	 Zentrale Biomaterialbank
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2 Definitionen

WP	Workpackage = Arbeitspaket
DIKI	Drug induced kidney injury (Medikamenten-induzierter Nierenschaden) WP1
DILI	Drug induced liver injury (Medikamenten-ind. Leberschaden) WP2
DIPI	Drug induced pancreatic injury (Medikamenten-ind. Pankreasschaden) WP3
DIVI	Drug induced vascular injury (Medikamenten-ind. vaskulärer Schaden) WP4
DINI	Drug induced CNS injury (Med.-ind. Schäden des Zentralnervensystems) WP5
HV	Healthy volunteer = gesunde Probanden
eCRF	Elektronischer Case Report Form (Prüfbogen für Studiendokumentation)

Weitere Definitionen und Abkürzungen bitte dem [AG-01_01.02 Abkürzungsverzeichnis](#) entnehmen.

3 Prozessverantwortung / Schnittstellen

3.1 Prozessverantwortung

ZeBanC

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IT Anton Behnke, Tel.: 450636170 E-Mail: Anton.behnke@charite.de

Technische Mitarbeiter: Tel.: 450 636353, E-Mail: zebanc-labor@charite.de

Transbioline

Siehe [Kontakt Projektpartner](#)

3.2 Schnittstellen

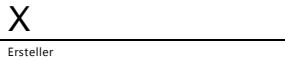
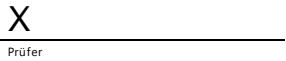
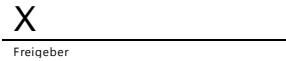
ITTM

ABX/CRO

4 Prozessbeschreibung

4.1 Allgemeine Informationen

TransBioLine ist ein fünfjähriges Programm zur Erzeugung explorativer und bestätigender Daten bei medikamenten-abhängigen Organverletzungen für fünf Zielorgansysteme (Niere, Leber, Bauchspeicheldrüse, Gefäß- und Zentralnervensystem) zur Anwendung in der Arzneimittelentwicklung. Das TransBioLine-Projekt ist ein Konsortium aus 27 Partnern aus Pharmaunternehmen, kleinen und mittleren Unternehmen und akademischen Einrichtungen aus 10 europäischen Ländern.

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An den verschiedenen Rekrutierungszentren werden Biomaterialien wie Serum, EDTA-Plasma, Urin und Liquor gesammelt, zwischengelagert und in Chargen auf Trockeneis an die ZeBanC versendet. Die Proben sammlungen der einzelnen Workpackages unterscheidet sich in Anzahl und Art der Proben. Daher müssen je nach Workpackage verschiedene Sample Kits zusammengestellt und versendet werden.

Nach Ankunft der Proben in der Biobank erfolgt die Dokumentation der Probendaten sowie die Einlagerung bei -80°C. Nach Anfrage der Leiter der Arbeitsgruppen bzw. der Analysepartner werden die Proben herausgesucht und an die Analysefirmen versendet.

4.2 Prozessübersicht

4.3 Prozessbeschreibung

Die Gewinnung der Biomaterialien erfolgt an den unterschiedlichen Rekrutierungszentren in ganz Europa. Pro Patient ist zu verschiedenen Zeitpunkten die Abnahme von Blut (Serum und EDTA-Blut) und die Sammlung von Urin vorgesehen.

Die Auswahl der Patienten, Aufklärung und Einholung der Einverständniserklärung erfolgt in den jeweiligen Zentren. Die Mitarbeiter vor Ort prozessieren die Proben je nach Vorgabe/Studienprotokoll ([KP-08_04.29a SD Transbioline Processing Manual](#)) und füllen den Probenbegleitschein aus bzw. dokumentieren die Daten und Barcodes im eCRF. Die Proben werden möglichst zeitnah prozessiert und bei -80°C zwischengelagert. In regelmäßigen Abständen oder nach Absprache werden die Proben nach Vorankündigung als Charge auf Trockeneis an die ZeBanC versandt.

Retrospektive Proben sammlungen

Die Proben für das WP5 (DINI) sind größtenteils schon gesammelt worden. Einige dieser Proben sind bereits in der Biobank in 2D Barcode Tubes gelagert (Projekt Neurologie/Liquor). Diese werden nach Benachrichtigung von WP5 an die Analysefirmen gesendet und unter Probenabgabe Transbioline ([LINK](#)) vermerkt.

Eine andere Sammlung von WP5 kommt aus Michigan, USA. Diese Proben werden zuerst an die Analysefirmen gesendet. Wenn nach der Messung Proben übrig bleiben werden diese zur ZeBanC gesendet. Diese Proben sind in Kryovials eingefroren und haben nur aufklebte Etiketten. Bitte vor Einlagerung die Koordination befragen.

