TransBioLine
Translational Safety Biomarker Pipeline

821283 – TransBioLine

Translational Safety Biomarker Pipeline

WP7 – Assay and Sample Management

D7.01 Design and setup workflows

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	V1	11/09/2017

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Document History

Version	Date	Description
V1.0	20.05.2019	First Draft
V2.0	15.11.2019	Second Draft
V3.0	12.02.2020	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. Hoffman-La Roche Ltd. Switzerland

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

SARD. SANOFI-AVENTIS RECHERCHE & DEVELOPPEMENT. France

TBL. TransBioLine

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

(Max ½ page)

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

In this project, there is a 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 the fundamental processes.

The first major deliverable of work package 7 was defining all procedures of biomaterial acquisition and processing, including ID-management to facilitate standard handling of biomaterials cross all partner sites. This harmonization will lead to samples and related data of high quality.

1. Introduction

Outcome of this deliverable are harmonized workflows, which will define the entire process from sampling to processing, documentation and shipment to the biobank for all recruitment sites including specification of all responsible persons/institutions. The resulting documents serve as a guideline for all participants and guarantee the smooth and harmonized collection of samples and data.

2. Methods

2.1 Evaluation of the status quo

In a first step, all processes necessary for sampling, processing and documentation of the samples as well as the institutions and persons involved were identified and defined. In addition, it was checked whether all participants had the necessary personnel and technical infrastructure.

The necessity of the involvement of third parties, e.g. a transport company, was also examined.

The collection strategy of the various TBL studies is also decisive for the creation and description of the workflows. This information, which also has influence on further milestones (D7.2 to D7.4), was also requested from WP1 to WP5.

2.2 Generation of Documents/time schedule

Based on the *status quo*, the individual process steps and their participants can be defined. In the following, it was determined which internal and external documents have to be worked out, which persons/groups of persons have to be involved in this process. A raw time schedule for the provision of documents, training material and consumables for smooth realization of all process steps was also developed.

3. Results

3.1 Internal and external processes

In order to facilitate a uniform approach, we have prepared several documents (see table 1) describing all internal processes (internal workflows, overviews and standard operating procedures, SOPs) as well as interfaces to the recruitment sites and third-party companies (e.g. transport service). The internal documents include the description

of the internal biobank workflows for instance preparation of sample kits and sample data sheets, receiving of samples and their documentation. The external documents include the sample request form and sample data sheets. For a better understanding and reproducibility of the processes, videos for the main processes such as sampling, sample processing and shipment were prepared and uploaded to Sharepoint.

Document name	**Document use**
KP-08_04.29 VA TBL-Process manual external	internal
KP-08_04.30 VA TBL-Prozesse intern	internal
KP-08_04.31 SD TBL-Data Management	internal/external
KP-08_04.30a SD TBL-Shipping addresses Contact list	internal/external
KP-08_04.29a SD Transbioline Processing Manual	external
VL-12_05.61h FB TBL-Order form sample kits	external
VL-12_05.61i FB TBL-Order form_Samples for analysis	external
Individual sample data sheets for recruitment sites (examples)	
VL-12_05.61b FB TBL WP2_DILI - Sample data sheet	internal/external
VL-12_05.61g FB TBL WP4_DIVI - Sample data sheet	internal/external
VL-12_05.61j FB TBL Pfizer HV V1_V2-sample data sheet	internal/external
Workflows	
Flowchart_1.0_Data_Management	internal/external
Flowchart_2.0_Sample_Management	internal/external
Flowchart_2.1_Sample_Kit_Request	internal/external
Flowchart_2.2_Shipment	internal/external
Flowchart-Overview	internal/external
Videos	
Sampling	external
Processing of blood samples	external
Shipping	internal/external

Table 1: Overview of documents and videos created by the biobank for internal and external use in TransBioLine.

3.2 Sampling at recruitment sites

Documents (SOP, sample data sheet, videos) on sampling, processing and documentation for the recruitment sites are part of D7.2.

