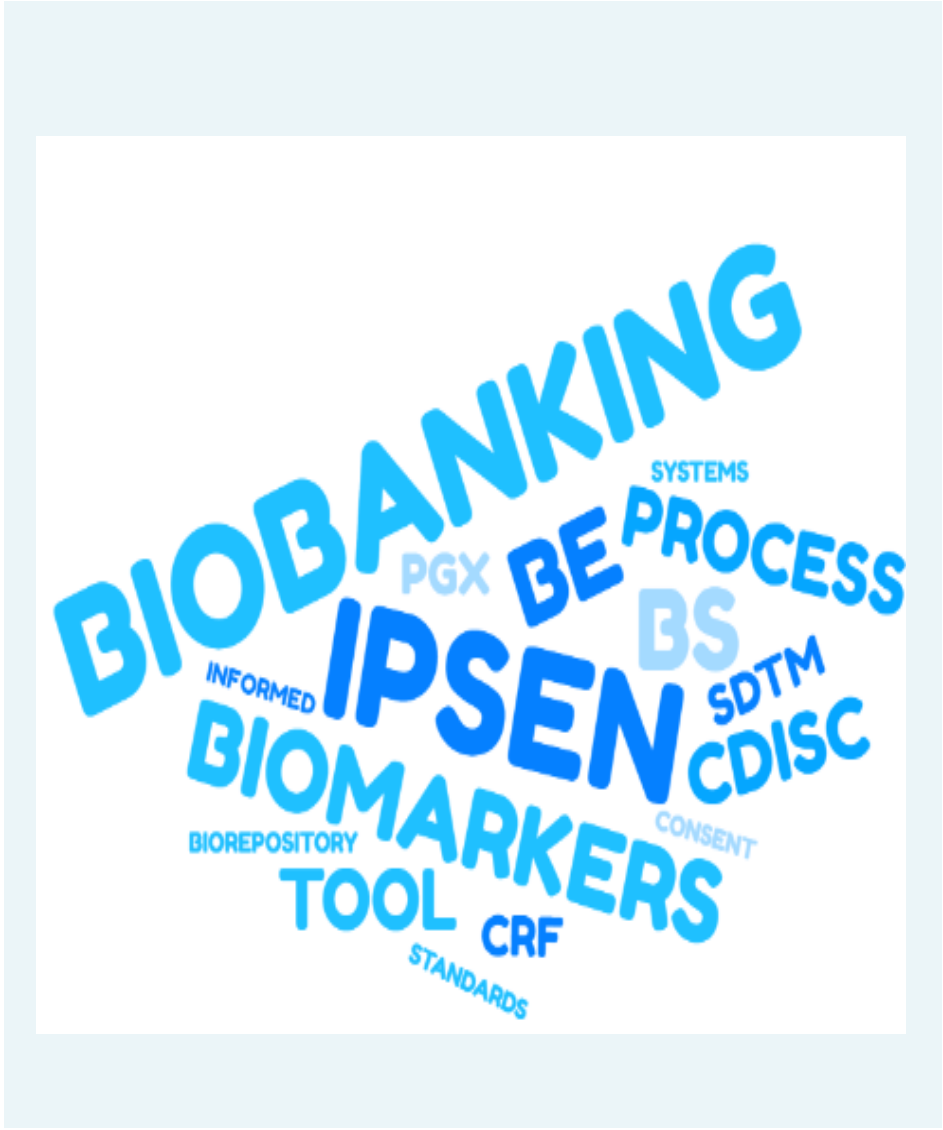


BIOBANKING – INVENTORY TOOL BASED ON SDTM

VALERIE PIERRON – CATHERINE BOULARD - IPSEN

24 JUNE 2019

Agenda

01 IPSEN CONTEXT

02 BIOBANKING WHAT FOR?

03 IMPACTS FOR IPSEN

04 CHALLENGES / NEXT STEPS

IPSEN CONTEXT

01 IPSEN CONTEXT

Outsourcing

All clinical studies are outsourced to CROs under the oversight of IPSEN (full-service and functional CROs)

