

9th EBF YSS

Reconciliation: the unsuspected challenge for clinical trials

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Agenda

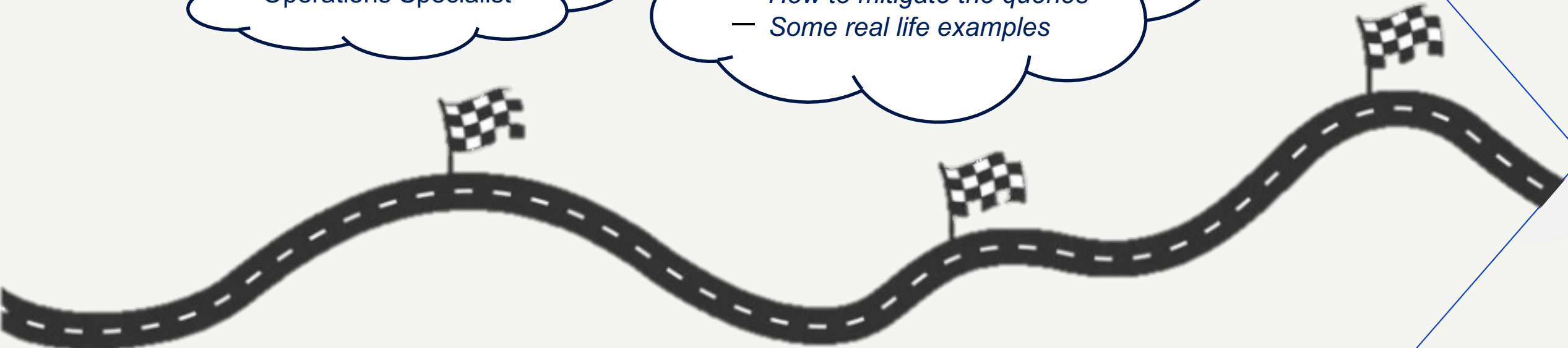
Roche

Role of a Biosample
Operations Specialist

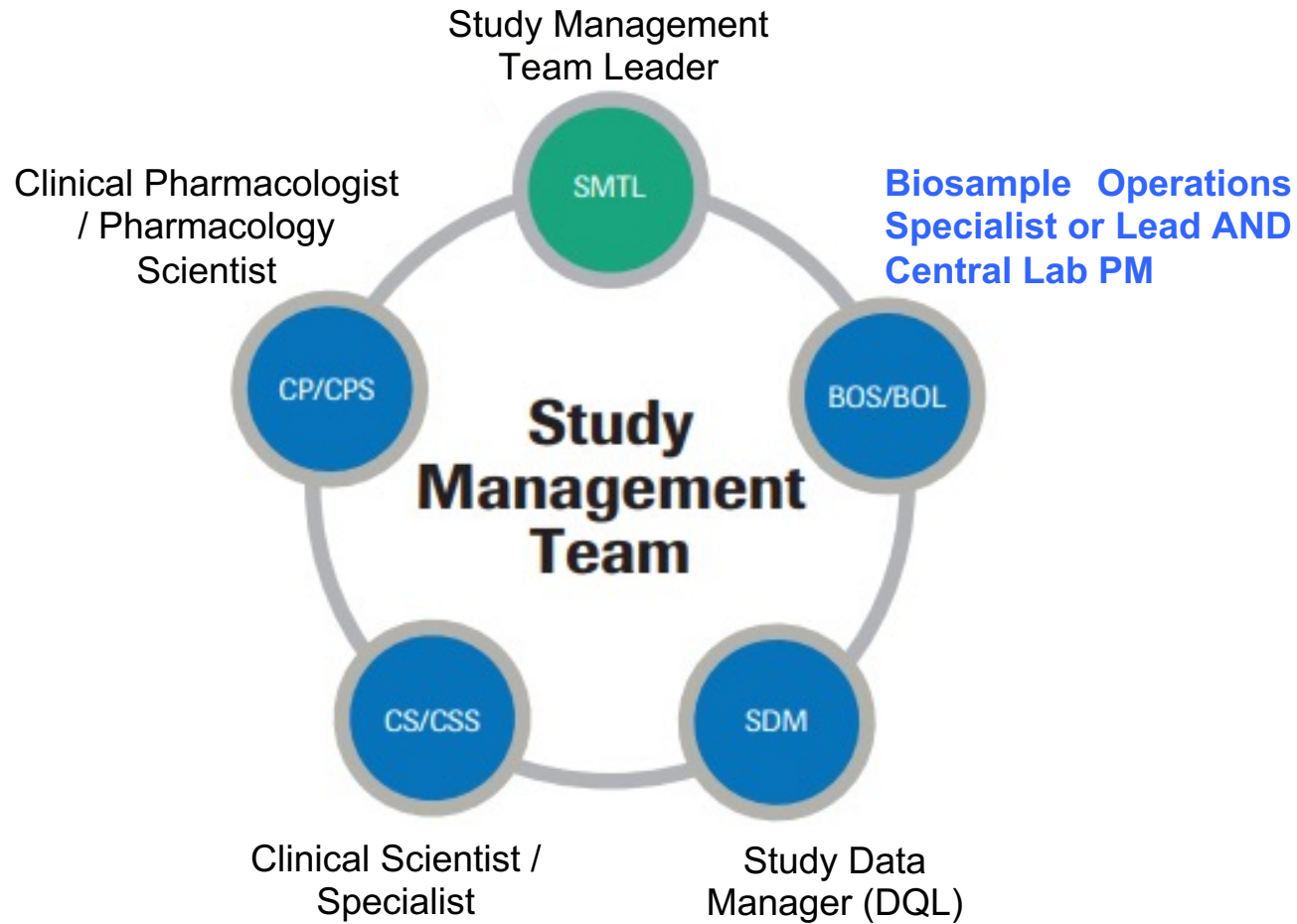
Reconciliation

- *Ideally*
- *What could go wrong?*
- *How is it done?*
- *How to mitigate the queries*
- *Some real life examples*

Next steps



Role of a Biosample Operations Specialist



Implement the biosample sample strategy from the protocol into operation during...

