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Paper PD06

Program-level Programming Strategy – Oh, I Wish I'd thought of that Beforehand!!

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ABSTRACT

This paper will provide an overview of the principal differences between planning and delivering statistical analyses for a development program versus a single study. The focus of this paper will be on program level fundamentals, providing insight into strategy and approaches implemented at ICON. Topics considered in this paper will be program team structures and roles, program governance, program management, and program infrastructure and planning. We will also present case studies and lessons learnt, giving particular insight from a CRO perspective.

INTRODUCTION

Our industry uses different terminology such as study/ project / program / portfolio, and sometimes interchangeably depending on the organization. In this paper we will consider 'Studies' and 'Programs' per the below definitions

> *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.*

This aim of this paper is to describe some of the fundamental principals of program management, and how we can relate it to the Statistical Programming work we deliver on Clinical Trails. We also look at this via 2 case studies, and also give some considerations from a CRO perspective.

PROGRAM FUNDAMENTALS

The program funamentals considered in this paper will be considered under the below categories:

GENERAL CONSIDERATIONS

At the onset of the program, it is useful to make some general considerations.

Considerations	Statistical Programming Examples
Is it necessary for the studies to be grouped? What is the goal/benefit? What are the risks? 	Do we need to pool data from multiple studies? Do we need the analysis to be consistent? Is there a need to keep programming costs down? Do the programming/reporting timelines make sense? Do we have parallel or overlapping reporting events? Will an upfront programming investment be needed? Will we realize the benefits of any upfront work? Are there other programs in place that can be leveraged? Have we worked on similar studies in the past? Has the sponsor worked on similar studies in the past?

GROUPING

Once we have determined that there is a need, or indeed a benefit, to managing the studies as a program, some consideration can also be given to the grouping of the studies within the program.

Considerations	Statistical Programming Examples
Is there a need to group the studies within the program? If so, how should the studies be grouped? What is common across all studies? What is common across some studies (or partially overlapping)? 	Group by drug compound, indication or phase? Does the timing of the studies overlap? Are there resourcing constraints or considerations? 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? Is the data coming from the same / different source systems or vendors? Do all studies have the same CRT data structures (e.g. SDTM)?

GOVERNANCE

Good governance is critical to the programs success. Avoid overlapping roles and having too many decision makers. Endless attempts to achieve consensus, can prevent a program from achieving sustained momentum.

Considerations	Statistical Programming Examples
What structures are needed? What are the relationships within the structures? Who are the decision-makers? What controls are needed? What practices are required? 	Independent study teams or a program level team? Domain experts working across studies e.g. Safety/Efficacy or more granular (AE/Lab/../Eff)? Is a Lead programmer for the program required? If so, what is their role and responsibilities? Will program level reviews be needed? If so, who will perform these reviews and when? How is the program being managed within the sponsor company? Do the roles between the CRO and Sponsor align? Do they need to? What processes and tools are required? Is consistency a consideration? Will we create program level code or utilities? How will program level code be controlled and maintained?

HIERARCHY

Considerations should be given to the responsibilities of the Program versus the Study Level Lead Programmers.

Study Level: Programming Lead		Program Level: Programming Lead
• Review, agrees the delivery schedule for the study • Estimates the programming resources • Provides study specific training and support • Assigns programming tasks to the team • Ensures study deliveries are met on schedule, on quality • Manages study budget and costs (programming hours) • Maintains study documentation • Maintains reports (e.g. project plans, status reports, KPIs)		• Sets and reviews the program objectives w.r.t analysis and programming strategy • Establishes program level processes, tools, training. • Establishes 'Roll up' reports (project plans, status, KPIs). • Coordinates activities across studies to ensure program level objectives are met. • Oversees the set-up, integration, reuse and maintenance of program level derivations (e.g. program level ADaM specs). • Oversees the set-up, integration, reuse and maintenance of program level code / macros. • Contributes to program level standards (e.g. review of SAP/mocks/ADaM specs/TLGs)

PLANNING

Study level planning is assumed regardless of whether the study stands alone or within a program. Hence, for this paper, we will be considering Program level planning considerations of the Program Manager(s).