3.3. Sample transfer recruitment sites / EFPIA partners to biobank

A further important process step is the initiation of the sample transfer from the recruitment sites and EFPIA partners to the biobank. The ZeBanC designs, prepares and provides sample data sheets and sample kits for all recruitment sites, which are collecting prospectively. Retrospective collected samples will be managed by the individual work packages (e.g. WP5). Most EFPIA partners will use the ZeBanC sample kits (except Johnson & Johnson).

The workflow for ordering the sample kits is described in the document KP-08_04.29a SD TransBioLine Processing Manual (see Deliverable D7.2). The manual and the respective request form are available on Sharepoint or upon request from the ZeBanC (see annex 1).

The processing will be performed according to the Transbioline Processing Manual and processing video.

After collection, samples will be put into intermediated storage at -80°C at the respective sites. Samples will be shipped in batches according to instruction (see Manual, video shipment). Sample shipment to the ZeBanC has to be announced in advance. The aliquoted samples (filled sample kits) will be regularly transferred to the ZeBanC (exceptions e.g. WP5 retrospective collection). Aliquoted samples are documented and stored in the biobank.

Regarding the necessary data transfer, we are in close contact with ABX-CRO and ITTM in order to enable a safe and efficient way of data transfer for all parties involved. It is important that data integrity is maintained and that the transfer takes place in accordance with GDPR. It is important be noted that we only receive pseudonymized (coded) data allowing to track back to the patient under certain conditions. Here also the consented ID management plays an important role.

3.4 Provision of samples to the biomarker companies

The provision of samples for biomarker analysis must also be harmonized and transparent for all parties involved. In cooperation with the other WPs and the biomarker companies, a comprehensive list of number of patients, sample types, sample quantities and the biomarkers to be analysed was compiled for each work package.

General data (including demographics, clinical and sample data) will be transferred to the Clindex Database, ABX-CRO (eCRF or data transfer), cleansed and minimal data

transferred to the ZeBanC via the OwnCloud provided by ITTM. All data will be stored in TranSMART (see figure 1).

The ZeBanC will manage the sample data in the LIMS-system CentraXX. Regular reports will be prepared giving overview about sample entry. Reports can be monitored by WP leads and/or the TBL consortium who will decide which samples are going to be analysed. The analysis partners will be informed about the sample choice and can request samples from the biobank. This workflow has not been finalised and is still under discussion. Upon request from the work packages, the aliquots will be picked and shipped to the respective analyses partners. The respective document will be prepared whenever the final decision is made. The sample and data transfer are depicted in figure 1.

3.5 Data sharing

In the working group WPX2 all sample and data management processes were harmonized. Data transfer will be managed by ABX-CRO and ITTM and described in D8 processes. The data sharing processes are established. Due to the large number and heterogeneity of the data capture, there are different ways of data transfer.

1) Data entry into TransBioLine-eCRF: data will be cleansed at ABX-CRO. Sample information data will be send to ZeBanC.
2) Data entry into study-specific eCRF or other device: data extraction will be uploaded to OwnCLoud provided by ITTM. ABX-CRO will assign a TBL-specific patient ID that will be linked to the respective study ID. Sample information data will be uploaded to ITTM OwnCloud and after verification of data quality uploaded into the Biobank LIMS CentraXX (ZeBanC).
3) Data from retrospective collections: data extraction will be uploaded to the OwnCloud of ITTM after it has been uploaded to ABX-CRO Clindex TransBioLine database. The data is then standardised by us and then loaded onto OwnCloud for ITTM to import onto TranSMART. ABX-CRO will assign a TBL-specific patient ID that will be linked to the respective study ID. After verification of data quality, the sample data will be importet into the Biobank LIMS CentraXX (ZeBanC).

For further comparison and to prevent errors, the ZeBanC will receive filled-in sample data sheet together with the samples.

General ID-management is in place. IDs compose of WP, recruitment site, study population etc. Every patient ID and sample ID will be unique.