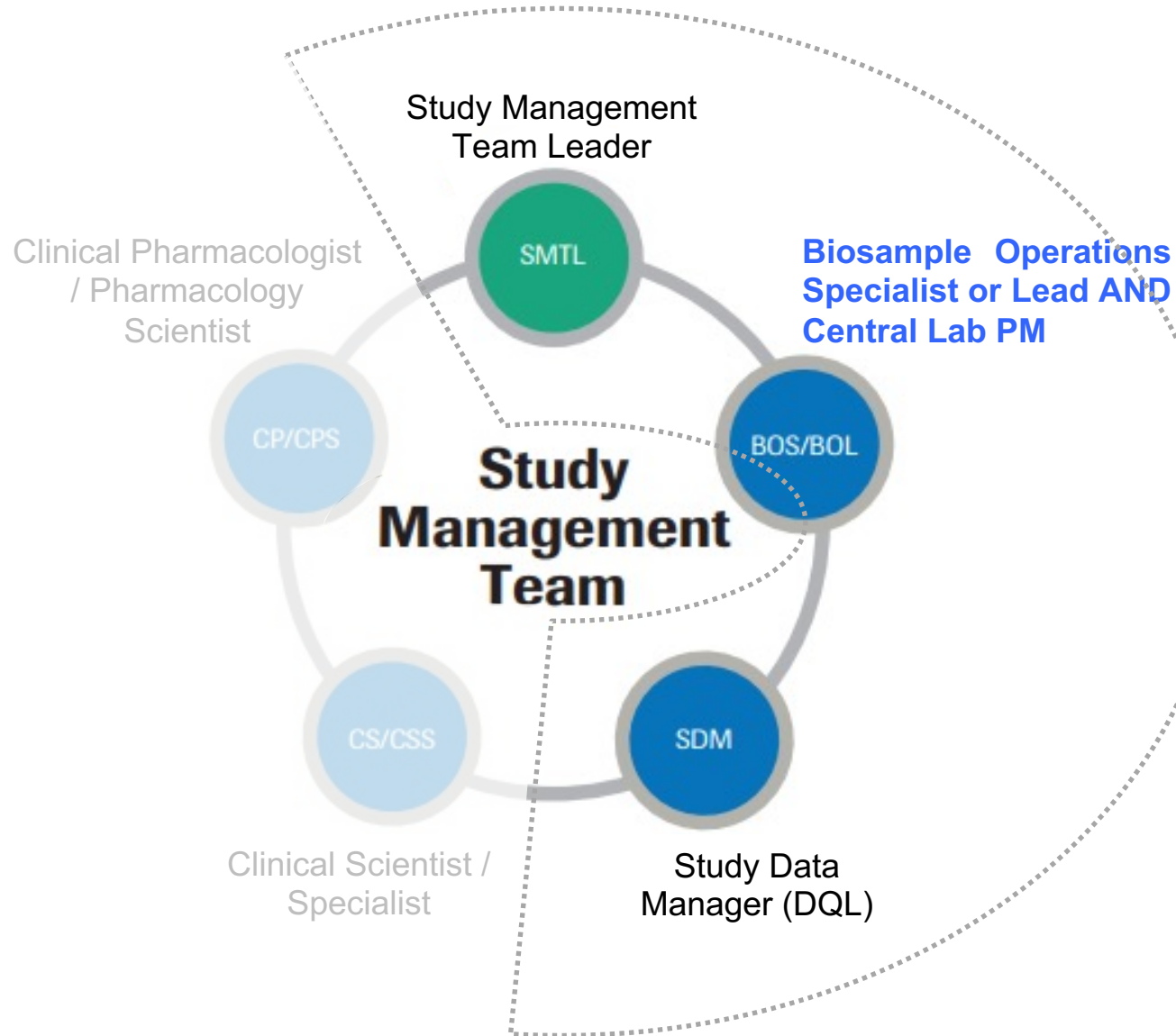
... **the study set up:**

- Set up the central labs
- Set up the histology labs
- Set up the biomarker testing lab
- Coordinate the PK/ADA strategy
- ...

... **the study maintenance:**

- Manage/oversee the sample flow
- Oversee the vendor activities
- Oversee the reconciliation
- ...

Role of a Biosample Operations Specialist



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- **Oversee the reconciliation**
- ...

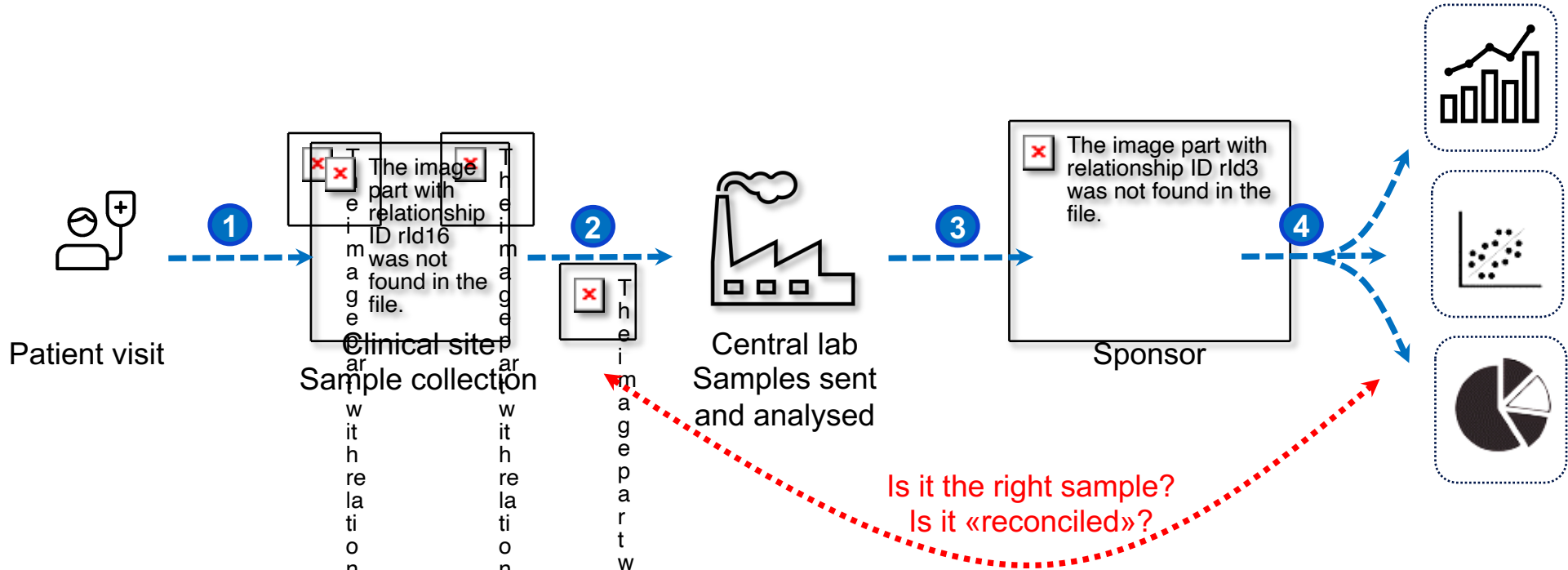
Reconciliation – Ideally



“Sample reconciliation is a process which compares the sampling information of blood or tissue samples entered into the eCRF against the physical sample identification data from the sample Vendor/analytical lab to ensure that both databases match; it is following the sample from site collection to laboratory receipt”

Reconciliation – Ideally

“Sample reconciliation is a process which compares the sampling information of blood or tissue samples entered into the eCRF against the physical sample identification data from the sample Vendor/analytical lab to ensure that both databases match; it is following the sample from site collection to laboratory receipt”



- 1 Patient visit the hospital to be enrolled in the study
- 2 The clinical site collect the sample and send them for analysis
- 3 The results are transfer to the sponsor and analysed
- 4 Analysis and interpretation