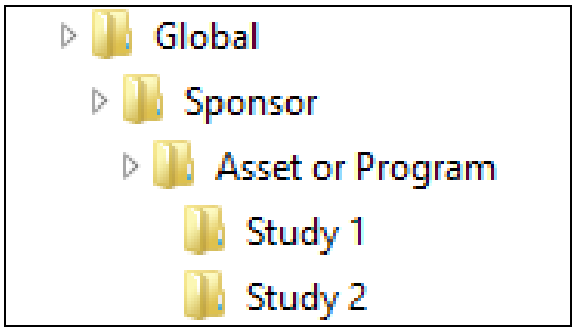
- Planning tools and templates for scheduling, status, resourcing, metrics, financial reporting, and so on, should be established in advance by the Program Manager(s).
- Create risk management and change management plans for the program.
- The process and schedule for each report should be developed.
  - Who do the program manager(s) need to communicate to?
  - On what frequency?
  - What information needs to be available from the study teams?
- Consider a 'bottom up' approach for plans and reports.
  - Program level reports should not be an additional overhead on individual study teams.
  - Consider what the studies are currently using, what can be leveraged / rolled-up?
  - Try to use same tools and reports for study level activities, as would be needed for the program.
  - Likely to receive current information and higher compliance

INFRASTRUCTURE

Under the context of this paper we will consider people, tools, and processes as infrastructure.

People	Tools	Processes
Consider the people required, for example: • Management • Program Leads • Study Leads • Programming Team • Support and Administrative Staff 	Consider the tools required, for example: • Platforms / Shared Workspace • Macros and utilities • Tools and templates • Bottom Up Reporting 	Consider the processes require, for example: • Training/on-boarding • Communication Plans • Program Level Standards • Review Processes • Change Management Processes 

Considering statistical programming infrastructure, there is likely to be a desire / need to share programs, macros, utilities, documentation across the program. At ICON, we have the below hierarchy in operation, with security controls at each level. Utilities, macros, template code and documentation can be stored at each level, accessed by other levels with the hierarchy, and we can apply read-write / read-only access controls as appropriate.



Global
Contains the global (non-sponsor specific) macros suite (DIAMOND macros). These are a set of modular TLG macros that are used across sponsors and studies. This area also contains the ICON ADaM template code, along with other utilities and documentation.

Sponsor
Contains sponsor level programs, macros, utilities and documentation.

Asset or Program
Contains asset or program level programs, macros, utilities and documentation.

Study X
Contains study level programs, macros, utilities and documentation.

At the Sponsor / asset level, these items are either created in advance of the study programming, or can evolve over time (e.g. created at a study level and 'promoted' upward).

Consideration should be given to time/effort/impact associated with maintenance and backward compatibility when establishing program level code. However the benefits are maintaining consistency and reduced effort for program level changes (making changes in one place)

FINANCIAL MANAGEMENT
Financial management is also a consideration. Whilst sponsors expect to receive discounts on subsequent studies within a program, considerations should also be given to the extra effort (and cost) required to manage a program of studies.

Considerations	Statistical Programming
Will program governance have a cost/overhead? Is it budgeted? If so, where? How will the costs be managed? By whom? How and when will they be reported? How will future costs be requested and approved? How will program versus study profitability be calculated? 	• Sponsors will expect discounts on subsequent studies due to anticipated synergies within the Program. • Ensure any assumptions underpinning the synergies are clear, agreed and documented. • Agree with the sponsor the implications of synergy assumptions being over/under realized. • At ICON additional costs to cover work effort of managing the program is applied evenly across the studies within the program. • We can anticipate higher effort during program start-up, and that the first study may not be as profitable as subsequent ones. • Consider reporting profitability of the program overall, as this may be a better indicator. • Also consider all risks within this model e.g. Study cancellation.

CASE STUDIES AND LESSON LEARNED

We have selected 2 case studies from within ICONs portfolio to demonstrate how we have implemented some of the Program Management Fundamentals; in this section, we also cover the successes and challenges for each case study.

