

Contents



Nycomed: a Takeda Company

1. Integrating clinical trial data
2. Working with CROs
3. Current operating model in Data Integration Standards
4. Conclusion and experience

Legacy Nycomed

- Focus area: Core expertise in gastroenterology, inflammatory, respiratory and pain
- Partnering was an essential part of the business model
- The pipeline was built from own research and through co-developments with partners.
- Effective from October 1st 2011, Nycomed is part of the Takeda group



Disclaimer



Nycomed: a Takeda Company

The shared content of this presentation is that of legacy Nycomed.
It does not reflect the R&D or CRO experience of legacy Takeda.

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The data asset of Nycomed

- Clinical Trial data are an essential asset of Nycomed.
- Providing integrated data collected from Clinical Trials requires data conversion and standardisation processes
- So far CDISC CDASH, SDTM and ADaM standards were adopted
- The data are stored and integrated in a Clinical Data Warehouse (compliant to Nycomed QMS and GCP / ICH E6)

Nycomed Data Standards

- CDISC SDTM and ADaM
- Code lists
- Processes / rules

Data Warehouse

- Data integrity, comparability
- Controlled access to data
- Data security and compliance

Data Integration Standards team

- Data Integration Manager (DIM)
- SAS programmer
- Data Warehouse Manager

Data Exchange

- Definition of standards and management of data exchange
- Support data submissions to regulatory authorities

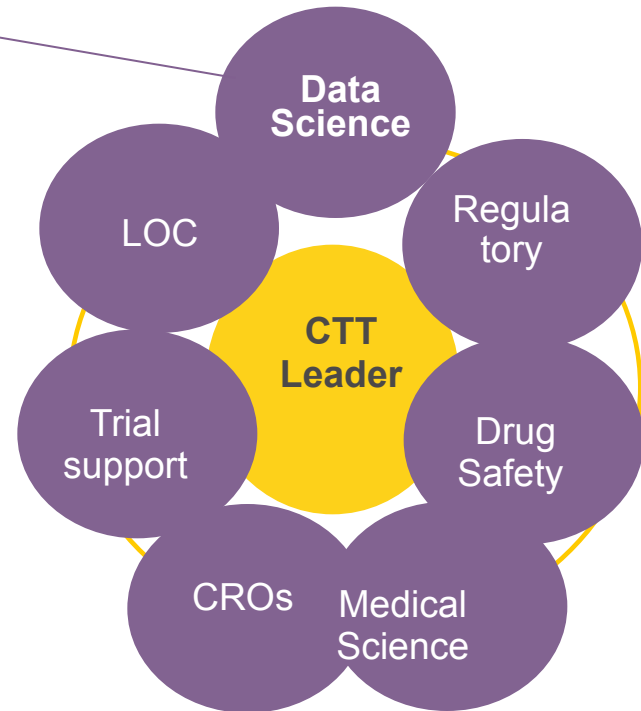
CRO collaboration

- Planning of data standardisation
- Definition of deliverables and processes
- QC agreement and oversight