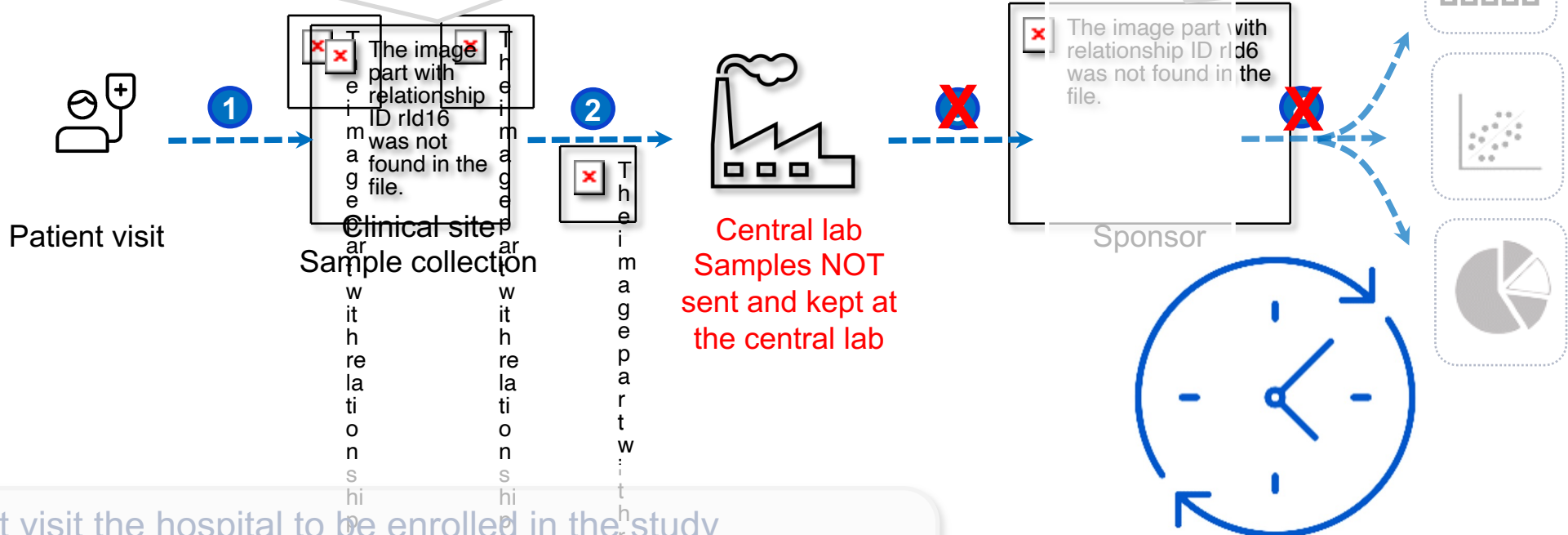
Reconciliation – What could go wrong?

Sorry but, ...

- ... we used the wrong kit / tube
- ... sent the wrong sample
- ... not sure the patient ID matches the tube
- ... did not take the samples, can we do it now?

Also, ...

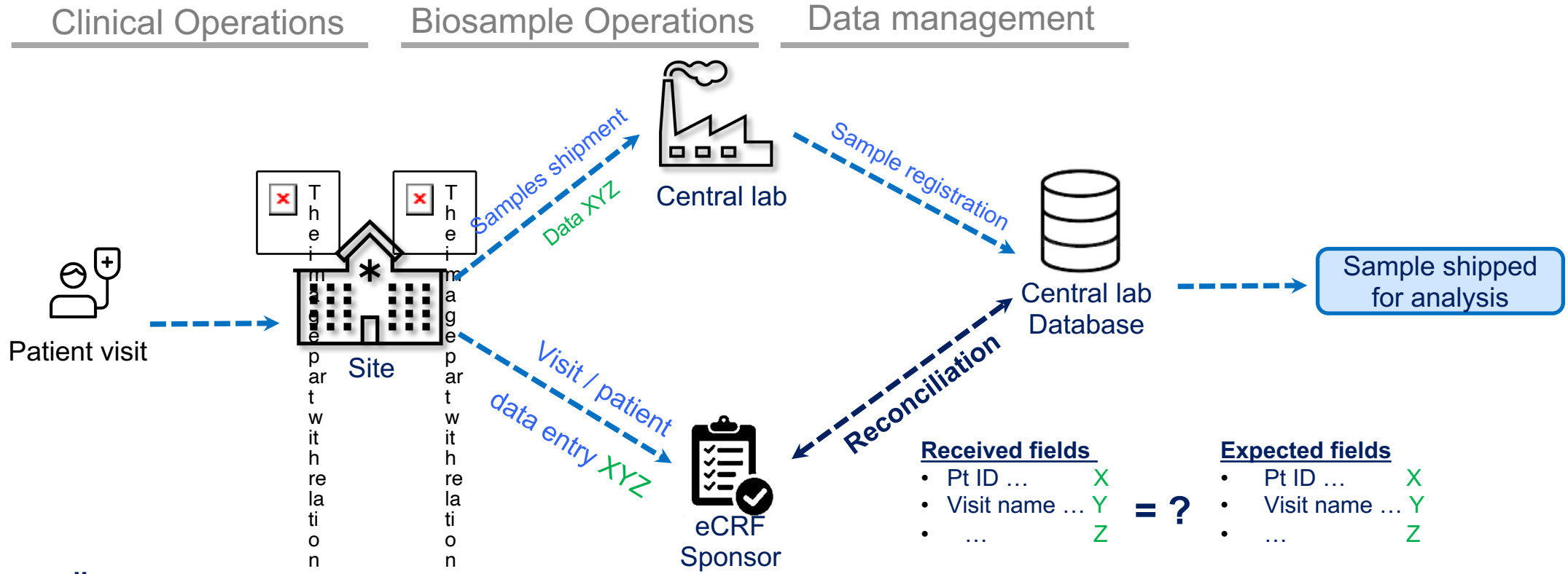
- ... the sample you sent was not supposed to be taken
- ... can you confirm the sample collection date?
- ... we do not see the sample registered in the eCRF