Ipsen is under contract with 2 Biorepositories

Biomarkers analysis is outsourced to CROs

Key actors

BIOMARKERS TEAM
BIOMETRY
CLIN OPS
CROs (full-service / functional)
CENTRAL LAB
BIOREPOSITORIES
CROs BIOMARKER
QUALITY
IT

Standards and Tools

Standard model in production (IPSEN SDTM) : July 2015

Clinical DWH in production - CTDC : August 2016

Biobanking tool in production : December 2018

Biobanking : what for ?

02 BIOMARKERS DEFINITIONS

A biomarker is a biological entity that is objectively measured and evaluated as an indicator of a normal or pathogenic process, or pharmacological responses to a therapeutic intervention

Predictive Biomarkers

Patient selection / stratification

« Identify right subset of patient which could respond to the drug »

Pharmacodynamic / Efficacy Biomarkers

(PoM, PoP, PoC)

« reflect biological consequences of target engagement to monitor drug »

Safety Biomarkers

« Identify subsets of patients experiencing a particular safety concern »

Prognostic Biomarkers

« Identify subsets of patients most likely to have a particular outcome »

Biomarkers Identification, Confirmation, Validation and Assay Validation can be done during clinical study and/or supported by Biobanked samples

02 BIOBANKING FOR FUTURE RESEARCH

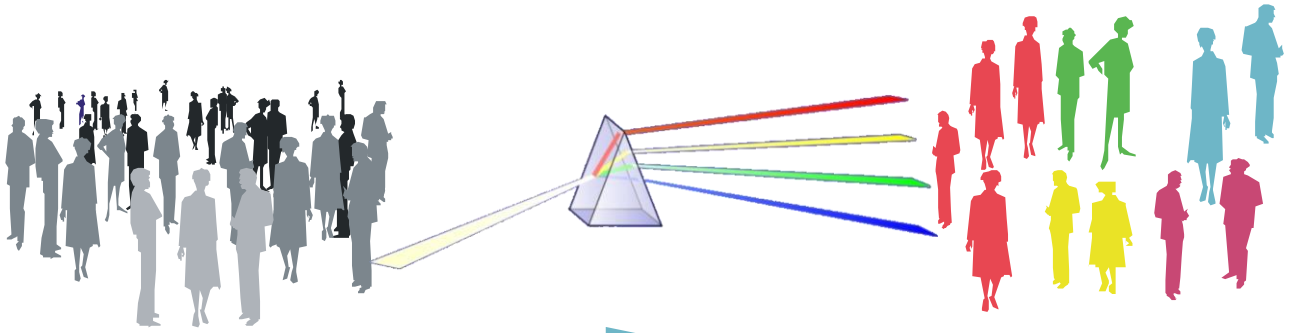
Exploratory Biomarkers

- Part of the exploratory objectives of the study protocol
- Biomarker measurements are therefore planned as part of the clinical trial
- Data is captured in the clinical database (samples + results)
- Biomarker analysis are planned in a dedicated SAP and as such reported in the TFL & CSR

Biobanking Activities

- Described in the exploratory objectives of the study protocol
- Biobanking is optional for subject engaged in the study and subject sign the optional consent for biobanking
- Samples are collected during different study visits (samples only in the clinical DB) and sent to a Biorepository
- Samples are stored for 15 years and used for research purposes
- This exploratory activity of biomarker research is not part of the clinical trial thus not part of the SAP, TFLs neither the CSR

02 BIOBANKING OBJECTIVES – TO SUPPORT PERSONALIZED MEDECINE



Derisking the unexpected clinical trial results

- You often do not get out from a Clinical trial (phase I, II, III) what you expected….
- Unexpected results means unpredicted markers

Biomarkers evaluation along the clinical study

- Validation of early biomarkers hypothesis to drive better patient identification and treatment efficacy monitoring

