

The background is a collage of medical and scientific imagery. It includes a stethoscope, several white pills, a calculator, and a line graph. The overall color scheme is a mix of teal, blue, and light green, with a semi-transparent grid overlay.

Health Science, Clinical Research

Time goes fast, are you really ready for unblinding?

DH05

Health Inspired,
Quality Driven.

Stijn Vermeylen
Team Manager Secure Data Management
Phuse EU Connect - 13-16 NOV 2022

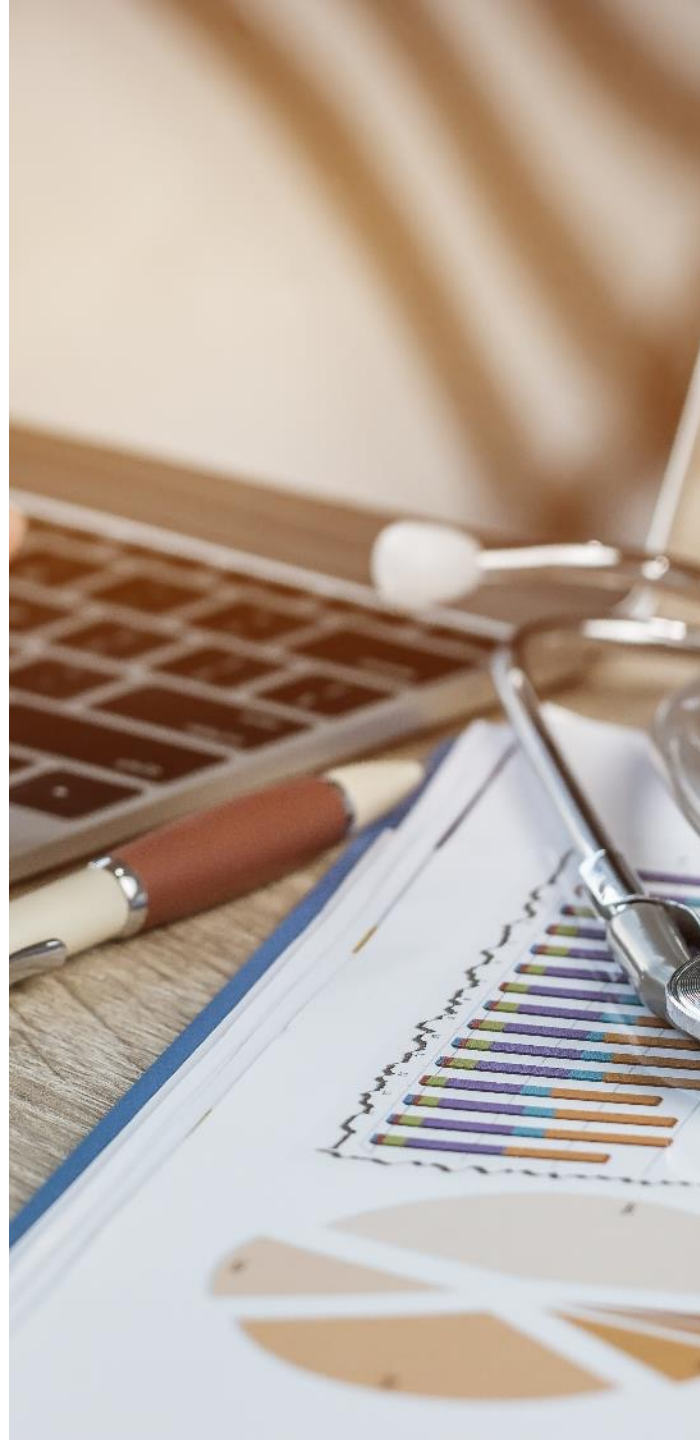


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Agenda

- Introduction
- Data Flow
- Handling Unblinding Data
- Conclusion



01 INTRODUCTION



Clinical research today

- Complex study designs
- Complicated data and multiple datastreams
- Numerous stakeholders
- Strict regulations
- Short timelines



In drug development, time is precious ...