- 1 Patient visit the hospital to be enrolled in the study
- 2 The clinical site collect the sample and send them for analysis
- ~~3 The results are transfer to the sponsor and analysed~~
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- As long as the «issue» or query is open, the samples impacted remain in storage and cannot be shipped for analysis in the corresponding lab
- It can take **up to 2 months** to resolve -> study milestones!

Reconciliation – How is it done?



When all goes well:

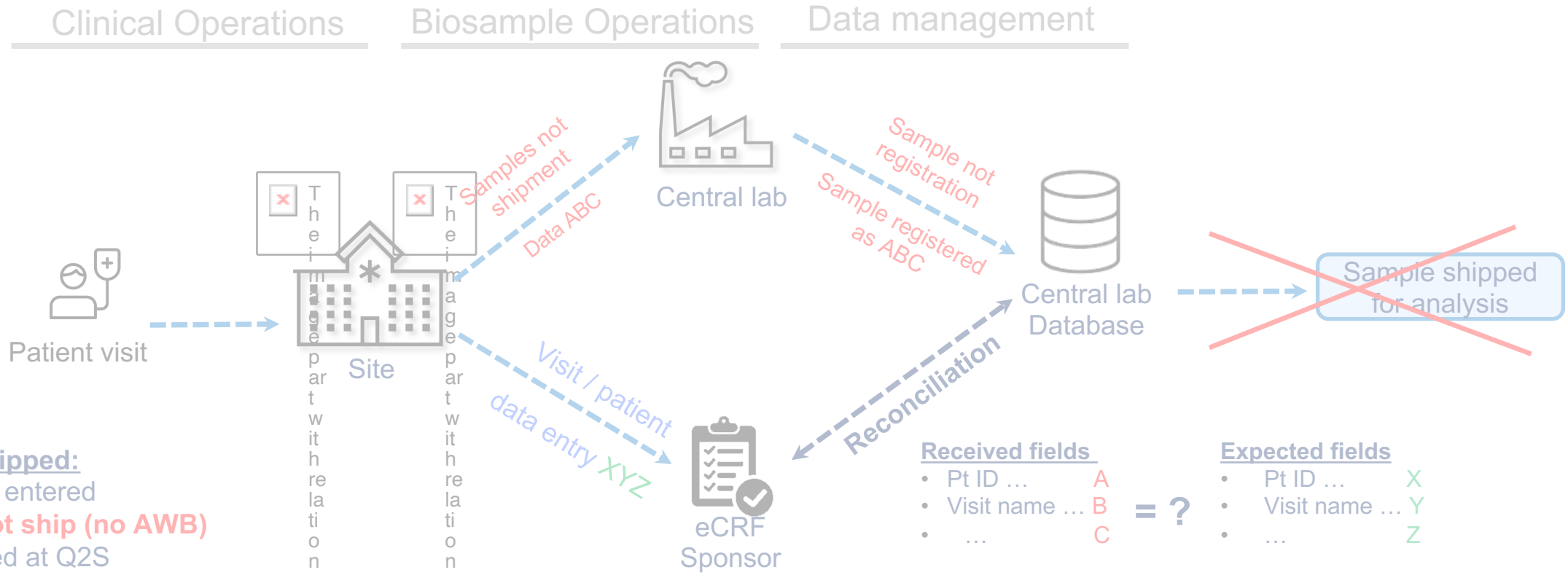
- eCRF data entered
- Site shipped sample
- Sample received at Q2S
- Received match the expected
- Reconciliation is performed

Conclusion at the reconciliation:

Samples received and clean

No query raised

Reconciliation – How is it done?