Biobanking for research

- Disease understanding
- Validation of new targets
- Support Biomarkers research towards personalized therapy: (safety, efficacy, selection, prognostic Biomarkers…)

3

IMPACTS FOR IPSEN

03 IPSEN NEEDS RELATED TO BIOBANKING

To ensure proper management of samples from their collection to their destruction in respect to ethical and regulatory guidelines, it is necessary to develop / define :

WORKFLOW – PROCESS SOP
STANDARDISATION FROM COLLECTION UP TO STORAGE

UPDATE INFORMED CONSENT

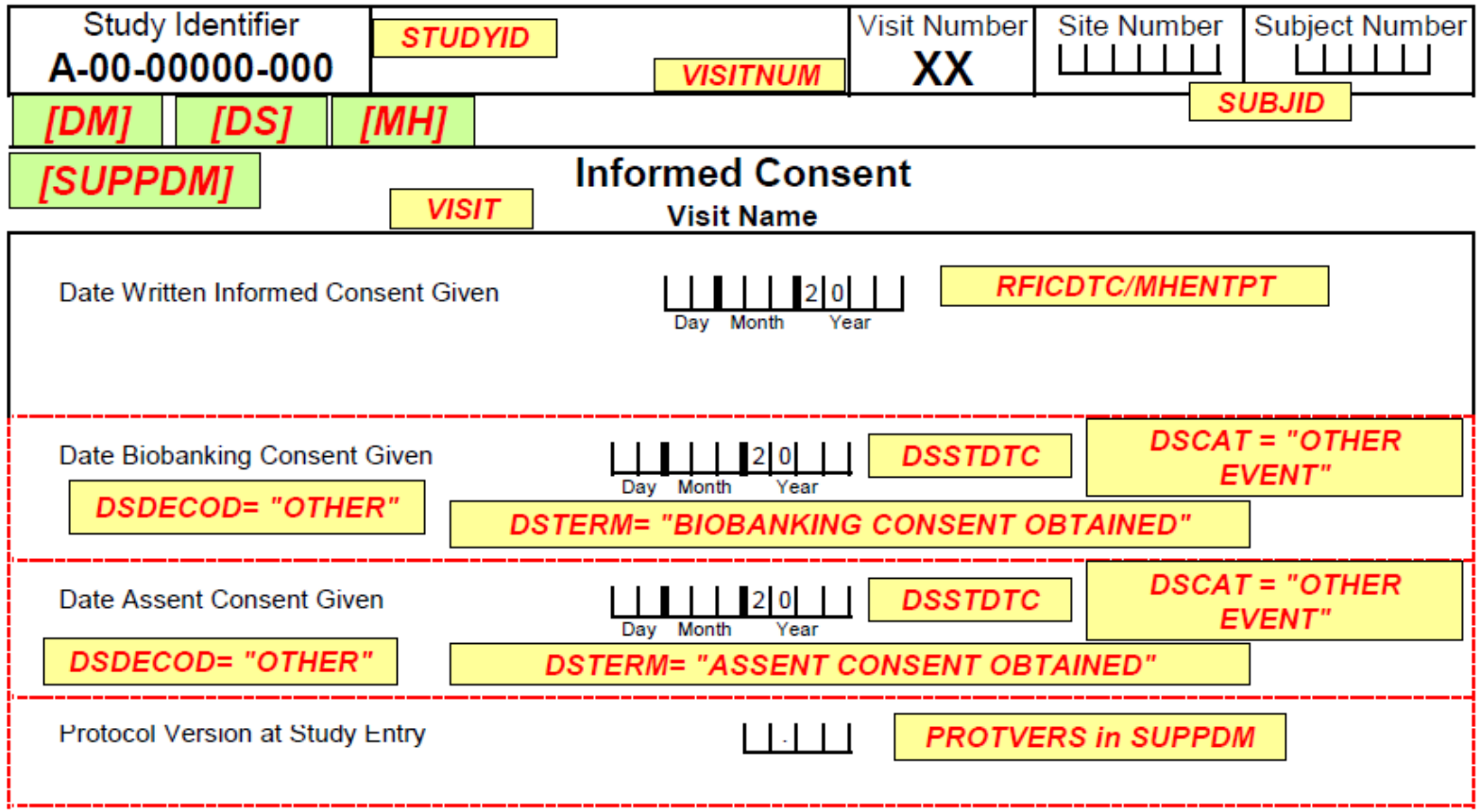
SPECIFIC CRF PAGES FOR SAMPLES COLLECTION
SDTM METADATA

IT TOOL WITH AN INVENTORY DB

Data Privacy – Data Protection – Sample Traceability – Respect Subject Consent

Decision to track samples based on BS and BE domains (SDTM domains from PGX)