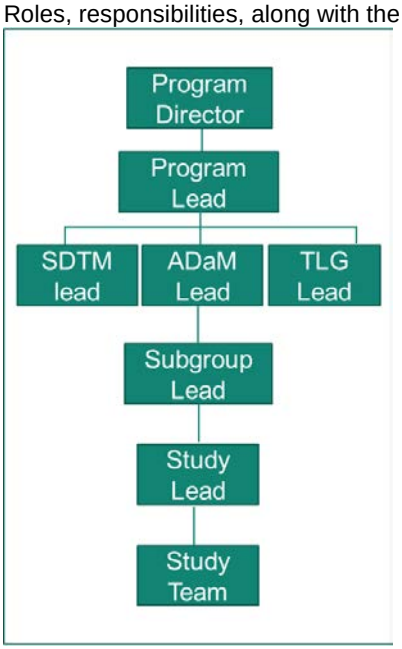
CASE STUDY A

Our case study A is a 44 study legacy conversion project. All of the studies are for the same drug compound, across different indications and phases. The objective was to convert the legacy studies to CDSIC SDTM and ADaM for individual study submission and also to pool some of the studies for an ISS/ISE. There was also a need to regenerate the TLGs, and perform quality control by comparing the reproduced TLGs to the original CSR TLGs.

<table>
<tr><th colspan="2">CASE STUDY A</th></tr>
<tr><td>General Considerations
  </td><td>• Consistency across studies.
• Ability to pool data.
• Ensure consistent results post conversion when compared to original study results.
• Quality/Time/Efficiency/Costs.
• All studies to be delivered as a final product.
• No one study had priority over another.
• Program to be broken down into sub-groups due to scale.</td></tr>
<tr><td>Grouping
  </td><td>• Sub-grouping criteria identified as
  • Indication
  • Phase
  • Number of Subjects
  • CRF pages
  • CRF domains

• Each study assessed against the criteria
  • 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.
• This purpose of the pilots was to validate the processes, resource algorithms, and timelines.</td></tr>
<tr><td>Governance and Management
 

  </td><td><u>Oversight and Structure</u>
• Roles, responsibilities, along with the required expertise was defined
 
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	Communication Plan
	• Counterparts and Relationships identified
	• Decision and Escalation Paths defined
	• Communication Plans and Tools defined
	  • Meetings (attendees, frequency, minutes, rules etc.)
	  • Timelines
	  • Reports (Status, Metrics, Financial)
	• Process controls identified and listed
	
	Risk Management Plan
	• Actual and Potential Risks identified
	• Risk Assessment performed (High/Medium/Low)
	• Mitigation / Action / Change Management Plans defined
	
	Resourcing Plan
	• Types of technical and non-technical support staff required identified
	• Resourcing forecast algorithms and assumptions defined

Infrastructure  	People • Lead Personnel identified/hired based on the expertise defined • Technical and non-technical resource forecasts determined and fulfilled Tools • Shared Platforms and Workspaces created for the Program and studies • Electronic Document Repository created • Standard Programming Directory structures defined • Shared utilities identified, developed and tested • Study Timeline (Project Plan) Template developed • Study Report Templates developed (status, KPI, issue/decision logs, financial reports). Process Processes developed including: • Management of Study Files and Programming Directory Structures • Inventory process (tracking versions of documents, source data etc.) • Version Control Process (documents, source data, programs, outputs) • Process for Creation and Validation of CDISC SDTM and ADaM Deliverables • Process for Verification of Published CSR Results • Core Process for the Production and Review of CDISC Deliverables (program level consistency review) • Training plans

CASE STUDY A: SUCCESSES AND CHALLENGES	
Studies within the subgroups were mostly consistent, but inconsistencies did appear across the subgroups.	
Program level review was required to harmonize across the program, but this task was a bottle neck.	
Sponsor review was expected, but limited capacity so again a bottle neck.	
Pilot study approach was beneficial as this provided insight on resource forecasts, timelines, processes etc.	
Budget, Resourcing, Tools and Processes changed/adapted over time, and for various reasons	
Roll-up reporting worked well (study to subgroup to program to sponsor)	
Too many leads / decision makers within the structure.	

CASE STUDY B

Our case study B is an example of a more standard type of Program that we would see at ICON. In this program there are 6 studies, all studies are for the same drug, however for different indications and across phase's I-III. The objective was to meet the reporting needs for each study, ensure consistency across studies, and also realize time and cost efficiencies.