Healthcare 2019: Expert Expectations for the New Year

The Financial & Business Case for Transformation

Monkeypox Virus outbreak in UK



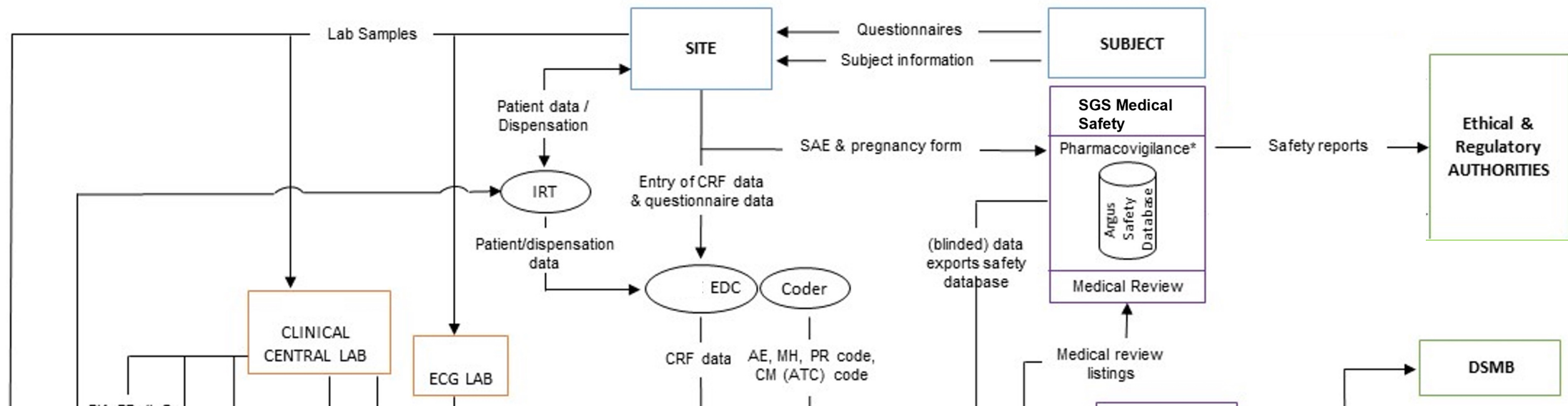
by Ankit Agrawal



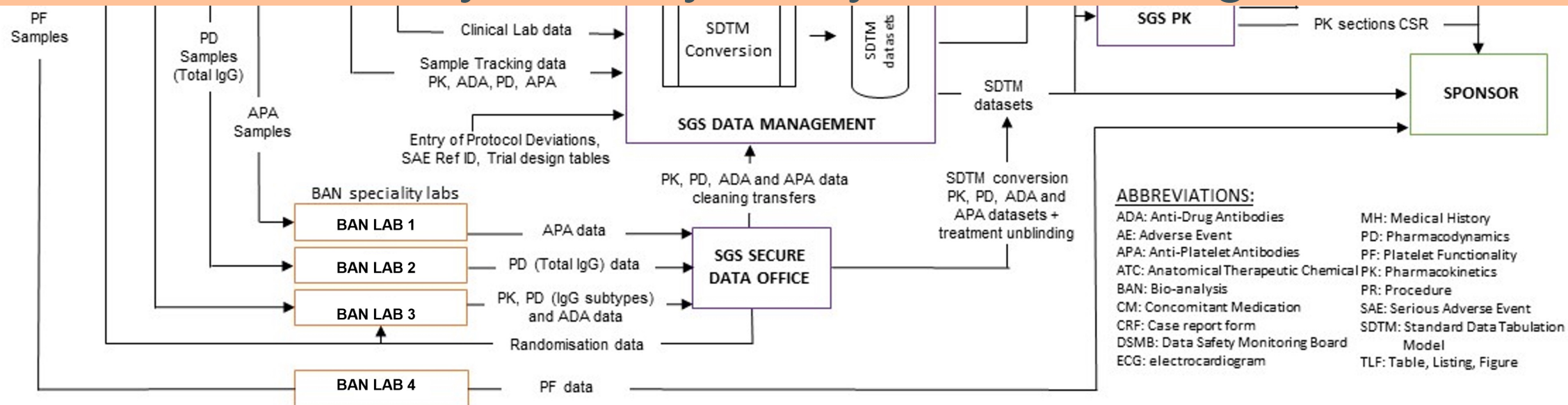
MEDICINES SHORTAGES NEARING CRITICAL POINT



SGS



Are you really ready for unblinding?