03 CRF PAGE FOR BIOBANKING INFORMED CONSENT - EXAMPLE



Biobanking informed consent in DS domain

03 SDTMIG – PGX DOMAINS

2.1 SDTM Domains

The domains introduced in this document are intended to hold data that fall into one of three general categories: data about biospecimens, data about genetic observations, and data that define a genetic biomarker or assign it to a subject.

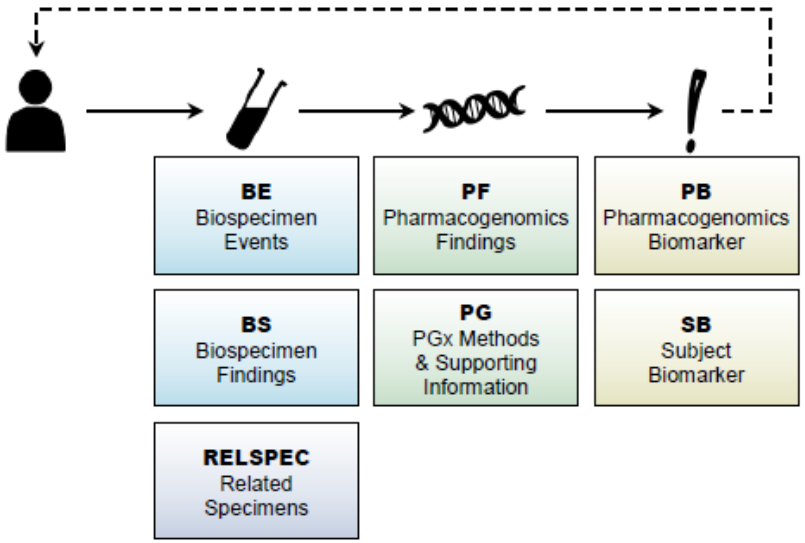


Figure 2: SDTMIG-PGx Domains and Datasets

BE = life cycle of the sample

BS = characteristics of the samples / biospecimens

Class / Category	General Observation Class		Special-Purpose
	Event	Finding	
Data about biospecimens	BE	BS	RELSPEC
Data about genetic observations		PF, PG	
Data that define a genetic biomarker or assign it to a subject			PB, SB