Alle weiteren retrospektiv gesammelten Proben der WPs verbleiben bis zur Analyse beim jeweiligen Projektpartner.

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KP-08_04.30 VA TBL-Prozesse intern**4.3.1 Erstellung und Koordination der Probensets**

Die Mitarbeiter der ZeBanC erstellen für die jeweiligen WPs die Probensets aus Anfrage ([KP-08_04.30 FB Order form TransBioLine sample kits](#)). Ein Probenset besteht aus 1ml 2D Barcode Tubes der Firma FluidX/Brooks mit unterschiedlichen Deckelfarben (siehe unten). Außerdem werden 5ml 2D Barcode Tubes der Firma Ratiolab (Lagerraum 1.0008) für Serum und Urinproben verwendet, die an die Firma MLM gehen.

Probenbegleitscheine werden mit Hilfe des „Barcode Generator“ (Eigenentwicklung der ZeBanC) erstellt. Für jeden Patienten stellt die ZeBanC Probensets zur Verfügung. Die Anzahl und Zusammensetzung der Tubes unterscheidet sich zwischen den Workpackages, die Farbcodierung sollte aber immer gleich sein:

Röhrchentyp (Firma)	Farbe	Biomaterial
0,8 ml (FluidX)	orange	Serum
	grün	EDTA-Plasma (1x zentrifugiert)
	blau	EDTA-Plasma (2x zentrifugiert), hier: Liquid biopsy
	gelb	Urin
5,0 ml (Ratiolab)	weiß	Serum
	weiß	Urin

Erstellung der Probensets am Beispiel WP2 - DILI

- 1) Rack laut Aliquotschein (hier Beispiel WP2, Abb. 1d) stecken und entsprechende Anzahl 5ml Tubes raus suchen

Probenbegleitscheine/Aliquotscheine

Workpackage	Standort	PBS/Aliquotschein
WP1		
WP2	Nottingham, Malaga	VL-12_05.61a Aliquotschein Transbioline_WP2.docx VL-12_05.61b FB Aliquotschei Rack Transbioline_WP2.docx
WP3		
WP4		
WP5 -HV	Charité Pfizer, Brüssel	VL-12_05.61c FB TBL WP5_DINI - Sample data sheet.docx VL-12_05.61d FB Probenbegleitschein TBL_WP5_DINI_HV.docx
HV	Pfizer J&J	VL-12_05.61j FB TBL Pfizer HV V1_V2-sample data sheet VL-12_05.61k FB TBL Pfizer HV V3-sample data sheet

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Lilly/Covance

[VL-12_05.61I FB TBL Lilly/CONAVANCE HV-sample data sheet](#)

- 2) **Etiketten** im Ordner, sonst ausdrucken und kleben (Abb. 1a): je ein Etikett mit Kit-Nummer (fortlaufend, siehe Übersicht Versand) und WP für Rack, Tüte mit 5ml Tubes und Folie für Probengeleitscheine pro Kit. Ausserdem je ein Etikett für 5ml Tubes (Kit mit Tube-Nummer, Abb. 1b) und 5 ml Box (nur WP Nummer, Abb. 1c).
- 3) **Achtung:** Rackscan erstellen und dann im WPF nicht gleich exportieren, sondern die 5ml Tubes nacheinander einscannen. Dann Exportieren (**Fertigstellung** PBS je nach WP)! Aliquotscheine doppelseitig und bunt ausdrucken!
- 4) Ein Kit (je nach WP, hier WP2) beinhaltet 1 Rack mit Tubes für 8 Patienten, 1 Tüte mit 8 x 5ml Tubes und 1 Folie mit 8 PBS
- 5) Je nach Anforderung werden mehrere leer Racks (für 1ml Tubes) und 1 Rack für 5ml Tubes mitgesendet. Dies bitte auch dokumentieren.

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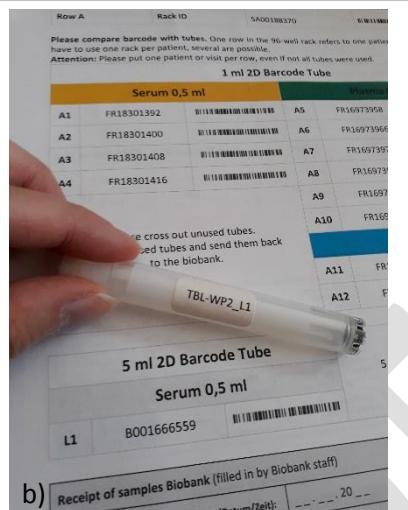
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Abbildung 1: Zusammenstellung Sample-Kits für Transbioline a) Etiketten drucken und kleben, je ein Etikett für Rack, Tüte mit 5ml Tubes und Folie für Probengeleitscheine b) 5 ml Tubes bekleben c) Tüte und Rack für 5ml Tube labeln d) und e) fertiges Set für WP2: 1 Rack mit Tubes für 8 Patienten, 1 Tüte mit 8 x 5ml Tubes und 1 Folie mit 8 PBS

Achtung: Bitte Sample data sheets nach dem Drucken kontrollieren (alle Barcodes vorhanden, Kit Nummer, nichts verrutscht).

