

Collaborative Clinical Trial
Management Through
Cross Functional Training

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Agenda

- Objectives
- Introduction
- Presentations
 - △ Protocol Review Using Cross-Functional Training
 - △ Cross-Functional Training on Study Conduction
 - △ Integrated Global Databases
- Question & Answer Time

Objectives

- Define Cross-Functional Training
- Define Advantages of Cross-Functional Training
- Provide three examples of cross-functional training in a clinical trial setting

What is Cross-Functional Training?

- Training employees to perform a wider variety of tasks in order to gain flexibility in work scheduling and improved coordination

△ Kermit R. Davis, Ph.D., Auburn University,
College of Business

Why do we do it?

- Speed
- Complexity
- Customer Focus
- Creativity
- Organizational Learning
- Single Point of Contact

△ Glenn M. Parker, *Cross-Functional Teams: Working With Allies, Enemies and Other Strangers*, Jossey-Bass, Inc., 1994.

When should we do it?

➤ Three recommendations:

△ Study Start Up

→ Protocol Review Using Cross-Functional Training

△ Study Conduct

→ Cross-Functional Training on Study Conduction

△ Program Close Out

→ Integrated Global Databases



Protocol Review Using Cross-Functional Training

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Agenda

- Objectives
- What is Protocol?
- Protocol Elements
- Information on Study Specifics
- Protocol Review Exercise
- Protocol Review Exercise – Follow Up Discussion

Objectives

- Identify key elements of a protocol
- Determine key elements of the protocol that other functional areas focus on and why

Objectives

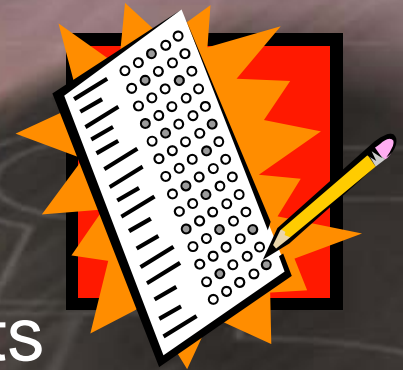
- Review the statistical plan of the protocol to determine how the clinical trial will be evaluated
- Identify the critical success factors and incorporate them into planning activities

Study Start Up

- Review the protocol
- Review other key study documents such as CRFs, proposals, and client specifications

Protocol Elements

- Key protocol elements include:
 - △ Phase of Clinical Trial
 - △ Investigational Product
 - △ Study Objective
 - △ Study Population
 - △ Study Design
 - △ Duration of Study
 - △ Primary and Secondary Endpoints



Phases of Clinical Trials

- Phase I
- Phase II
- Phase III
- Phase IV

Study Specifics

➤ **Investigational Product**

△ Name of the Study Drug

△ Classification of study drug

△ Client may have sent resource materials



Study Specifics

➤ **Study Population**

△ Number of patients to be enrolled

△ Description of population

△ Adults, pediatric, ages, gender

Study Specifics

➤ Study Design

- △ Blinding or Masking
- △ Treatment Sequences
- △ Controls
- △ Subject Assignments



Study Specifics

➤ **Study Duration**

△ Length of study

△ Timelines

△ Number of Treatments

△ Visit schedule

Study Specifics

➤ **Study Objectives**

△ What is the clinical trial trying to prove?

△ Example: If giving the anti-flu drug decreases the flu

➤ **Primary and Secondary Endpoints**

△ Critical to the analysis of the study

Study Specifics

➤ **Statistical Plan**

△ Discusses the statistical methods

△ Determines the level of significance to be used

△ Determines the power of the trial and clinical justification

Protocol Review Tools

- Get a highlighter and start to capture key information within the protocol
- Compare key information with other leads and determine if this key information is common in other functional areas



PROTOCOL REVIEW EXERCISE



Protocol Review Exercise

- Protocol Name/Number
- Phase
- Study Objective
- Primary & Secondary Endpoints
- Study Population
- Study Design
- Study Duration
- Investigational Product
 - △ Drug Description
 - △ Dosage
 - △ Administration
- Critical Success Factors
- Plans to ensure Critical Success Factors

Protocol Review Exercise – Follow Up Discussion

- What concerns did you not consider for this study?
- How do these new concerns impact your functional group?
- How do you think you will manage these concerns?
- What would you plan for?

Cross-Functional Training on Study Conduction

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Cross-Functional Training on Study Conduction

1. Who?
2. What?
3. When?
4. Where?
5. Why?
6. How?

Who Should be Trained on Study Conduction Issues?