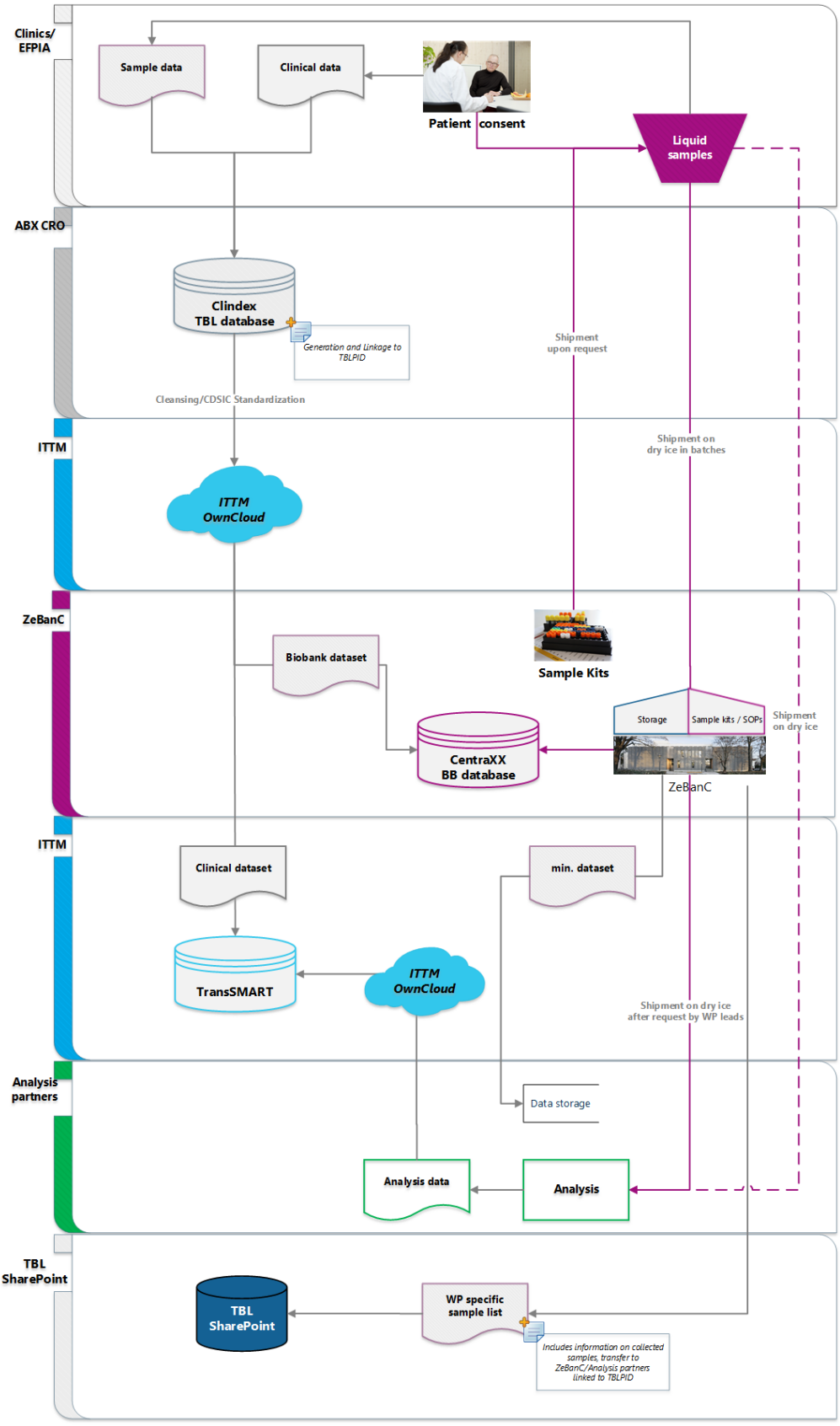


Figure 1: Overview workflow sample and data management

4. Discussion

The ZeBanC is intrinsically responsible for the creation/provision of the sample kits, for the permanent storage including the documentation of the samples and the provision of the samples for analysis.

However, we can only successfully plan and implement these tasks in close coordination with the other WPs. Decision making processes, such as which samples go when and where to which analysis, also play an important role in the successful implementation of the TransBioLine project objective. The ZeBanC acts as an interface between sample collection and biomarker analysis in close coordination with all WPs.

