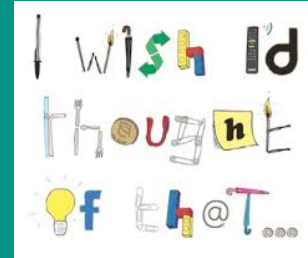




PhUSE 2016

**PD06: Program-level
Programming Strategy**



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Program Management

Program Objective

Grouping of Studies

Governance

Hierarchy

Planning

Financial Management

Infrastructure



Terminology

A **Program** will be **two or more Studies**, grouped together based on a set of key characteristics, and managed collectively.

Studies within a program do not necessarily need to be interdependent or even related, but are managed together to achieve a collective objective.



Program Objective

Is it necessary for the studies be grouped?

What is the goal?

What are the benefits/risks?



Consistency

Do we need to pool data from multiple studies?

Do we need the analysis to be consistent?

Are there other programs in place that can be leveraged?

Have we worked on similar studies in the past?

Time

Do the programming/reporting timelines make sense?

Do we have parallel or overlapping reporting events?

Cost

Is there a need to keep programming costs down?

Will upfront programming investment be needed?

Will we realize the benefits of any upfront work?

Grouping

Is there a need to group the studies within the program? If so, how?

What is common across all studies?

What is common across some studies or partially overlapping?

What is different or unique?

Commonalities and Differences

Group by drug compound, indication or phase?
What components of the analysis are the same or different (safety/efficacy/other)?

Is there known differences in the data?

Standard versus non-standard eCRF design?
SDTM versus non-standard?



Timing

Does the timing of the studies overlap?
Are there any ordering or prioritization factors?
Will there be a first or benchmark study?

Governance

What structures are needed?
What are the relationships?
Who are the decision-makers?

What controls are needed?
What practices are required?



People

Program Level Lead Programmer?
Do the roles between the CRO and Sponsor align?
Do they need to?
Independent study teams or a program level team? Domain experts working across studies?

Controls & Practices

Is consistency an objective?
Are program level reviews needed? If so, by whom?
What program level code or utilities are required?
How will program level code be controlled and maintained? How will use be monitored?

Hierarchy



Program Level: Lead Programmer

- Program Level coordination with the Biostatics Program Lead
- Sets and reviews the programming implementation strategy in line with the program objective(s)
- Establish program level processes, tools, and training relative to programming.
- Establish / Contribute to templates (e.g. project plans, status reports, metrics, KPIs) relative to the programming effort.
- Coordinates activities across studies to ensure program level objectives are met.
- Ensures program level code is released into production according to the timing needs of each study
- Contributes to program level standards (e.g. review of SAP/mocks/ADaM specs/TLGs)
- Oversees the set-up, integration, use and maintenance of program level derivations (e.g. program level ADaM specs) and program level code / macros

Planning 'Best Practices'

- Establish Planning Tools and Templates for the Program in advance.
- Develop a process and schedule for each.
 - Who does the Program Level Lead need to communicate to?
 - What information needs to be shared?
 - On what frequency?
- Consider a 'bottom up' approach for plans and reports.
 - Program level reports should not be a burden on individual study teams.
 - Consider the tools and reports that the study team will be using, then consider what can be leveraged / rolled-up?
 - More likely to receive current information and gain higher compliance



Infrastructure

People

- Sponsor
- Management
- Program Leads (Clinical, DM, Biostatistics, MW)
- Study Leads
- Programming Team
- Support and Administrative Staff



Tools

- Platforms
- Shared Workspace
- Macros and utilities
- Tools and templates
- Reports

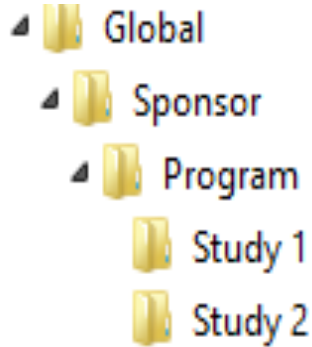


Process

- Training/on-boarding
- Communication Plans
- Program Level Standards
- Review Processes
- Change Management Processes



Programming Environment



- **Global**
Contains global macros, ADaM template code, utilities and documentation.
- **Sponsor**
Contains sponsor level programs, macros, utilities and documentation.
- **Program**
Contains program level programs, macros, utilities and documentation.
- **Study X**
Contains study level programs, macros, utilities and documentation.