- No sample shipped:**
- eCRF data entered
 - **Site did not ship (no AWB)**
 - Not received at Q2S
 - No storage + no data base update

- Sample shipped (wrong data)**
- eCRF data entered
 - Site shipped sample **AWB** known
 - Sample received
 - **Received vs expected not matching**

Clinical site, ClinOps, BPL, DM and Central lab should work together to resolve the query asap to allow the sample to be shipped and analysed ...

... it can take up to several months!!!

<u>Received fields</u>			<u>Expected fields</u>	
• Pt ID ...	A	= ?	• Pt ID ...	X
• Visit name ...	B		• Visit name ...	Y
• ...	C		• ...	Z

Conclusion at the reconciliation:

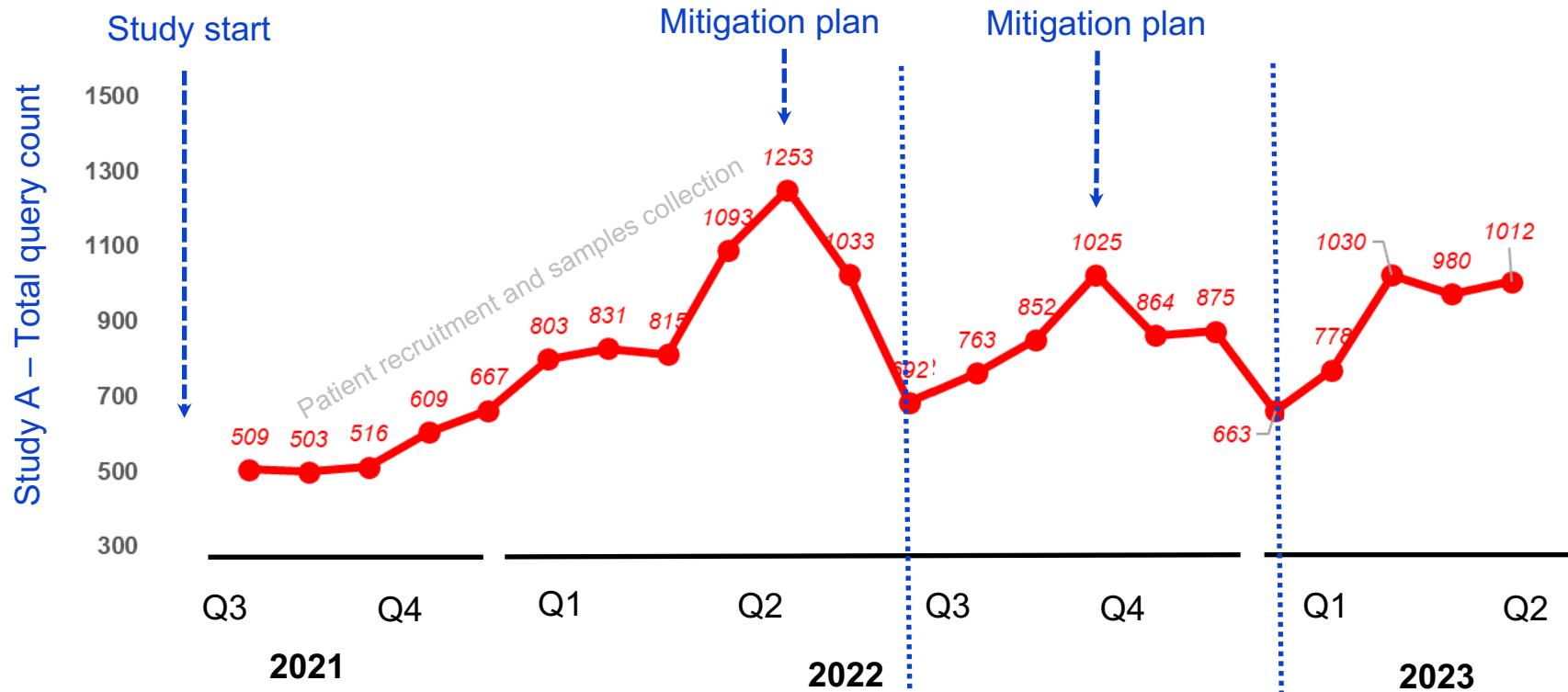
- 1 x query eCRF data since expected do not match the received
- 1 x missing sample query since expected fields empty