5. Conclusion

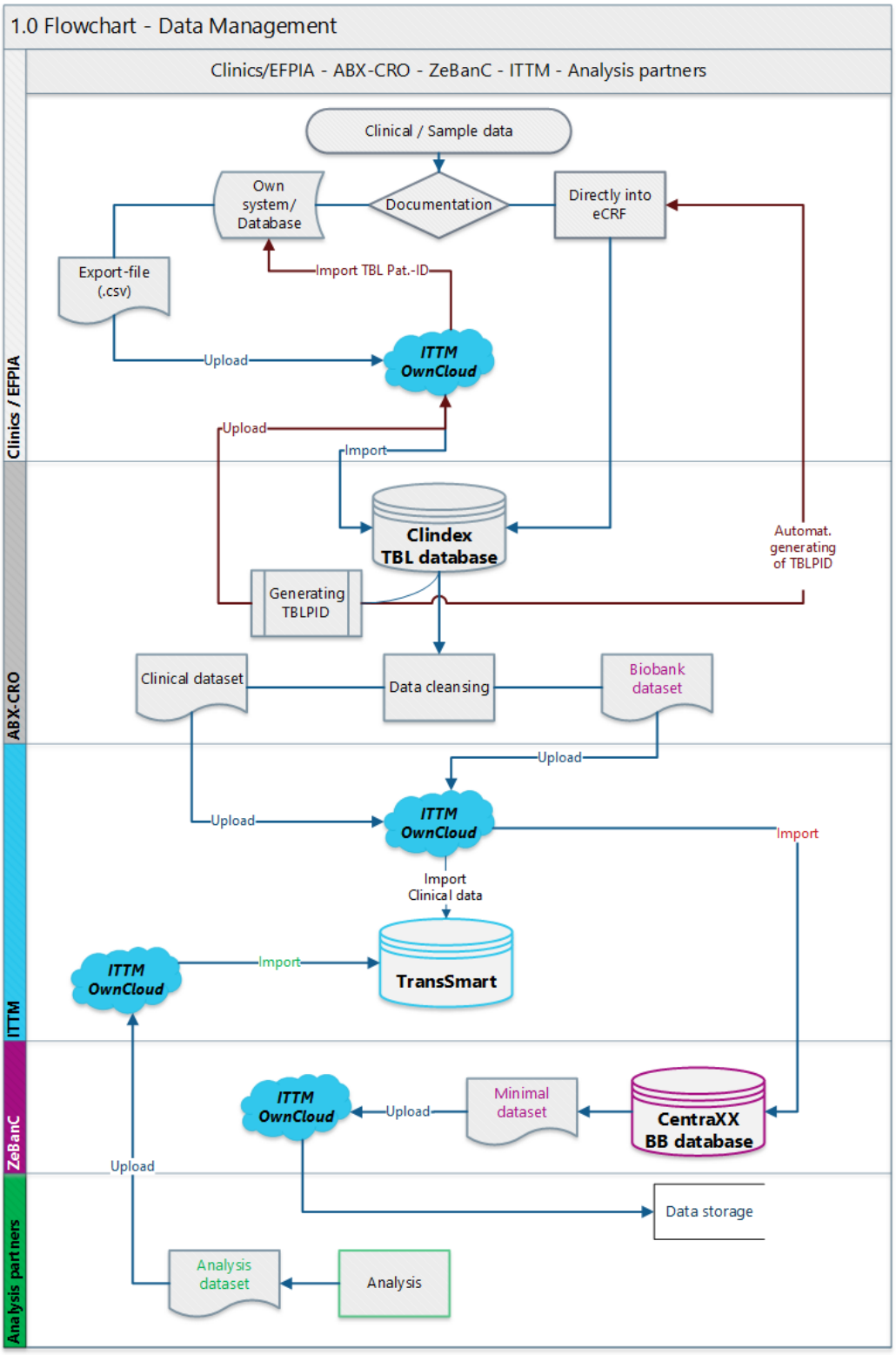
The workflows and interfaces are defined. The documents that harmonize important processes are available.