- At the Sponsor / Program level, items are either created in advance, or can evolve over time (e.g. created at a study level and 'promoted' upward).
- The benefits of this approach is greater consistency, plus reduced effort when program wide changes are needed.
- However, consideration should be given to time/cost/impact associated with maintenance and backward compatibility when establishing program level code.

Financial Management

Will program governance have a cost/overhead? Is it budgeted?

How will the costs be managed?

How and when will costs be reported?

How will future costs be requested/
approved?



How will program versus study
profitability be calculated?

- Ensure Program management is budgeted
- Sponsors will look for opportunities to provide cost efficiencies due to synergies.
- Ensure all assumptions underpinning the synergies are clear, agreed and documented.
- Make the sponsor aware that change orders may occur if synergy assumptions are under realized.
- Anticipate greater effort during program start-up, and on the first study.
- Consider reporting profitability for the entire program, as this may be a better indicator of financial performance.
- Be aware of the risks within this type of approach e.g. study cancellation.

Case Studies

Case Study A

CDISC Legacy Data Conversion

Same Compound

Multiple Indications

Phase I -III

44 studies

Objective: Convert 44 legacy studies to CDISC SDTM and ADaM for submission and ISS/ISE

Case Study B

Individual Study Analysis

Same Compound

Multiple Indications

Phase Ib/II

7 studies

Objective: Meet the reporting needs for each study, ensuring consistency across studies, realize time and cost efficiencies

Case Studies: Program Objectives



Case Study A	Case Study B
• Consistency across studies • Ability to pool data • All studies to be delivered as a final product • No one study had priority over another • Time/Efficiency/Cost was a consideration	• All studies to be delivered based on individual needs • No single study had priority over another • A benchmark study for the program was identified to establish the program standards • Consistency across studies was expected • Ability to pool data • Time/Efficiency/Costs were considerations • Additional studies to be added overtime

Case Studies: Grouping



Case Study A

- Initial sub-grouping criteria
 - Indication
 - Phase
 - CRF pages / domains
 - 9 subgroups became apparent
 - 2 studies selected as initial pilot studies (since both covered majority of CRF domains)
- Plan was
- to have one team work on the 2 pilot studies initially.
 - followed by the 9 subgroups working in parallel

Case Study B

- Initial sub-grouping criteria
 - Indication
 - Phase
 - 1 Benchmark Study
 - 5 studies considered similar for safety and efficacy
 - 1 study considered entirely unique
- Plan was
- for the first study in the program to set the standard
 - Followed by other studies that would adhere to the standard (with exception of the one study considered unique)

Case Studies: Governance and Management



Case Study A and B

Oversight and Structure

- Roles, Responsibilities and Expertise defined (e.g. Program Level Lead)

Communication Plan

- Roles, Counterparts and Relationships identified
- Decision and Escalation Paths defined
- Communication Plans and Tools defined
- Process controls identified

Risk Management Plan

- Actual and Potential Risks Identified
- Each risk assessed for impact and likelihood; Mitigation / Action Plans agreed

KPIs and Turn Around Timelines

- Project Plan Templates developed

Resourcing Plan

- Types of technical / non-technical support staff
- Resourcing forecast algorithms and assumptions defined