03 SDTMIG – PGX DOMAINS – BE and BS DOMAINS

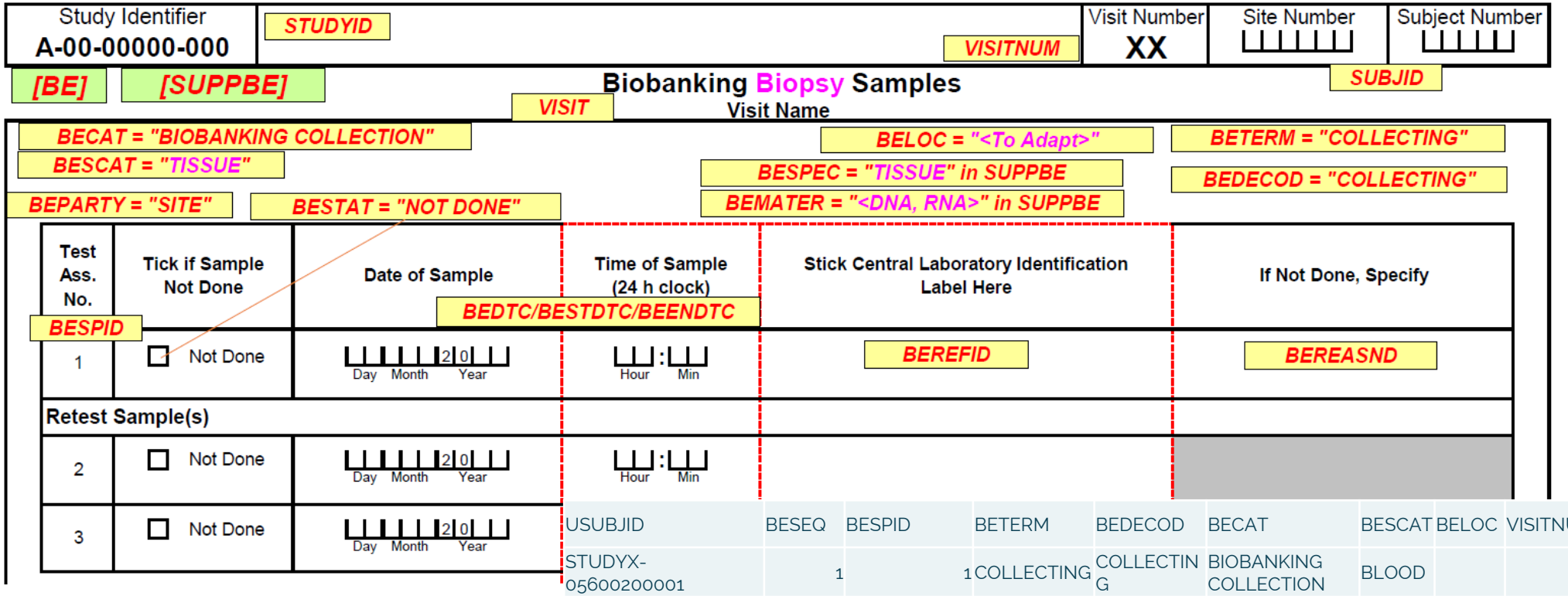
BE
Biospecimen Events Domain

- Events class domain used to capture information about actions taken that affect a specimen or alter its status
- Include what the action taken was (e.g., transportation, freezing, ……..), when the action occurred (the date/time associated with it), and who or what party became accountable for the specimen (e.g., site, laboratory)