Due to the large number of partners involved and the various diseases to be considered in this project, there is a high need for coordination within TransBioLine. This also applies to biobanking as the essential basis for reproducible and reliable biomarker analyses. The communication between the different partners is established. Efforts for improving communication between TransBioLine partners and for optimizing sample workflow will be a continuous ongoing process until the completion of TransBioLine.

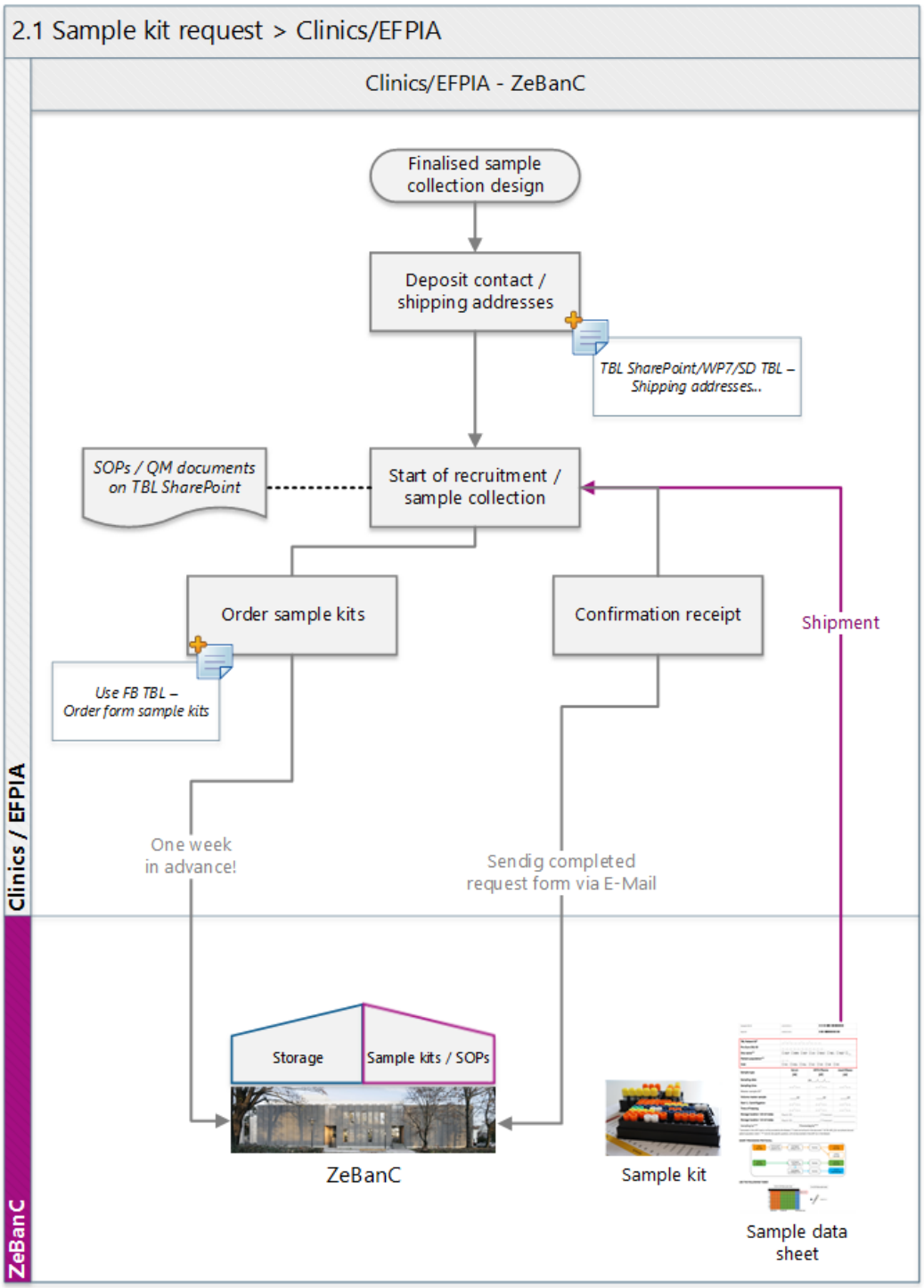
Annex 1

- Flowchart_1.0_Data_Management
- Flowchart_2.1_Sample_Kit_Request
- Flowchart_2.0_Sample_Management
- Flowchart_2.2_Shipment
- Flowchart-Overview