4.3.2 Versand der Probensets

Die Probensets werden von den Work packages mit folgendem Schein geordert: [VL-12_05.61h FB TBL- Order form sample kits.docx](#). Die angeforderten Sample Kits werden zusammen mit den 5ml Tubes und den Sample data sheets verpackt. Zusätzlich werden je nach Anzahl der angeforderten Kits leer Racks und Boxen hinzugefügt. Der Versand erfolgt über unsere Poststelle (Abholung Labor).

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Übersicht Adressen:

[KP-08_04.30a SD TBL - Shipping addresses contact list.docx](#)

Etiketten für Versand (nach WP geordnet):

[03 Versand und Beschriftungen](#)Der Versand der Probensets wird dokumentiert: [Übersicht ausgegebenen Probensets](#)**4.3.3 Lagerung und Dokumentation**

Die Biomaterialien werden nach Probeneingang auf -80°C zwischengelagert und nach CentraXX-Dokumentation an ihren Lagerort verbracht. Die Racks möglichst in den Liconic einlagern, Boxen (5ml und ohne Barcode) kommen in Velma. Als Havarie oder Zwischenlagerort kann Daphne verwendet werden.

Dokumentation 2D Barcode Tubes aus Probensets

Die Racks mit den Proben werden über den Rackscanner gescannt und mit den gelieferten Daten abgeglichen. Der Probeneingang und die Einlagerung werden mit Hilfe der Probenbegleitscheine oder bevorzugt (wenn möglich) über eine Datei mit dem CentraXX-Importer in CentraXX dokumentiert.

Dokumentation anderer Tubes

Die Proben von gesunden Probanden (healthy volunteers, HV) werden von Firmen geliefert. **ACHTUNG:** Einige dieser Firmen (z.B. Johnson&Johnson) nutzen nicht die Probensets der Biobank, sondern verwenden eigene Röhrchen und Barcodes. Diese müssten falls kein 2D Barcode vorhanden ist, einzeln eingescannt werden (Trockeneis!). Zu den Proben erhalten wir eine Datei mit Probendaten, die abgeglichen werden müssen. Diese Proben werden zusammen in eine TransBioLine Box (LINK?) gelagert.

4.3.4 Probenabgabe

Die Analysepartner (Signatope, MLM, TamiRNA und die Universität von Zürich (UZH)) bzw. die Leiter der WPs fragen Proben zur Analyse an. Dies wird dokumentiert (**Übersicht versendete Proben**), die Proben im CentraXX herausgesucht und mit dem Analysepartner abgeglichen.

Die Proben werden dann herausgesucht und nach der UN3733 (Versand von Biomaterialien) verpackt und versendet (Adressen).

TransBioLine Kurierservice: Charité Vorgabe DHL**4.3.5 Abrechnung und Datenübermittlung**

- Das TransBioline Projekt hat eine eigene Kostenstelle, eine Kostenaufstellung (Bestellungen, Versandkosten) erfolgt halbjährlich intern

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- Ein Update über die erhaltenen Proben wird regelmäßig nach Probeneingang bzw. –ausgang an die Übersicht/Tabelle in der OWN-Cloud (oder ITTM?) gesendet

5 Mitgeltende Unterlagen

[DS-02_01.02 SD Kontaktdaten ZeBanC](#)
[KP-08_04.30 VA TBL-Prozesse intern](#)
[KP-08_04.30a SD TBL - Shipping adresses_contact list.docx](#)

Probenbegleitscheine

siehe [Tabelle oben](#)

Probensets und Versand

[Adress-Etiketten](#)
[VA Versand von Biomaterialien](#) (Spezialbedingungen Luftfracht beachten!)
[Dokumentation Versand Sample Kits](#)
[Probenabgabe Liquor für TBL](#)
Dokumentation Versand Proben zu Analysepartner

6 Dokumentation / Verteiler

E-Mail-Verteiler:

zebanc-labor@charite.de, ownCloud, einzelne Recruitment Centre für Benachrichtigung Erhalt

Die Dokumentation erfolgt in CentraXX sowie auf dem internen Netzlaufwerk.

Die Dokumente werden den Biobank-Mitarbeitern über SharePoint oder das interne Netzlaufwerk zur Verfügung gestellt.

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