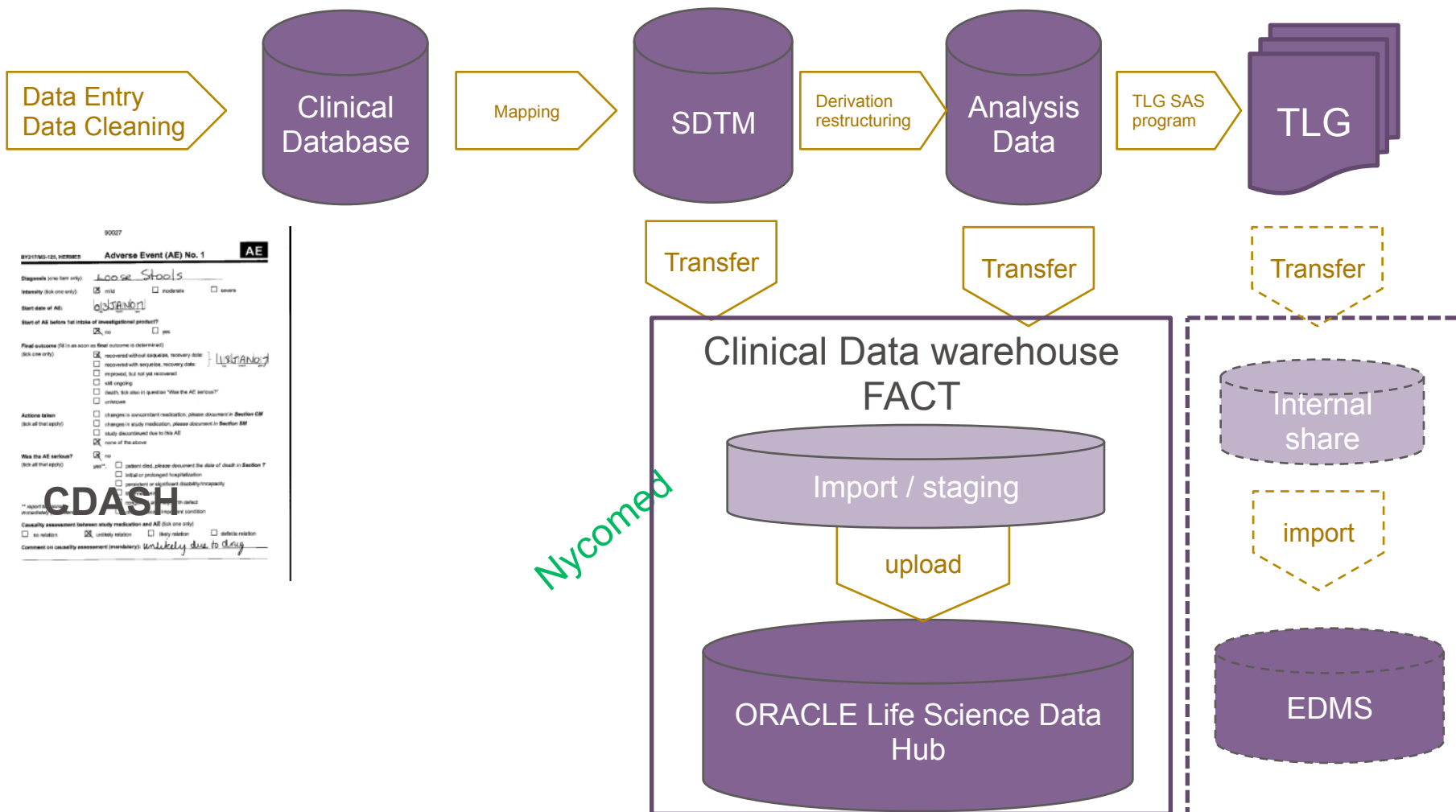
Our role in the Clinical Trial Team (CTT)

Data Science members / responsibilities:

- **Data Manager:** Data cleaning process and database set-up (to a large proportion)
- **Biostatistician:** Study specific statistical reporting and generation of analysis data bases
- **Data Integration Manager:** Data standardisation tasks



Trial data flow



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Outsourcing at legacy Nycomed



Nycomed: a Takeda Company

- Basis
 - High level outsourcing of non-strategic activities
 - lean R&D and CRO oversight model with strategic partnerships
- The CRO is accountable to
 - Provide deliverables according to agreement
 - Work according to GCP and CSV principles
- Nycomed is accountable for
 - Compliance to regulatory requirements
 - Oversight of the CRO to ensure quality in regards to task conducted for Nycomed

Most of Data Science tasks are completely contracted out . That requires:

- Strong partnership with CRO
- Building expertise on both sides (CDISC, requirements of regulatory authorities, ...)
- Nycomed to specify user requirements and to define clear sponsor standards
- Clear QC concept including definition of quality levels to be met

Since Nycomed is accountable for the compliance of the deliverables in regards to GCP and CSV, the CRO processes must fit to the according requirements