BS
Biospecimen Findings Domain

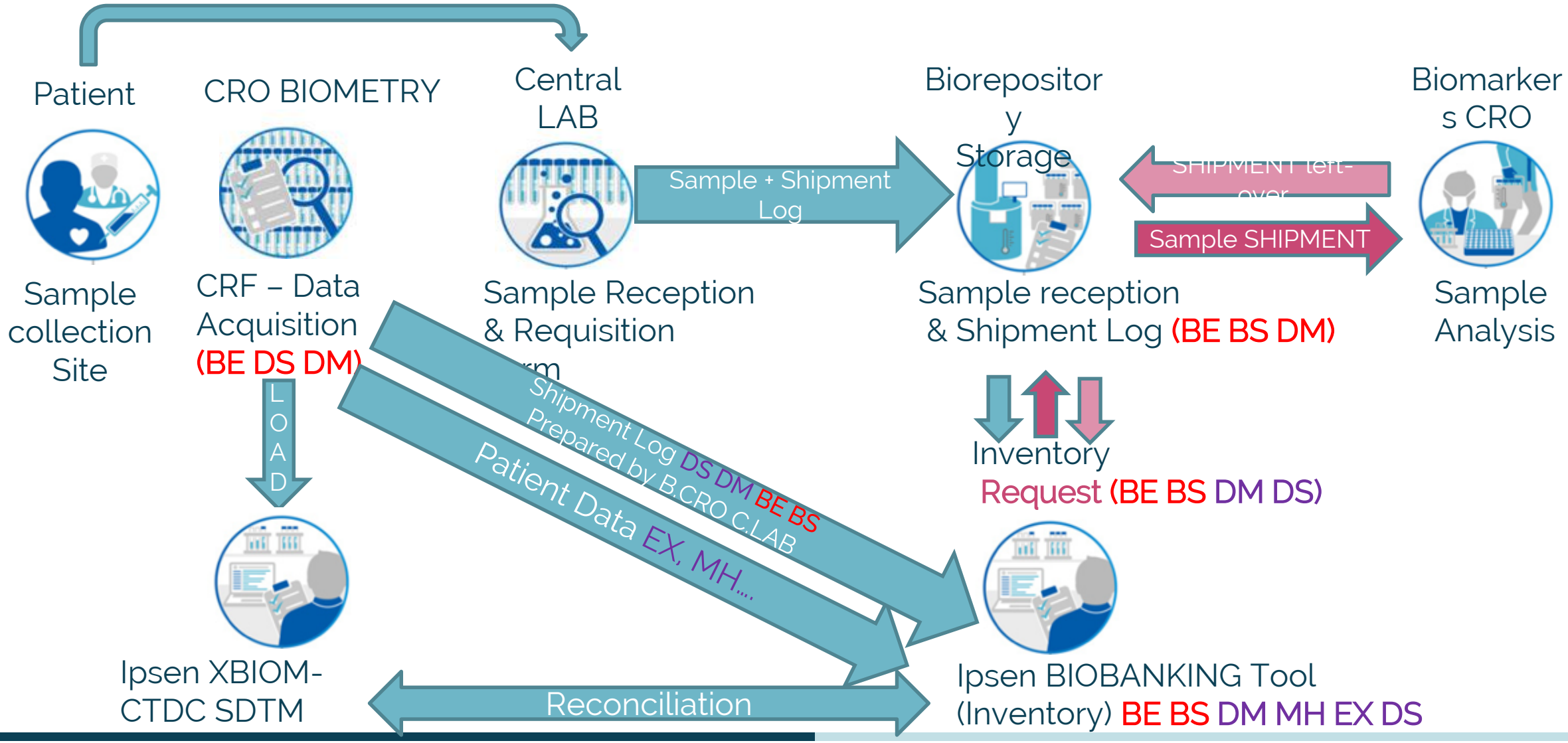
- Findings class domain contains the details regarding the characteristics of biospecimens and extracted samples (e.g., RNA, DNA) such as specimen volume, quantity of extracted sample, specimen condition and the sample quality or integrity of RNA samples….

03 CRF PAGE FOR BIOBANKING - EXAMPLE



USUBJID	BESEQ	BESPID	BETERM	BEDECOD	BECAT	BESCAT	BELOC	VISITNUM	BEDTC/BESTDTC/BEENDTC
STUDYX-05600200001	1	1	COLLECTING	COLLECTING	BIOBANKING COLLECTION	BLOOD		1	2013-01-08T11:25
STUDYX-05600200001	2	1	COLLECTING	COLLECTING	BIOBANKING COLLECTION	URINE		1	2013-01-08T11:25
STUDYX-05600200001	3	1	COLLECTING	COLLECTING	BIOBANKING COLLECTION	TISSUE	LIVER	1	2013-01-08T11:25
STUDYX-05600200001	4	1	COLLECTING	COLLECTING	BIOBANKING COLLECTION	BLOOD		1	2013-01-08T11:25
STUDYX-05600200001	5	1	COLLECTING	COLLECTING	BIOBANKING COLLECTION	BLOOD		1	2013-01-08T11:25

03 BIOBANKING PROCESS & DATA FLOW



03 BIOBANKING TOOL OBJECTIVES = INVENTORY DATA BASE

During the Sample life cycle, the following information is collected, tracked and imported in the IPSEN BIOBANKING TOOL (DB) with an SDTM structure :