<table>
<tr><th colspan="2">CASE STUDY B</th></tr>
<tr><td>General Considerations
  </td><td>

All studies to be delivered based on individual needs
No one study took priority over another
Consistency across studies was expected
Potential/Desire to pool data
Quality/Time/Efficiency/Costs were considerations
A benchmark study for the program was identified
The benchmark study would be the basis for all other studies
Programming for other studies would occur in parallel
Additional studies to be added to the program later
Regional alignment of staff required

</td></tr>
<tr><td>Grouping
  </td><td>

Sub-grouping criteria was identified as

Indication
Phase

Each study was assessed against the criteria

3 studies considered similar for both safety and efficacy
2 studies considered similar for at least safety
1 study considered entirely unique

Plan was for

The first study in the program was to set the standard
Other studies where to then follow the standard (with exception of the outlying study considered unique)

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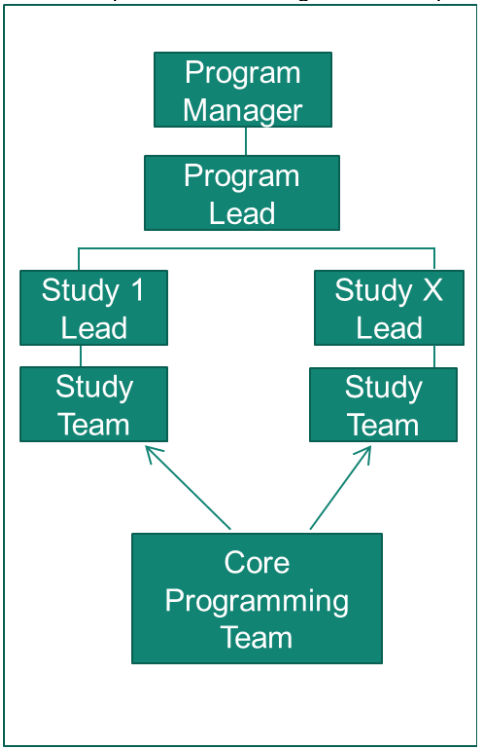
<tr><td>Governance and Management
 

 </td><td>
<u>Oversight and Structure</u>

Roles, responsibilities, along with the required expertise was defined



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	Program + Study Communication Plans
	• Counterparts and Relationships identified
	• Decision and Escalation Paths defined
	• Communication Plans and Tools defined
	  • Meetings (attendees, frequency, minutes, rules etc.)
	  • Timelines
	  • Reports (Status, Metrics, Financial)
	• Process controls identified and listed
	
	Resourcing Plan
	• Types of technical and non-technical support staff required
	• Resourcing forecast algorithms and assumptions defined
	
	KPIs agreed

Infrastructure 	People • Lead Personnel identified/hired based on the expertise defined • Core team of programmers established Tools • Shared Platforms and Workspaces created for the Program and studies • Electronic Document Repository created • Programming Directory structures fixed across all studies • Standard TLG mocks developed for the program • Shared utilities/macros developed on study 1 and 'promoted upward' • Template code developed based on study 1 and added to the program level • Study Timeline (Project Plan) Template developed. • Study Report templates developed (status, KPI, issue/decision logs, financial reports). Process • On-boarding / Training plans developed • Standard ICON development and validation processes used • Process for managing change requests on TLG standards developed • Process for Program lead review of ADaM specifications, ADaM and TLGs developed

CASE STUDY B: SUCCESSES AND CHALLENGES

Establishing standard TLG mocks for the Program was successful.
Change Management Process was well defined and implemented (often).
Timing was an issue, since the first study was subject to a lot of change, and subsequent studies were conditional on the stability of the first study.
Contracts and synergy assumptions where not always realized due to ongoing changes on the first study.
KPIs not met. Sponsor study team not always available for review /approval per the KPI.
No Roll-up Reporting in place, or was done manually, latest information not always available to the program lead.
Modular macros implemented, which enabled flexibility/change to programs and outputs within and across studies, without impacting the entire program.

CONCLUSION AND 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 both internal and external factors, as inevitably there will be a need to adapt / change the programs assumptions.
- Consider whether the sponsor is invested in program management, or if the individual study results will take priority. For example, in order to ensure program level consistency would the sponsor be willing to pause on a study? Or will the desire to report the individual study results always win out?
- Sponsors will expect discounts on studies within a program; 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 will be a cost overhead for managing the program.
- Remember good governance is critical to the success of the program.
- The role of the program manager is to satisfy the criterion for which the program was set-up, not to manage the individual studies.
- A poorly articulated management structure, overlapping roles and decision-making authority, with endless attempts to achieve consensus, can prevent a program from achieving sustained momentum.

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

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