Basic assumption at legacy Nycomed

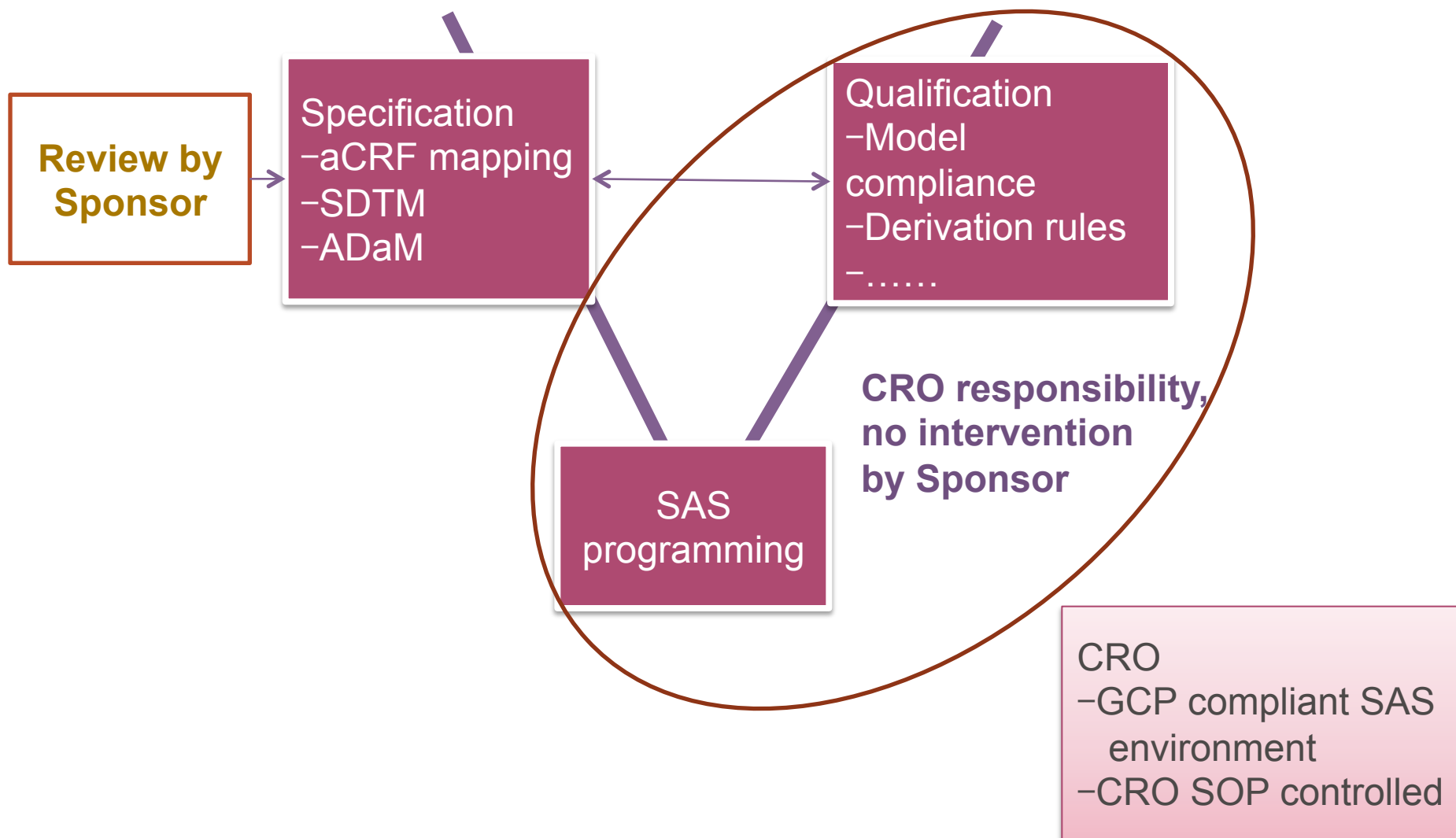
- The sponsor has the ultimate accountability for all outsourced processes
- The CRO works according to his processes and rules
 - The sponsor needs to know how the CROs works
 - The sponsor must ensure that all processes are covered by SOPs
 - The sponsor must ensure that the CRO SOPs do not contradict own standards

Creation of SDTM and ADaM datasets is basically a SAS programming task!

What does that mean?

- Nycomed adopted the V-model for computerised systems validation (CSV)
- Since a SAS program is a small Computer System we require that
 - CSV principles will be applied and thus
 - software development lifecycle documentation (SDLC) will be created for the validation of SAS programs