ABBREVIATIONS:

ADA: Anti-Drug Antibodies

AE: Adverse Event

APA: Anti-Platelet Antibodies

ATC: Anatomical T

BAN: Bio-analysis

CM: Concomitant Medication

CRF: Case report form

DSMB: Data Safety Monitoring Board

ECG: electrocardiogram

MH: Medical History

PD: Pharmacodynamics

PF: Platelet Functionality

al PK: Pharmacokinetics

PR: Procedure

SAE: Serious Adverse Event

SDTM: Standard Data Tabulation

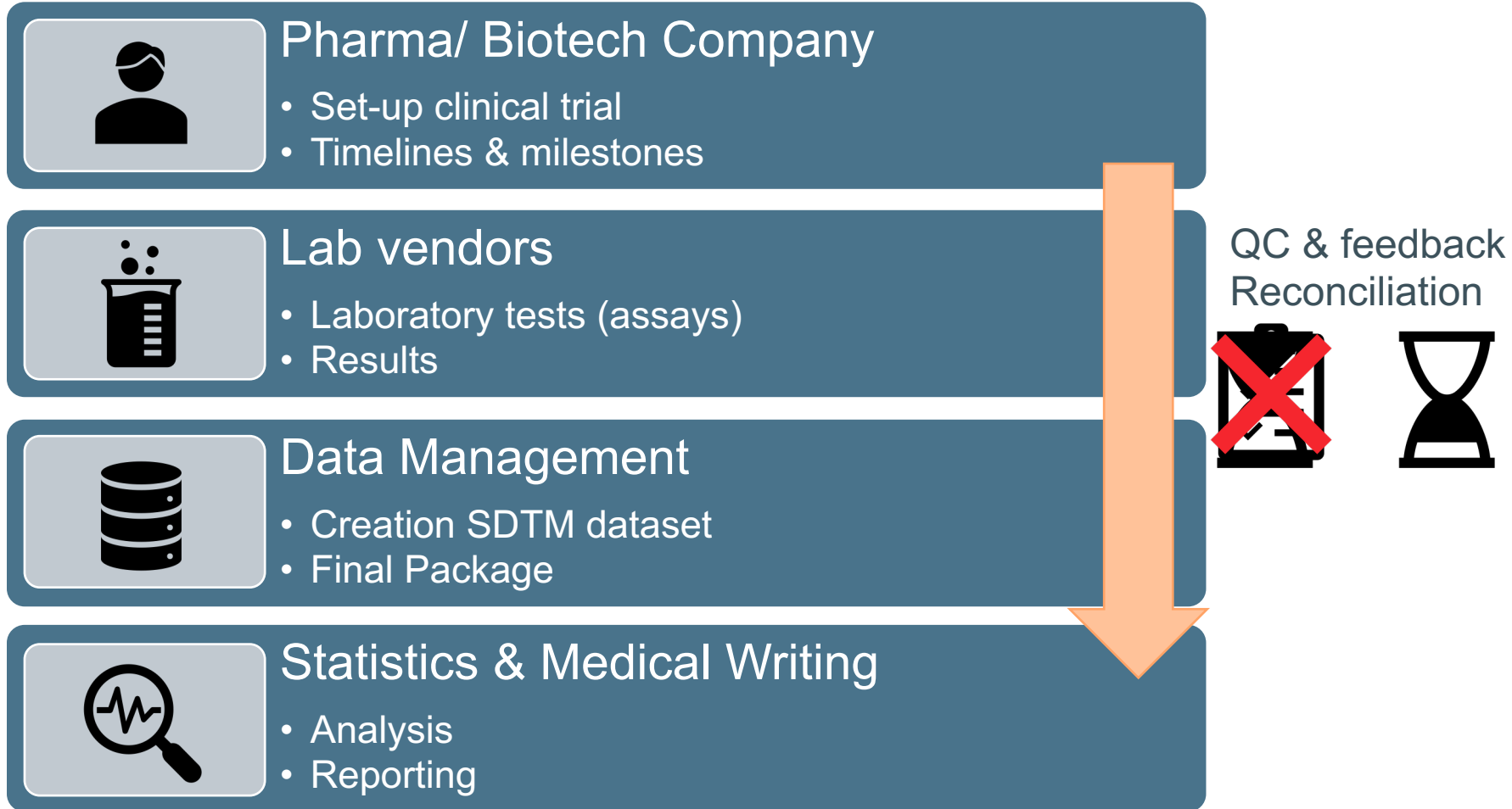
Model

TLF: Table, Listing, Figure

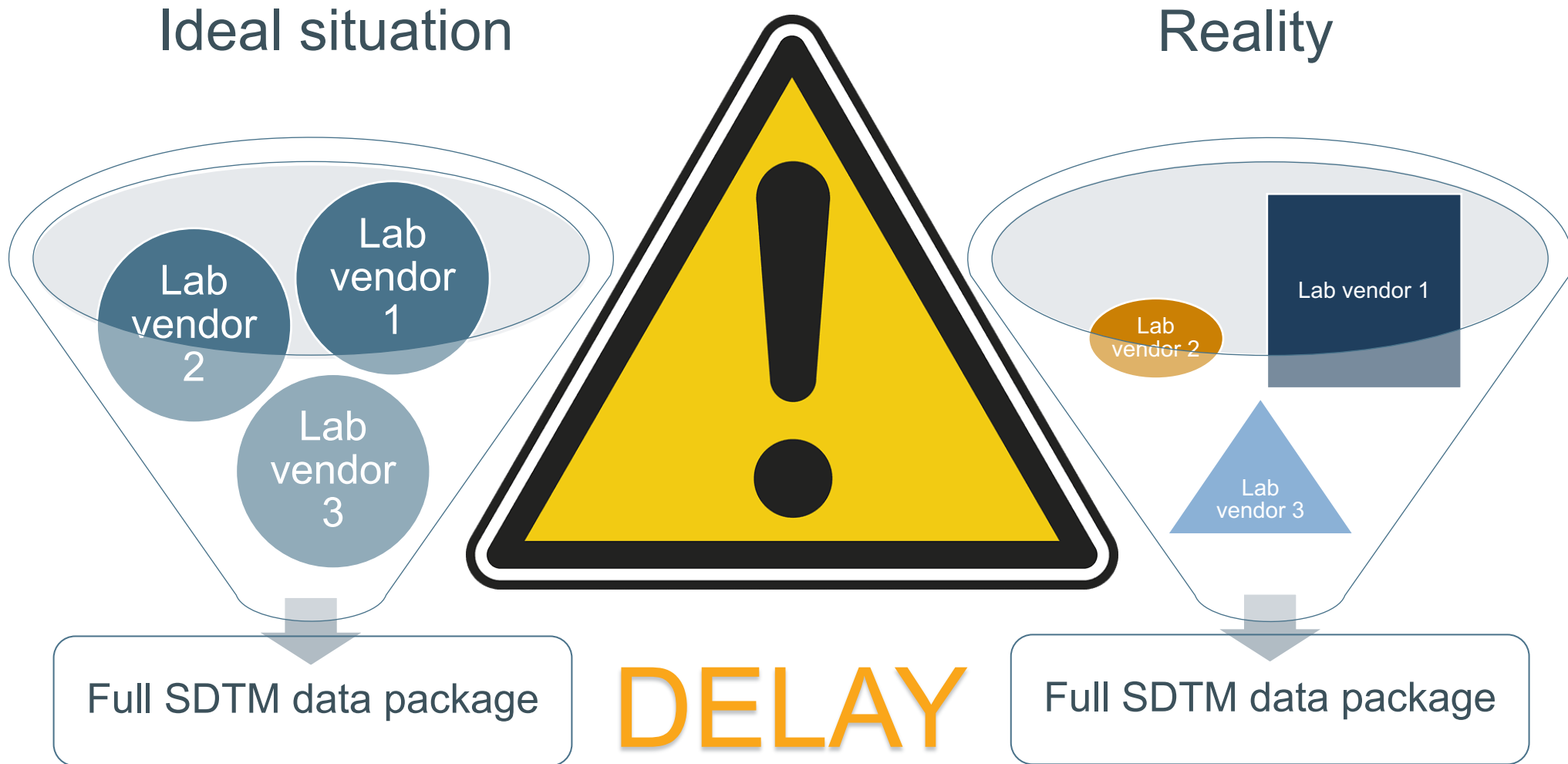
02 DATA FLOW



Data Flow



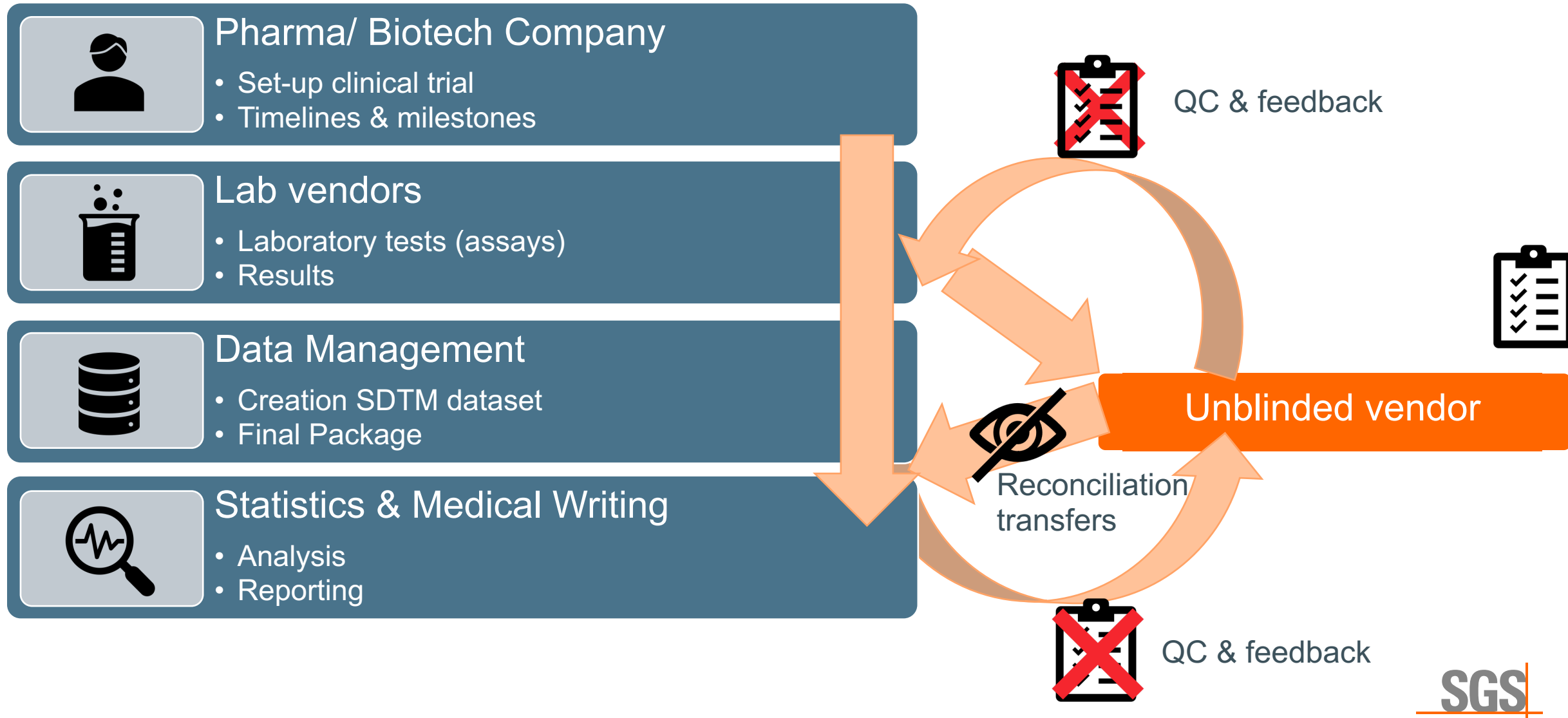
Data Flow



03 HANDLING UNBLINDING DATA



Handling unblinding data



Handling unblinding data

- At start of a clinical trial
 - Vendor database vs CRF database
 - Creation of DTA between vendor, unblinded vendor and DM CRO
 - Format of transfer
 - Frequency of transfer
 - Completeness of transfer (CDISC and statistical compliance)
 - Transfer location
 - Contact information
 - Test transfers