Reconciliation – How to mitigate the queries



- **At study set up:**
 - Make sure the collection of the sample is clear, understandable and correct
 - Engage with the clinical sites and train them
 - Question the feasibility of the sampling and gather any concerns
- **Once the study started:**
 - Partner with the study management team and the central lab!
 - Provide proactively support and guidance to them
 - Engage with the clinical sites 1:1 and help them to address:
 - *Questions*
 - *Miscommunications*
 - Request guidance form the science team
 - *Sample prioritization?*
 - *Timelines to resolve the queries*

Reconciliation – some real life examples



- Around 800 samples impacted
- 2/3 were PK samples required for decision making

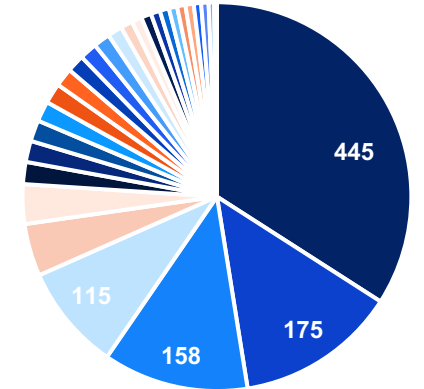
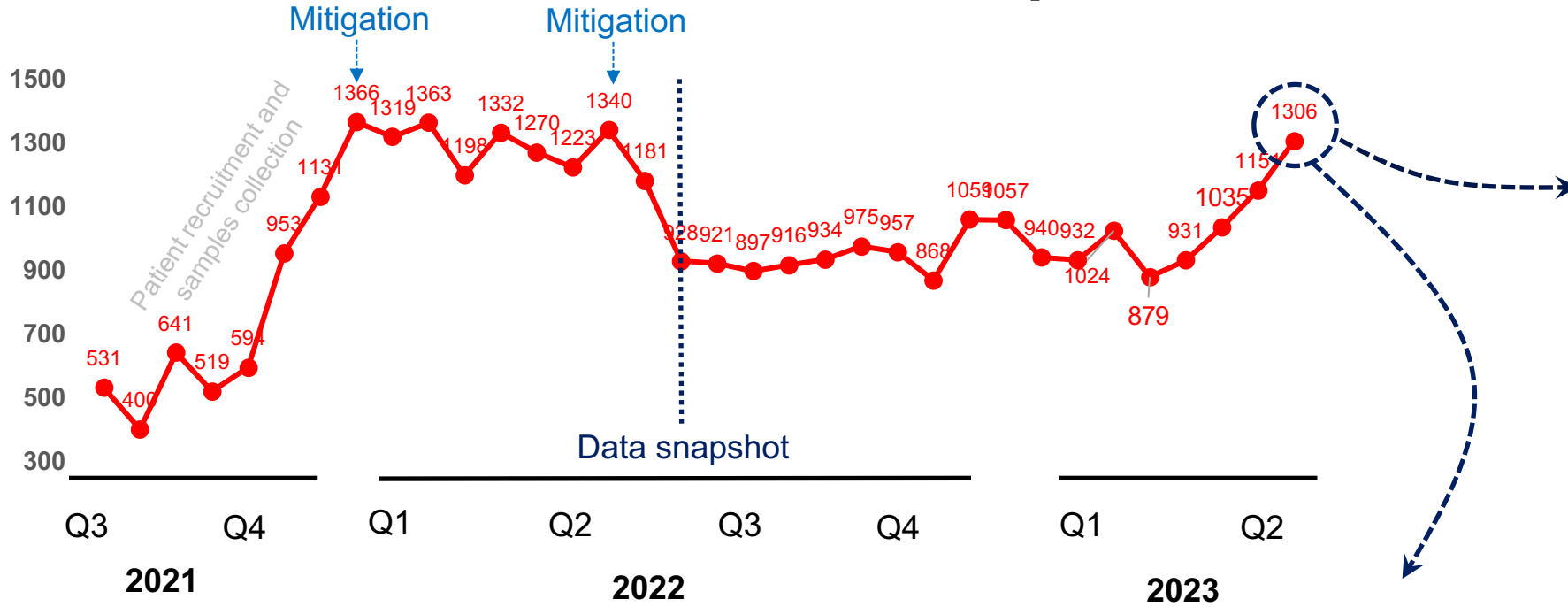
Data snapshot occurred here

- Focused on PK we rescued around **400** data points
- Cytokines were also targeted
- Focused on PK again, another **200** data points rescued
- Histology focus as well