Categorize training by job function related to the activity:

- ***In-depth*** for full ownership
- ***Job-dependent components*** for direct interaction; overview of the remainder
- ***Overview level*** for indirect interaction

Who Should Do the Training?

- Trainers with subject matter expertise
- Subject matter experts who are effective trainers

What Should be Included in the Cross-Functional Training on Study Conduction?

- Subject Enrollment
- Informed Consent
- Essential Documents
- Monitoring
- Data Queries
- Adverse Events
- Drug Supply Documentation
- Analysis and Reporting

Sample Training Level Matrix

	Clin Res	Stat CDM	Project Mgmt	Pharm Supp	Reg Affairs	Safety
Subject Enrollment	I-D	J-D	O	J-D	O	J-D
Informed Consent	I-D	O	O	O	O	O
Essential Documents	I-D	O	O	O	J-D	O
Monitoring	I-D	O	O	O	O	O
Data Queries	I-D	I-D	O	O	O	O
Adverse Events	I-D	O	O	O	J-D	I-D
Drug Supply Documentation	I-D	O	O	I-D	O	O
Analysis and Reporting	I-D	I-D	O	J-D	I-D	I-D

I-D: In-depth J-D: Job-dependent O: Overview

When Should Cross-Functional Training on Study Conduction Occur?

- Early enough to enable the trainee to learn, assimilate, and optimally apply the knowledge and skills into their job activities.
- Not so early that the learning is not able to be effectively applied on the job.

Where Should Cross-Functional Training on Study Conduction Occur?

- As close as possible to the actual job setting.
- Where hands-on, experiential learning can occur.

Why Should Cross-Functional Training on Study Conduction Be Done?

- Team function
- Clinical development is a highly-interdependent process.
- A competitive advantage

Recommendations on How to Do Cross-Functional Training

- Identify functions/persons needing training.
- Evaluate the job-requirements of the training participants.
- Define the training content.
- Design the training to fit the experience level of the participants, as well as the job-requirements.
- Deliver the training “just-in-time, rather than just-in-case.”



Integrated Global Databases

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Agenda

- Objectives
- What is Data Integration?
- What are common misconceptions about Data Integration?
- Data Integration Realities
- Holistic Team Approach
- Data Integration Process

Objectives

- Upon successful completion of this session, all participants will be able to:
 - △ Define Data Integration & Prospective Data Integration
 - △ List the Data Integration Process steps
 - △ List three Data Integration critical success factors

Data Integration

What is
Data
Integration?

- **Data Integration** is the process of bringing databases together so that a meaningful analysis of data across different clinical trials may be conducted
 - △ The product of a data integration is a **Global Database**
- **Prospective Data Integration** incorporates database designs and processes that help build databases that are easily integrated

Data Integration

What is
Data
Integration?

- The ISS, or **Integrated Summary of Safety**, is a product of an Integrated Safety Database
- The ISE, or **Integrated Summary of Efficacy**, is a product of an Integrated Efficacy Database

Data Integration

What Are
Common
Misconceptions
About Data
Integration?

- Data Integration is a Simple Activity that Does Not Take a Lot of Planning and Time
- Data Integration Takes a Minimal Effort if the Information is Similar Across Studies
- Data Integration is Something One Thinks About Once All of the Clinical Trials Have Been Completed
- Data Integration is Easier if the Number of Studies to Integrate is Small
- Identical Case Report Form Items from Various Studies Can All Be Merged

Data Integration

Data Integration Realities

- It is a Tremendous Undertaking
- Never Wait Until all Studies are Complete to Start Designing and Building a Global Database
- Begin Early (During Protocol and CRF Design)
- All Like Data Can Not Be Pooled

Data Integration

A Holistic
Approach
Builds a
Better
Database,
Faster

- Integration is not just a programming task
- It is imperative that the meaning of the data is understood and preserved throughout the process
- A high level of expertise in each facet of the integration process is necessary
- A Global Database can serve many needs, and these all must be considered in the planning and execution of the database work

Data Integration

A Diverse,
Experienced
Team
Assures
That All
Aspects of
the
Integration
Are
Successful

A Typical Integration Team

Team Member	Responsibility
Data Manager	Assures that similar fields in the global database are populated with data that has been cleaned in an appropriate manner.
Physician	Assures that the clinical meaning of integrated data is preserved. Assures that appropriate standard unites and scales are chosen for the global database.
Lead Programmer	Provide oversight to the execution of the integration and assures that accuracy and quality are preserved in the global database.