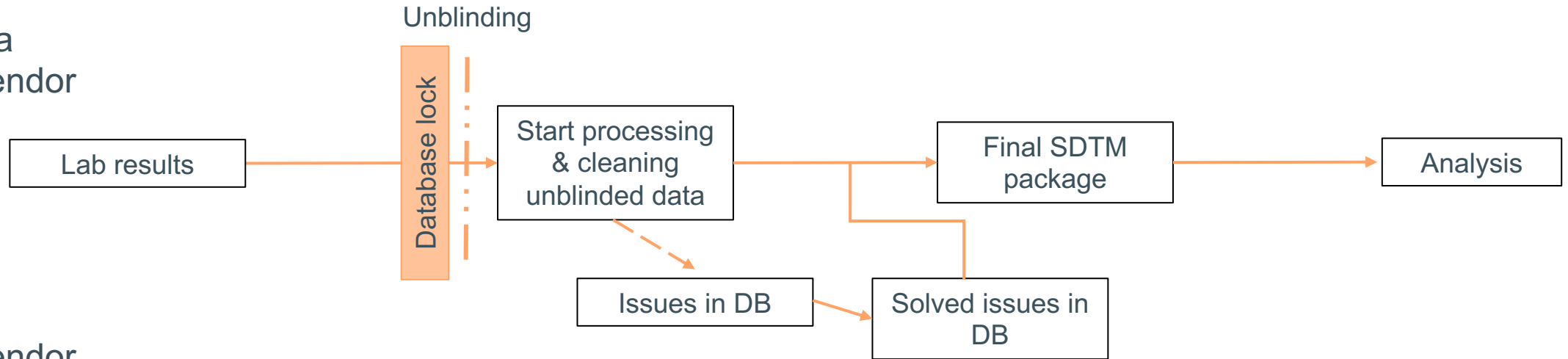
Handling unblinding data

- During conduct of a clinical trial
 - Transfers
 - Cleaning transfers
 - Reconciliation with sampling data from eCRF
 - Prior to starting analysis
 - Scrambled transfer
 - Early preparation of analysis programs
 - Prior to database lock
 - All transfers are QC'ed before release
 - Validated system
 - Data cleaning
 - Releases to Unblinded, independent group
 - Evaluations/ decision making
 - IDMC, DSMB, SMC release
- At time of unblinding
 - Transfer to DM CRO (at database lock)

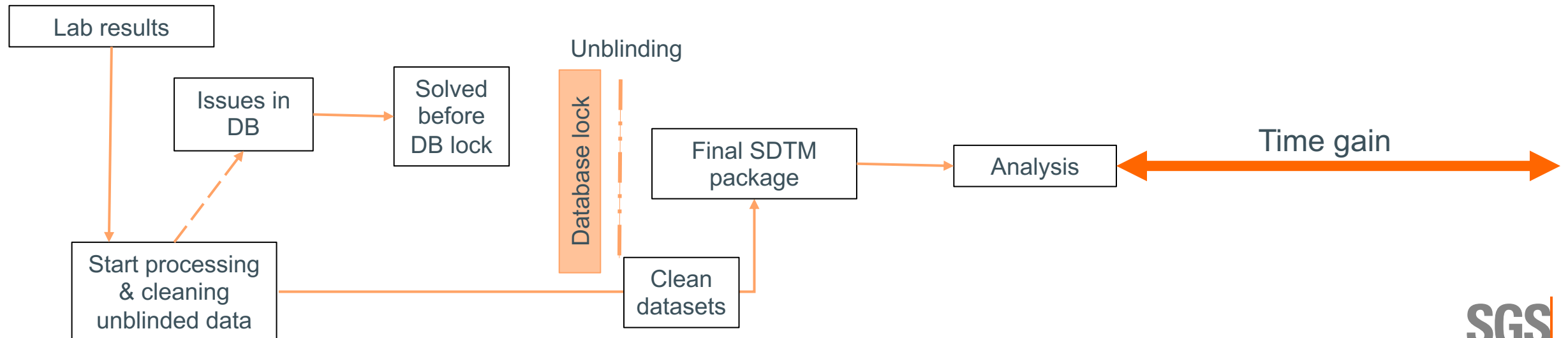


Database Lock Timelines for Blinded Data

Without extra
unblinded vendor



With extra
unblinded vendor



Case study examples

- Cleaning unblinding data on restricted eCRF page

USUBJID	Assigned Medkit n°	Dispensed Medkit n°
001	1234	1234
002	2345	2345
003	3456	4356