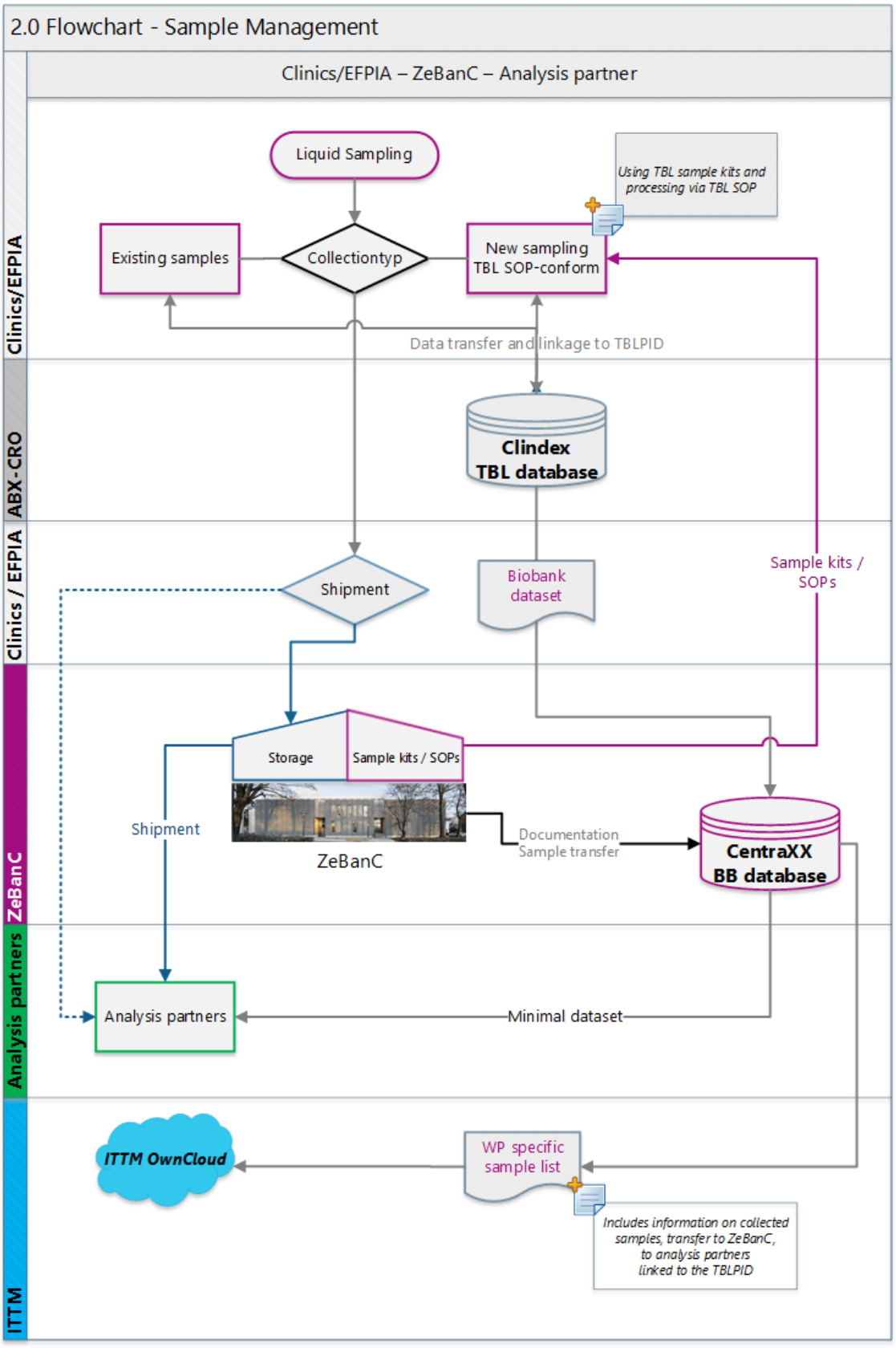
- Flowchart_1.0_Data_Management



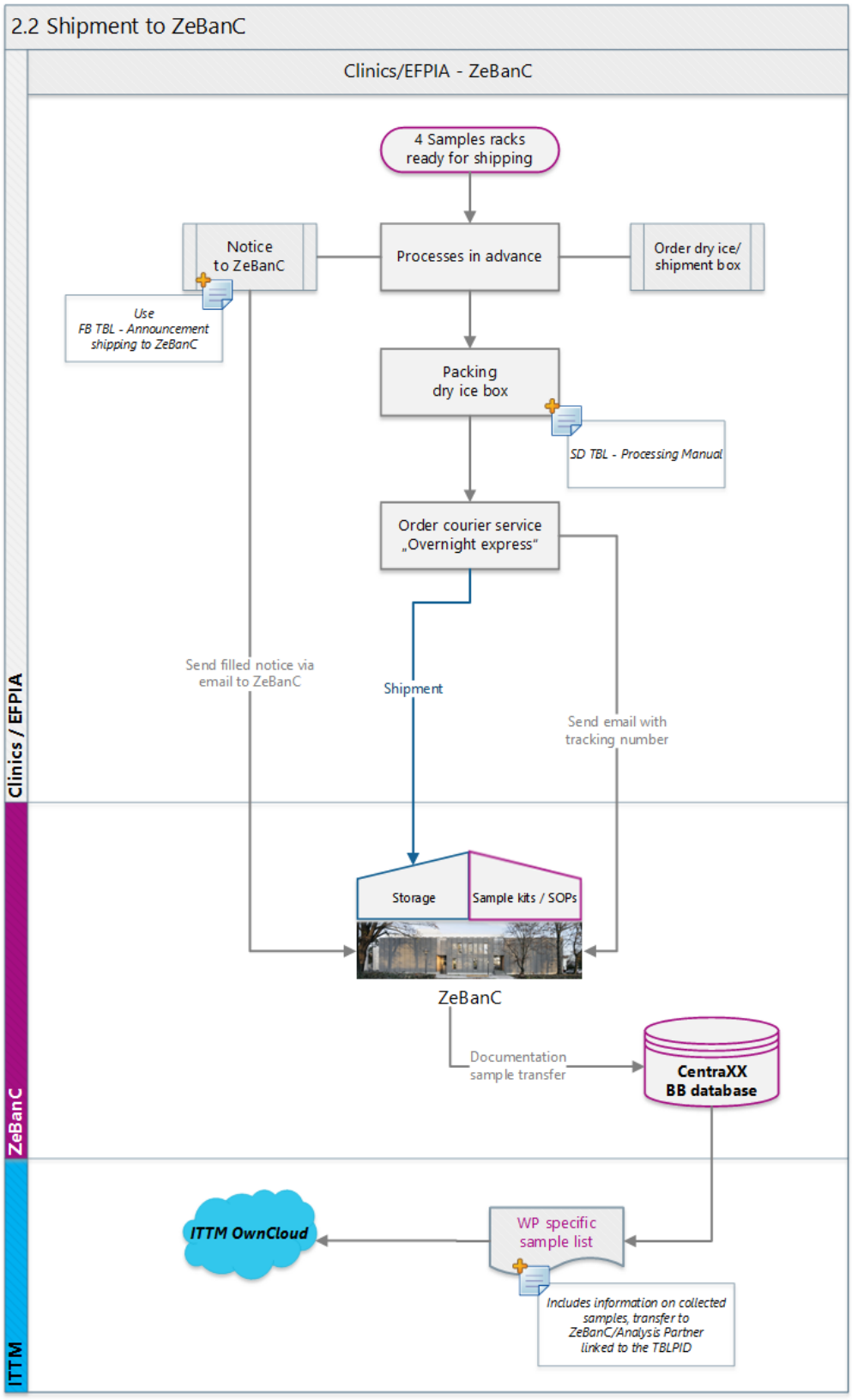
- Flowchart_2.1_Sample_Kit_Request



- Flowchart_2.0_Sample_Management



- Flowchart_2.2_Shipment



- Flowchart-Overview