Reconciliation – some real life examples



Study B – Total query count



- Serum PK
- Blood PD cytokines
- Whole Blood Flow 355/A562
- Serum ADA
- Whole Blood A721 Flow
- Tissue Sampling
- PD PBMCs Residual
- Blood cell Pellet
- Bone Marrow Flow
- BMA MRD
- BLOOD SMEAR
- PD PBMCs 1
- ctDNA
- BMA PLASMA 1
- BMA BMDCs PELLET
- BMA BMDCs CELLS 3
- PD PBMCs 2
- SM CD138+ ENRICHED CELLS
- BMA BMDCs CELLS 2
- BMA BMDCs CELLS 1
- PD PBMCs 3
- Serum TCZ PK
- RBR (RNA 2)
- RBR (RNA 1)
- Serum IL-6 PD markers 1

Count of Obs (query ID)	Column Labels																	Grand Total
	2021				2022				2023									
	Qtr2	Qtr4	Qtr1	Qtr2	Qtr3	Qtr4	Qtr1	Qtr2	Qtr3	Qtr4	Qtr1	Qtr2	Qtr3	Qtr4	Qtr1	Qtr2		
Row Labels	juin	oct	mars	avr	mai	juin	juil	août	sept	oct	nov	déc	janv	févr	mars	avr		
Missing eCRF data		9			40	9	47	7	20	4	21	11	13	78	210	171	640	
Missing sample		1	7	7	11	3	1		4	11	9	2	58	106	60	46	326	
Collection date/time inconsistent				5	1		1		5	2	3	22	23	17	44	38	161	
Erroneous Patient No.									1					1	40	14	56	
Unexpected condition															1	35	36	
Erroneous Sample											1			3	28	3	35	
Missing tissue eCRF data					1		1							5	21		28	
Missing tissue sample	2										4	1	1	8	1		17	
Consent Issue			2												2		4	
Time window				1			1				1						3	
Grand Total	2	10	10	12	53	12	51	7	30	17	39	36	95	218	407	307	1306	

Next steps to improve the query resolution



A lot of frustration in the way the queries are managed currently:

- Excel based:
 - *heavy complex files*
 - *challenging to deal with*
- Tracking of the queries is not on point
- Query shared with the teams in a redundant way:
 - *the same query can be flagged several times*
 - *the query can be reported through reports, CRA, eCRF and central lab systems*

On top of working on streamlining the protocol, train the sites and improve communication ...

... new approach needed ...

Next steps to improve the query resolution



... we are getting rid of excel and using case management system instead where the queries will be handled and all interactions will have an audit trail = improve the communication and oversight between the most important actors and improve the query resolution timelines

Case ID	Status	Assignee	Study	Site	Subject ID	Visit name	Case Type	Case subtype	Case title	Created	Due date	Vendor name	Dataset name	Tags
CDR0002957	Open	(empty)	WN42349	338954	850102	Week 24	Reconciliation	Sampling	Missing sample	24/05/2022 01:40:02		Eurofins Genomics Europe Genotyping A/S...	MNFCOVA	Add Tag...
CDR0003072	Closed	(empty)	WN42349	338954	850102	Week 48	Reconciliation	Sampling	Missing sample	24/05/2022 01:40:22		Eurofins Genomics Europe Genotyping A/S...	MNFCOVA	Add Tag...
CDR0003257	Open	(empty)	WN42349	338954	850102	Week 24	Reconciliation	Sampling	Missing sample	24/05/2022 01:40:54		Eurofins Genomics Europe Genotyping A/S...	MNFCOVA	Add Tag...
CDR0002254	Open	(empty)	WN42349	338954	850102	Screening/Baseline	Reconciliation	Sampling	Missing sample	24/05/2022 01:37:58		Eurofins Genomics Europe Genotyping A/S...	MNFCOVA	Add Tag...
CDR0003542	Open	(empty)	WN42349	338954	850102	Week 24	Reconciliation	Sampling	Missing sample	24/05/2022 01:41:45		Eurofins Genomics Europe Genotyping A/S...	MNFCOVA	Add Tag...
CDR0003473	Open	(empty)	WN42349	338954	850102	Screening/Baseline	Reconciliation	Sampling	Missing sample	24/05/2022 01:41:24		Eurofins Genomics Europe Genotyping A/S...	MNFCOVA	Add Tag...

CDR case - CDR0002957

Case ID: CDR0002957

Owner: [input field]

* Reported on behalf of: Sophie Bloemendal gaulties sophie.bloemendal@roche.com

Due date: [input field]

Case Type: Reconciliation

Case subtype: Sampling

* Case title: Missing sample

* Description: [Lab]: Sample collection is reported in eCRF but the corresponding sample has not yet been received by the lab. If the sample has been shipped please provide the airway bill number and the accession number that belongs to the sample into the response box of the query.

Status: Open

* Assignee: [input field]

Assignee Functional Group: [input field]

Internal ID: missing_sample.12801132.Biomarker serum.Predose

Imported from: RULEE

Protocol deviation: -- None --

Parent: [input field]

Doing now what patients need next