Specify all Unique Treatment Label Identifiers Used for this Preparation

Treatment Label ID

? Please verify medkit number

- Identify medication misallocations
 - Use of medication kit list to identify treatment switches

Case study examples

- Early detection of issues in vendor file
 - Format not according to DTA
- Preparation of SDTM compliant dataset
 - LBSTRESU: conversion to SI units in compliance with UNIT Codelist

Vendor result file
after conversion to
SDTM

STUDYID	DOMAIN	USUBJID	LBTESTCD	LBORRES	LBORRESU	LBSTRESC	LBSTRESN	LBSTRESU
STUDY-X	LB	1	TEST A	0.1	g/mL	100	100	g/L
STUDY-X	LB	1	TEST A	5	g/mL	5000	5000	g/L
STUDY-X	LB	1	TEST A	7	g/mL	7000	7000	g/L
STUDY-X	LB	1	TEST A	10	g/mL	10000	10000	g/L
STUDY-X	LB	1	TEST A	NEGATIVE	g/mL	NEGATIVE		g/L

Case study examples

- Dataset merging issues
 - Missing data in vendor result file or in sampling records from eCRF
 - Mismatches
 - Duplicate records

Sampling records
from eCRF



Vendor result file
after conversion to
SDTM

STUDYID	DOMAIN	USUBJID	PCREFID	PCTESTCD	VISIT	PCDTC	PCTPT	PCTPTREF
STUDY-X	PC	1	1	DRUG A	WEEK 1	2022-02-11T14:40	PREDOSE	DOSE
STUDY-X	PC	1	2	DRUG A	WEEK 1	2022-02-11T15:50	1H	DOSE
STUDY-X	PC	1	3	DRUG A	WEEK 1	2022-02-11T16:50	2H	DOSE
STUDY-X	PC	1	4	DRUG A	WEEK 1	2022-02-11T18:50	6H	DOSE
STUDY-X	PC	1	4	DRUG A	WEEK 1	2022-02-11T18:50	6H	DOSE

STUDYID	DOMAIN	USUBJID	PCREFID	PCTESTCD	VISIT	PCDTC	PCTPT	PCTPTREF
STUDY-X	PC	1	2	DRUG A	WEEK 1	2022-02-11T15:50	1H	DOSE
STUDY-X	PC	1	3	DRUG A	WEEK 1	2022-03-11T16:50	2H	DOSE
STUDY-X	PC	1	4	DRUG A	WEEK 1	2022-02-11T18:50	6H	DOSE
STUDY-X	PC	1	5	DRUG A	WEEK 1	2022-02-11T20:50	8H	DOSE

Case study examples

- Samples of placebo subjects not always analyzed
 - Sending result file to blinded party: unblinded
 - Populate with “not analyzed”

Sampling records
from eCRF



Sampling records
from eCRF, merged
with results

USUBJID	ISORRES	ISSTAT	ISREASND
001			
002			
003			

USUBJID	ISORRES	ISSTAT	ISREASND
001	1.5		
002		NOT DONE	NOT ANALYZED
003		NOT DONE	NOT ANALYZED

04 CONCLUSION



Conclusion

- Being ready for unblinding means
 - Reduction of data issues after unblinding
 - Increase in data quality
 - Less risk of unblinding during the study (unblinded vendor as buffer)
 - Fast timelines towards analysis
 - No unfortunate surprises
- How?
 - Ensure that there is a clear data flow
 - Clear timelines and communication between parties involved in that data flow
 - Handle and clean blinded data during study conduct (by an unblinded vendor)
 - Prepare datasets and input files for analysis prior to unblinding



Questions?

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