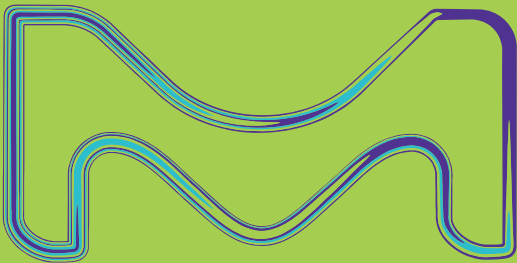


DH01: Finding the Right Balance – Data Management Surveillance in a Fully Outsourced Partnership Model

PHUSE connect, Amsterdam, 12-Nov-2019



*This presentation reflects the sole opinion and perspective of the presenter.
The slides do in no way present the position of Merck, their executive board
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MERCK

What does a „fully outsourced Partnership Model“ mean?

- » **Partnership Manual** describes the interface processes between the sponsor and the CRO
- » CRO is responsible for the operational execution of the clinical studies
- » CRO uses its own systems, processes, procedures and qualified vendors

What is the role of the Sponsor?

- » Merck Healthcare is mainly responsible for oversight tasks
- » According to ICH-GCP, the sponsor is responsible for the quality of the study, even if large parts are handed over to a CRO

Trial Oversight Plan (TOP)

**Documents
strategic
oversight approach
of all involved
sponsor functions**

- 1 In compliance with ICH-GCP and applicable regulations
- 2 Achieve defined levels of quality, timeliness and cost
- 3 Ensure inspection readiness

DM Vendor Surveillance Plan (DM-VSP)

...describes the planned surveillance activities to verify that the CRO is meeting the sponsor expectations regarding quality and timeliness.

DM-VSP Example

Trial Activities / Vendor Task	Surveillance Owner	Surveillance Method	Frequency	Expectation (if applicable)	Tasks Performed by Surveillance Owner	Documentation of Surveillance Tasks
Electronic Case Report Form (eCRF) development	SPDM	Review	on initial version and all amended versions	eCRF must match Clinical Study Protocol (CSP) requirements, eCRF should follow current Merck General Data Standards version and Therapeutic Area Data Standards version, if available. CRO will perform UAT of study database and provide summary report to Merck.	Merck will review draft eCRF and provide comments. Merck will also participate in the Design Review Meeting with trial team to finalize eCRF. Merck will review and sign off UAT summary report.	eCRF review log and UAT summary report (will be stored in the Clinical Data Repository)

Integrated Data Review Plan (IDRP)

...is used to identify, assess, control, communicate and review the risks associated with the clinical study during its lifecycle to provide quality data fit for purpose.

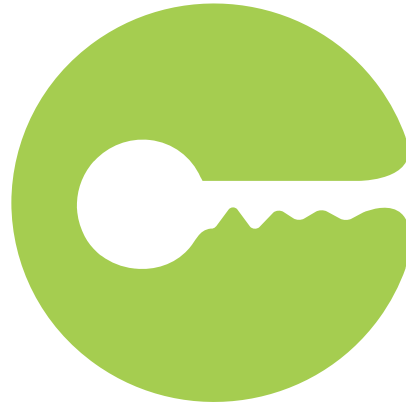
Aim of the IDRP



What is considered a Key Data Point?



Patient's safety



Primary & secondary
objectives



Special relevance

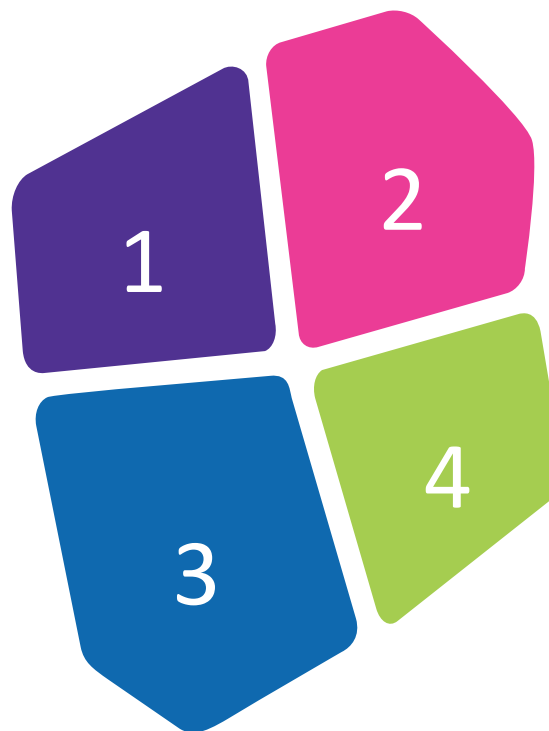
IDRP Structure

ID.No.	Data Point	eCRF form/ External vendor	Description of the failure/risk	Probability of Failure (1-3)	Severity of Failure (1-3)	Risk Criticality	Risk Mitigation Actions	DM	Medical	Safety	CRA	Stats	Vendor	Tool / Source of data	Study Plan
1	Assessment of Response to Treatment (based on RECIST 1.1)	SOLD/EOR/IRRC	Wrong EOR or target lesions calculation (sum of longest diameters for RECIST, modified irRC)	3	3	9	Queries raised by DM to capture wrong assessments Assessments reviewed by Medical	X	X					eCRF	Validation Specifications (e.g. Edit Checks) Medical Review & Supervision plan
2	Assessment of Response to Treatment (based on RECIST 1.1)	TMTL	Error when entering measures in eCRF (entry of longest diameters/short axis)	1	3	3	Queries raised by DM to capture wrong assessments Assessments reviewed by Medical	X	X					eCRF	Validation Specifications (e.g. Edit Checks) Medical Review & Supervision plan