SAS programming: SDTM / ADaM datasets

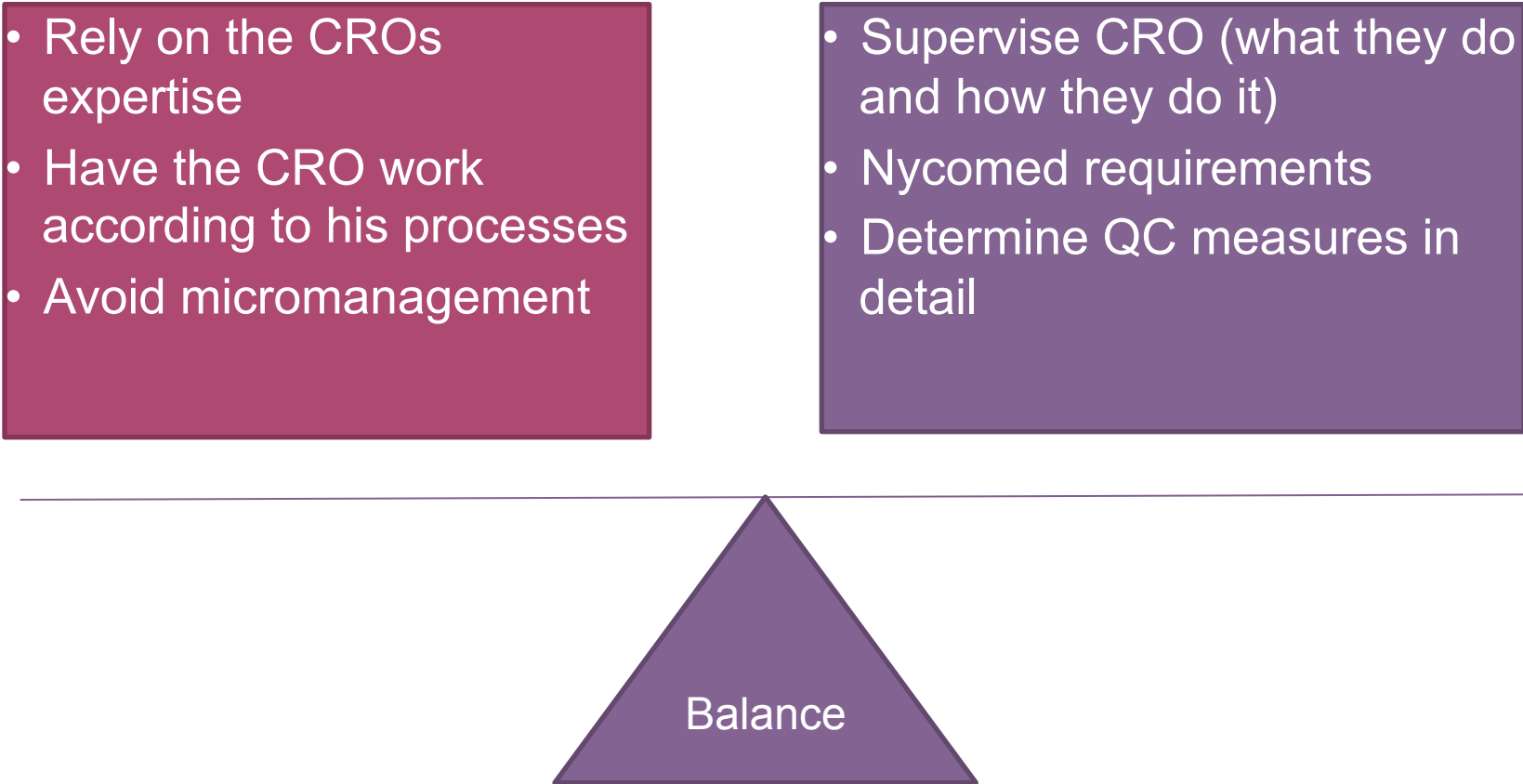


CRO efficiency

versus Nycomed oversight

- Rely on the CROs expertise
- Have the CRO work according to his processes
- Avoid micromanagement

- Supervise CRO (what they do and how they do it)
- Nycomed requirements
- Determine QC measures in detail



Balance

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Contracting out data standardisation tasks

The planning process and documentation for the data standardisation task is Nycomed SOP controlled

This SOP is mandatory for the CRO

The SOP basically describes the Data Integration Plan (DIP). This is the 'Data Management Plan' for data standardisation tasks

The Data integration plan (DIP)



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DIP content

General: Management plan for data standardisation

- Contacts and communication details
- Agreements about CDISC standards
- Details about deliverables and responsibilities such as
 - Timelines
 - SOPs to be used
 - QC planning and documentation

Deliverables

specifications

QC plan and
report

Datasets
(SDTM ADaM)

Define files

Integration
Report

QC and oversight on deliverables



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CRO

Nycomed DIM

Nycomed Biostatistician

Validation / QC

- GCP compliant SAS programming according to CRO SOP.
- Validation / QC documentation
- Compliance checks (run opendcdisc.org checks and deliver report for SDTMs / ADaMs)

Oversight

- Compliance (check opendcdisc.org report after receipt of data)
- Consistency (cross check of aCRF, SDTM specs, SDM, Adam specs, Adams, define files)
- Completeness (QC and SAS programs, according to agreements in the DIP)

Verification

- Checks primary and secondary endpoint variables (correct application of rules as specified in SAP and ADaM specifications)

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Examples of issues



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Deliverable	Potential issues	Nycomed measures
Data Integration Plan	Relevant CRO SOPs are not available to Nycomed	As a minimum, SOP list is required as well as a trial specific QC plan
SDTM and ADaM datasets	CRO starts programming without approved specifications	Nycomed will not accept datasets
SAS programs	No clear agreement on delivery CRO claims intellectual property	Clear specification in MSA, contracts, SOPs and DIP
QC documentation	Qualification documentation is not provided/available or only on general level	DIP requires proofed validation evidence per program

- Mature CDISC standards and CDISC knowledge on both side is crucial
- Sponsor standards and QC concept are available and aligned with CRO
- Clear definition of deliverables and QC concepts
- Communication and partnership building – preferred provider concept
- **Contracting CROs for CDISC data standardisation is more than just referring to the current SDTM/ADaM standards**

Thank you



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BACKUP SLIDES

Working with CROs