Data Integration

A Diverse,
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A Typical Integration Team

Team Member	Responsibility
Coder	Applies a single coding dictionary to Adverse Events and Medications. Assures that codes are used consistently.
Statistician	Assures that the design of the Global Database supports the statistical analysis
Project Manager	Coordinates the activities of the team, and provides the client with up-to-date progress.

Data Integration Process

- △ Understand the Trial(s) at Ground Level
- △ Define Database Structures
- △ Data Dictionaries
- △ Consistency and Coding
- △ Ensure all data is captured (Special Data)
- △ Determine the Structure of the Global Database
- △ Global Coding and Electronic Submissions
- △ Using and Validating the Database
- △ Project Management Tasks
- △ Summary of Critical Success Factors

Data Integration

The
Process

Understand
the Trial at
the Ground
Level

Objective: Ensure a High Level of Consistency in Processing Data Across all Studies to Facilitate Data Pooling and Analysis

Data Integration

The
Process

Understand
the Trial at
the Ground
Level

Tasks for Each Study:

➤ Review Documentation

- △ Review Study Designs
- △ Review Case Report
Forms (annotated, if available,
and representative completed
CRFs)
- △ Review Edit
Specifications
- △ Review Analysis Plans

Data Integration

The
Process

Define
Database
Structures

➤ Define Database Structures

△ In the **Prospective** Approach, design databases which capture the data in a manner that is most easily integrated with existing or future databases

Data Integration

The
Process

Define
Database
Structures

➤ Define Database Structures

- △ Provide a simple, clear method to display data specifications
- △ The variable name, its label, its type, associated codes (user-defined formats) and comments
- △ **“Data Dictionaries”**

Data Integration

Study 1234 – Demographics Dataset Variables

Variable	Label	Type	Codes	Comments
PATID	Unique Patient ID	Char		Page 3
SEX	Sex of Patient	Char	1=F 2=M	Page 3
RANDDATE	Randomization Date	Date		Page 3
AGE	Age of Patient at Randomization	Num		<pre>age = int((intck('month', dob, randdate) - (day(randdate) < day(dob))) / 12)</pre>

Data Integration

➤ Data Dictionaries

△ Guide the Database Development

△ Document Differences Between Databases

Data Integration

The
Process

Consistency
and Coding

- **Determine Edit Specifications**
 - △ Agree on Minimum Types of Checks
 - △ Rules for Creation of Derived Data Fields Necessary for Checks
- **Approve Coding Policies**
 - △ Select Fields to be Coded: Medical History, Adverse Events, Concomitant Medications
 - △ Review Coding Conventions
 - △ Review Lists of Coded Terms for Consistency
 - △ Maintain Global Coding Dictionaries
 - Determine the Impact of Changes to the Dictionary on Completed Studies
- **Review Serious Adverse Event Coding**
 - △ Reconciliation with Clinical Database
 - △ Review Lists of Coded Terms for Consistency

Data Integration

The
Process

Ensure that
All Data is
Captured

➤ Identify Special Data Sources

△ Some Examples

- Blood Level/PK Data
- Laboratory Data
- Imaging Data
- Quality of Life
- Serious Adverse Events
- Pathology Data
- Studies from: Client, Other CRO, Govt. agency such as NCI, NIH

Data Integration

The Process

Determining
the Structure
of the Global
Database

Objective: Produce a Global Safety and Efficacy Database that can be Efficiently Analyzed for Regulatory Submissions

Data Integration

Tasks:

➤ **Determine Contents of Global Database**

The Process

Determining
the Structure
of the Global
Database

- Relevant Demographic Data (incl. Body Surface)
- Overall Drug Exposure Data (incl. Plasma Levels, Dosage Regimen)
- Adverse Events
- Deaths
- Withdrawals
- Lab Data (Converted, Normal Ranges and Critical Limits of Clinical Concern)
- Efficacy Data
- Study Information (Design, Lot Number, Investigator, Treatment)

Data Integration

The Process

Determining the Structure of the Global Database

➤ **Define Structure and Format**

- △ May choose to map to the best existing structure, especially if a good set of summaries has been programmed using it
- △ May choose to build a less normalized, more easily summarized database, with the definitions of categories defined as part of the database structure
- △ Record these decisions in a data dictionary
- △ Include Units, New Computed/Derived Fields, Visit Windows, Improvement/Success Criteria
- △ Include special data, and assure that it is transferred completely

Data Integration

The Process

Global
Coding and
Electronic
Submissions

- **Adverse Event Coding**
 - △ Suggest Terms that may Need Re-coding
 - △ Identify Differences in Coding US vs. Europe