Shipment log - Sample flow : BE + BS domains
Demographic (DM) : SUBJID, DATE/TIME OF BIRTH, COUNTRY, STUDY SITE IDENTIFIER, SEX
Disposition (DS) : DSTERM (Biobanking consent obtained) + date
Exposure data (EX) , ARM
Medical History (MH)

This information will allow IPSEN to track the samples to locate them at any time :

- to know the quantity per sample type of specimen available
- to allow Scientist autonomous selection of biobanked samples according to clinical data,
- to analyze biobanking results in relation to associated clinical data and/or to exploratory biomarker results to comply with regulation, authority inspection and patient consent

03 INVENTORY DATA BASE: EXAMPLE – EXTRACT

DM	DM	DM	DM	DM	DM	DS	DS	BE	BE	SUPPBE	SUPPBE	BE	BE	BE
STUDYID	SUBJID	BRTHDTC	COUNTRY	SITEID	SEX	DSTERM where DSTERM= 'BIOBANKING CONSENT OBTAINED'	DSSTDTC where DSTERM= 'BIOBANKING CONSENT OBTAINED'	BEREFID	BETERM	QVAL where QNAM= BESPEC and QLABEL="Specimen Type"	QVAL where QNAM= BEMATER and QLABEL="Material"	VISIT	BESTDTC	BENDTC
Study Identifier	Subject Identifier for the Study	Date/Time of Birth	Country	Study Site Identifier	Sex	Reported Term for the Disposition Event	Start Date/Time of Disposition Event	Reference ID	Reported Term for the Biospecimen Event	Specimen Type	Material	Visit Name	Start Date/Time of Biospecimen Event	End Date/Time of Biospecimen Event
ABC134	25010300001	1971	FRA	250103	F	BIOBANKING CONSENT OBTAINED	2005-01-18	1234567XXX1	COLLECTING	BLOOD	RNA	VISIT 2 DAY1	2005-03-20	
ABC134	25010300001	1971	FRA	250103	F	BIOBANKING CONSENT OBTAINED	2005-01-18	1234567XXX1	SHIPPING	BLOOD	RNA	VISIT 2 DAY1	2005-03-20	
ABC134	25010300001	1971	FRA	250103	F	BIOBANKING CONSENT OBTAINED	2005-01-18	1234567XXX1	RECEIVING	BLOOD	RNA	VISIT 2 DAY1	2005-03-21	
ABC134	25010300001	1971	FRA	250103	F	BIOBANKING CONSENT OBTAINED	2005-01-18	1234567XXX1	STORING	BLOOD	RNA	VISIT 2 DAY1	2005-03-21	2005-05-25
ABC134	25010300001	1971	FRA	250103	F	BIOBANKING CONSENT OBTAINED	2005-01-18	1223567XXX1-R01	EXTRACTING	RNA	RNA	VISIT 2 DAY1	2005-05-25	
ABC134	25010300001	1971	FRA	250103	F	BIOBANKING CONSENT OBTAINED	2005-01-18	1223567XXX1-R01	STORING	RNA	RNA	VISIT 2 DAY1	2005-05-25	2005-07-25
ABC134	25010300001	1971	FRA	250103	F	BIOBANKING CONSENT OBTAINED	2005-01-18	1223567XXX1-R01	DESTROYING	RNA	RNA	VISIT 2 DAY1	2005-07-25	

4

CHALLENGES & NEXT STEPS

CHALLENGES

NEXT STEPS

- Complex project due to the involvement of many experts and different teams (biomarker, biometry, clin ops, quality, IT …)
- Process that requires training each clinical team and outsourced CROs every time
- Biorepositories : had to adapt to our data formats. They are not SDTM compliant
- Tool upgrade is needed : variables to be added
- Insufficiently automated reconciliation between clinical data and inventory data
- Standardization of results ongoing

THANK YOU !