IDRP Benefits

Common understanding
of quality expectations
at different study
milestones

Ensure alignment
across functions



One central document
referencing all cross-
functional cleaning steps

Focus on critical variables
impacting study endpoints

Clean Patient Tracker (CPT)

Monitoring of data collection & cleaning status on a patient level

Data Health Reports (DHR)

Cleaning status at site/country & study level

Projections to verify DBL readiness at a given timepoint

SDTM Review

**All aCRFs /
SDTM data sets
must follow the
sponsor data model &
the sponsor SDTM
Standards**

- 1 SDTM review checklist
- 2 Pinnacle 21 review template
- 3 Structure Quality Checks (SQSP)
- 4 Centrally stored consolidated issue log

Data Quality Surveillance Plan (DQSP)

...defines what kind of independently developed and programmed standard and study-specific checks will be performed on the delivered pre-cleaned SDTM data in order to check the level of data quality that has been achieved.

DQSP process

- 1 **Run** DQSP checks on pre-cleaned SDTM data
- 2 **Review** DQSP outputs
- 3 **Align** with different functions on the detected findings
- 4 **Provide** consolidated feedback to CRO
- 5 **Request** action plan & associated timelines
- 6 **Monitor** error rate over time

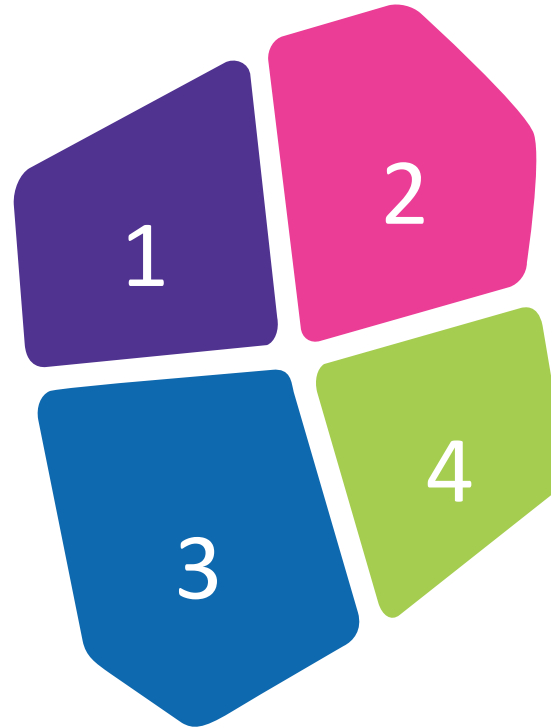
Periodic Data Review Meeting (PDRM)

...to assess on a regular basis the completeness and quality of all study related data as defined in the IDRP including the data status of discontinued subjects.

PDRM Benefits

Joint team review,
quality and risk
assessment

Database lock timelines
reduced for critical
database locks



Verification that all
cleaning activities are
conducted as planned

Common understanding
of quality expectations

Surveillance in a fully outsourced Partnership Model - What are the challenges?



Balance



Alignment



Communication



Resources

Balance



Challenges

- » micro-management vs. functional surveillance
- » find the specific points that trigger more in-depth reviews and activities

Balance



Possible solutions

- » define fixed quality gates for data content, SDTM structure & operational data
- » implement cross-site calls for knowledge sharing

Alignment



Challenges

- » CRO SOPs vs. Partnership Manual
 - » different approach on how to handle certain tasks
 - » mismatch of responsibilities
- » work not performed according to shared concept

Alignment



Possible solutions

- » align processes
- » conduct regular F2F cross-company alignment meetings

Communication



Challenges

- » decisions are taken at different levels of the partnership
- » multiple communication channels

Communication



Possible solution

- » define cross-company communication pathway across all relevant stakeholders

Resources



Challenges

- » retention of dedicated resources
- » intensive training on sponsor standards needed

Resources



Possible solutions

- » increase team stability at program level to...
 - » profit from synergies across studies
 - » cover for unforeseen shortages
 - » flexibly assign resources to projects

Conclusion

- ✔ excellent cross-functional & cross-company collaboration is key
 - ✔ awareness of data context & immediate cross-functional communication of critical findings
 - ✔ communication of lessons learnt to ensure cross-study consistency
 - ✔ model allows for working hand-in-hand & continuing to grow together
-
- » Sponsor retains overall ownership & accountability for the study
 - » Sponsor is ultimately responsible for the quality of the study



Any Questions



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