- **Electronic Data Submission**
 - △ Recommend What Can be Stored Electronically
 - SAS Datasets
 - Programs
 - Reports
 - Scanned CRF Images
 - Other Images
 - Graphs

Data Integration

The Process

Using and
Validating
the
Database

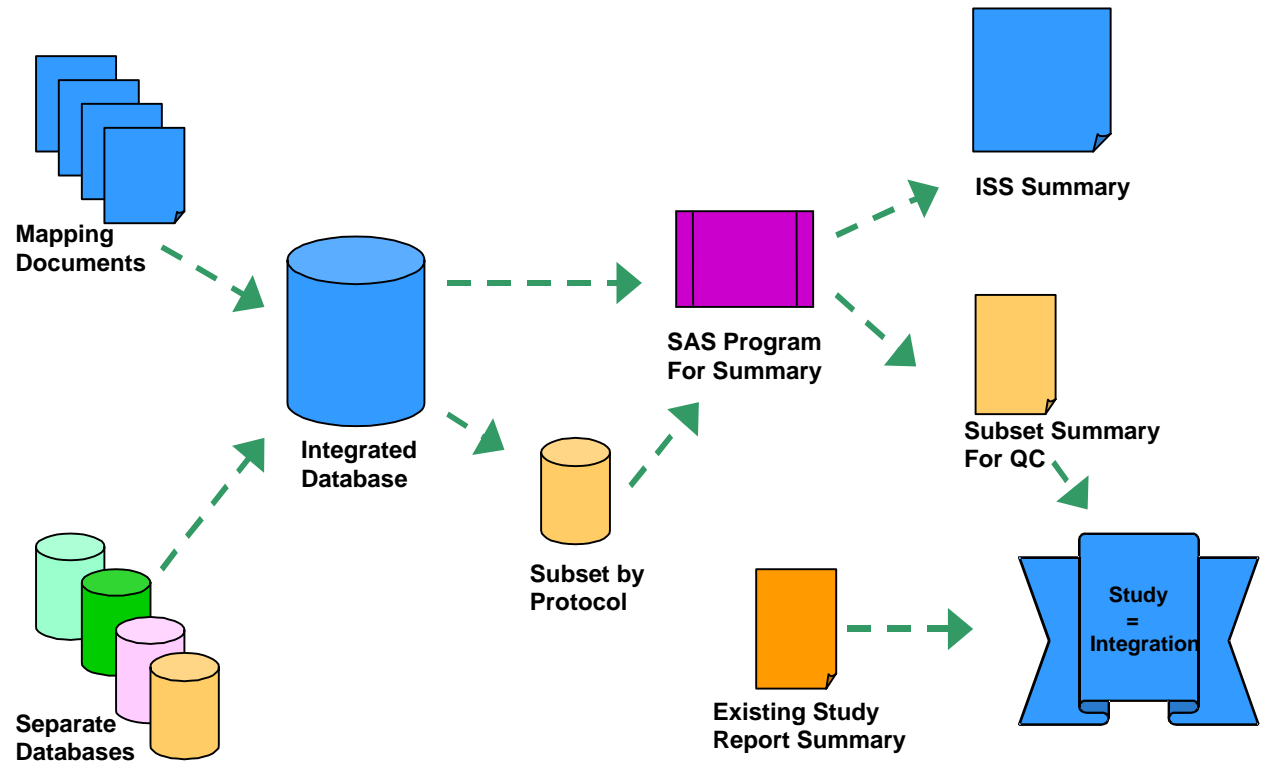
➤ **Output**

- △ Prepare Analysis Plan
- △ Provide Detailed Table, Figure and Listing Specifications for ISS and ISE.
- △ Use Tables/Listings to Review Contents of Global Database
 - Validate the integration of large databases by comparing subsets of the integrated output to tables from existing reports for the individual study databases

Data Integration

QC
Process

Best QC for Data Integration



Data Integration

The Process

Project
Management
Tasks

- **Identify Rate Limiting Tasks and Milestones**
- **Set and Monitor Timelines**
- **Determine Appropriate Resources Needed to Meet Timelines**
- **Ongoing Review of Output**
- **Make Recommendations and Obtain Approval from Senior Level Decision Makers**

Data Integration

Critical
Success
Factors

➤ Summary

- △ Start as Early as Possible
- △ Leverage Project Management
- △ Build an Experienced and Diverse Team
- △ Work to Well-Established Endpoints
- △ Document and Program, in that order
- △ Validate Rigorously



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Questions?

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