Case Studies: Infrastructure



	Case Study A	Case Study B
People	Lead Personnel identified/hired	
	Subgroup Teams established (internal and outsourced)	Core team of programmers established
Tools	• Shared Platforms / Workspaces / Repositories created for the Program and studies. • Programming Directory structures fixed across all studies. • Templates developed (project plans, status, KPI, issue/decision logs, financial reports).	
	• CDISC compliance and harmonization utilities identified, developed and tested	• Standard TLG mocks developed • Program level ADaM specification, including derivations • ICON global reporting suite (DIAMOND) used for TLG code • Program specific macros/template code, developed on the first study and 'promoted upward'

Case Studies: Infrastructure



	Case Study A	Case Study B
Process	Processes developed including: • CDISC SDTM and ADaM Deliverables from legacy data • Verification of Published CSR Results • Core Review of CDISC Deliverables (program level consistency review) • Others • Management of Study Files and Programming Directory Structures • Inventory process (tracking versions of documents, source data) • Version Control Process (documents, source data, programs, outputs) • Training plans	Processes developed including: • Governance of change requests on TLG standards • Set-up, use and maintenance of program level macros/code/utilities • Program Lead review process • SAP/mocks/ADaM and TLGs • Ensuring compliance with standards • Confirming study specific deviations • Others • On-boarding / Training plans • Standard KPI / TAT / Project Plans • Standard ICON documentation and quality control processes applied

Case Study A: Challenges & Successes



Success	Challenge
Subgroups enabled parallel activity and flexible resourcing	Inconsistency appeared across subgroups (e.g. SDTM mapping assumptions, extended controlled terminology)
Program Level Review successful in identifying and resolving inconsistencies	Program Lead review was a bottleneck in the process. The process required review and approval by the sponsor which was also a bottleneck.
Pilot study approach was successful as it provided early insight into resource needs, timelines, processes etc.	Budget, Resourcing, Tools and Processes changed/ adapted over time, and for various reasons
Risk management Plan well outlined	Unforeseen challenges arose
Roll-up reporting worked well (study to subgroup to program to sponsor)	Possibly too many leads / decisions makers / reviewers within the structure

Case Study B: Challenges & Successes



Success	Challenge
Standard Program level TLG mocks established.	Sponsor had not included all stakeholders / decision makers
The Change Management Process was well defined and implemented (often)	Governance from the sponsor was limited, and study teams deviated (often) from agreed standards.
The modular macro approach allowed flexibility for change.	Whilst the sponsor set the expectation for use of standards, they also wanted flexibility for change.
List of Tables (LoT) for each study classified the use of standard and non-standard usage, so metrics readily available to support change of scope	Under-realization of synergies resulted in change of scope.
Our standard turn around time included a milestone for 'TLG programs ready', so that we were in a position to react once reporting events were requested	Sponsor did not always know when their first reporting event would be needed, and delivery requests often communicated late.

Case Studies: CRO (My) Perspective

- Case study A is an example of a standalone piece of work entirely managed within the CRO, with limited stakeholders and decision makers.

- Case study B is the reality of drug development!



- Even with the best upfront processes in place, studies will be subject to change.
- Sponsor study teams will have multiple stakeholders, and many decision makers, with fast decisions and turn around needed.
- CROs should get to know their sponsors, and consider whether the sponsor is invested in a program approach. For example, will work pause whilst consensus is reached, or will an individual study always take priority?
- CROs should also consider if their sponsors are invested in standards. Will upfront investment in code/macros/utilities result in realization of any anticipated time / cost / efficiency benefits?

Closing Remarks



- Just because studies can be grouped together doesn't mean they should
 - Carefully consider all assumptions underpinning the program.
 - Stress test / risk assess these assumptions.
 - Consider all internal and external factors, as inevitably there will be a need to adapt / change.
- Sponsors will look for cost efficiency opportunities due to synergies; ensure that any synergy and discount assumptions are clear and documented.
 - Consider any overhead for managing the program. Whilst synergy discounts may lead to a cost saving for an individual study, there is a cost to managing a program.
- The role of the Program Level Programming Lead is to satisfy the criterion for which the program was set-up, not to manage the individual studies.

Thank you for listening.
Any Questions?



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