



Perfecting the Game Plan

The Hand-off from Programming and Statistics to Regulatory Operations

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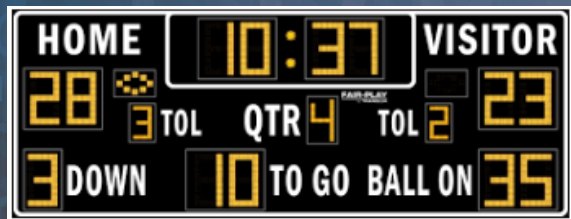
**PRACTICE DOES NOT
MAKE PERFECT.
ONLY PERFECT PRACTICE
MAKES PERFECT.**

~ VINCE LOMBARDI



Introduction

- Our Team
 - Cross-functional ‘data hub’ support for multiple global trials
 - Programming and Statistics
 - Regulatory Operations
 - Data Management, Medical Writing, Pharmacovigilance
- Our Goal
 - Prepare and submit a New Drug Application (NDA) to the FDA under compressed timelines



Submission Numbers

NDA Study Data at a Glance

Legacy Format	CDISC Format	Integrated	Other
17 Phase 1 CSRs	3 Global Phase 3 CSRs	Safety	25 Preclinical Studies
	5 Phase 1 CSRs	Efficacy	BIMO
1 Phase 2 CSR →	Converted Phase 2	2 Pop-PK	
1 Phase 3 CSR →	Converted Phase 3	PK	

- Data packages made up 41% of files and 33% of eCTD folders in NDA



Submission Challenges

Data Package Conversion

- Programming and Stats deliverables cannot be submitted without conversion to acceptable file formats for the eCTD

Deliverable Type	File Format Produced	File Format Required
Tables, Listings, Figures	.rtf	.pdf
Datasets	.sas7bdat	.xpt
SAS Codes	.sas	.txt
Annotated CRF	PDF with annotations	No annotations allowed

Source Files

- Several sources of data for CSRs completed over a decade-long span
 - Past and current in-house Sponsor programmers
 - Previous CRO partners
 - MMS Programming group
- Review of legacy/raw data for completeness
 - Datasets without STUDYID
 - Missing define files
- Preclinical data available only in PDF format

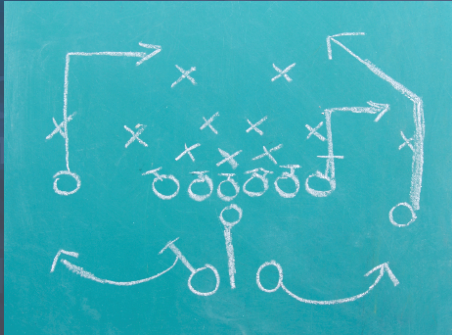
Ineligible Receivers

- Programming/Stats and Regulatory groups work in separate validated systems
 - Programming outputs are stored on a locally hosted server
 - eCTD submissions are published in a cloud system
 - Access limited by role

Interference



- Last-minute changes and requests for additional tables
- Sponsor providing outputs unexpectedly
- Teams are located in different sites, in different time zones, and could easily form siloes
- Overlapping priorities that shifted constantly



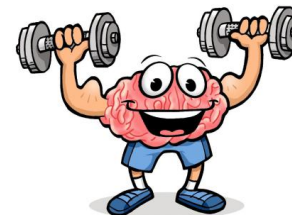
The Game Plan

Communication Plan



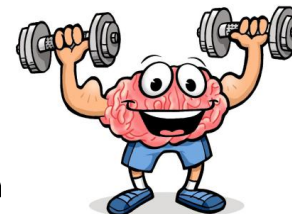
- Weekly meetings between Programming, Stats, and Reg Ops leads:
 - Agreed on table numbering strategy for integrated datasets to most easily facilitate hyperlinking to tables
 - Regular discussion of upcoming deliverables, shifting priorities, and potential impacts to timeline
- Reg Ops was included on meetings between data team and Sponsor and cc'd on all emails related to data package deliverables
- Shared Agency interactions with all team members
- Reviewed Study Data Standardization Plan to understand data requirements prior to submission kickoff

Cross-Functional Training and Support



- Programming, Statistics, and Regulatory teams trained together on FDA updates for data requirements
 - Small Business & Industry Assistance webinars
 - Joint review of FDA guidances for shared understanding and interpretation (eg, Data Tech Conformance Guide)
- Granted read-only access in each other's systems to key stakeholders so workflow was not disrupted
- Ensure all team members have access to same time-saving tools
 - TRS Toolbox for creation of PDF outputs
 - eValidator tool for eCTD submissions to spot potential errors

Cross-Functional Training and Support



- Trained Programmers on using the submission index.xml to review
- Populated spreadsheets together for creation of TS domains for all clinical and preclinical studies
 - Reg Ops provided Study ID and Study Start Date information
 - Programming provided TS.xpt quickly
- Reviewed all BIMO listing and dataset requirements as a team
 - Determine best bookmarking strategy (automated vs. manual)
 - Used functionality of eCTD publishing tool to avoid duplications (protocols and aCRFs)

Advanced Planning



- Documents
 - Reviewer's Guide templates and SAP templates are pre-formatted for easy publishing
- Data
 - Programming provided list of datasets and relative size of files to prepare submission build in advance of files being complete
 - Agreed on most efficient way to produce define.pdf files for legacy studies (ie, proc_contents)
- Timing and Coordination
 - Reviewed deliverable timelines over a critical 3-month period to choreograph handoff of datasets during slower document publishing times

File Organization and Storage

- Datasets, programs, aCRFs, CSDRG, ADRG, defines all have specific locations and e-submission 'codes' within the eCTD structure
- Programming and Stats leads prepared a detailed spreadsheet to organize data package and streamline Reg Ops assembly

Deliverable	Location	Notes	Ready for Reg Ops	Reg Ops Complete?
Analysis - ADaM	S:\IS\ADaM\Source\Define		Yes	No
Analysis - ADaM Data Definition	S:\IS\ADaM\Source\Define		Yes	No
Analysis - ADaM Reviewer's Guide	S:\IS\ADaM\Source\Define	adrg.pdf	Yes	No
Miscellaneous Dataset Data Definition	S:\IS\ADaM\Source\Output\Misc_Transport	File name: PROC CONTEN	Yes	No
Output - Tables	S:\IS\Tables\Source\Output	File name: ISM Final Tables	Yes	Yes
Output - Listings	S:\IS\List\Source\Output	File name: ISM Final Listing	Yes	Yes

Submission Build

Outline

Filter <none>

0000 0000 6 - 5 0 1

- 0000
 - 1 Administrative Information and Prescribing Information
 - 2 Common Technical Document Summaries
 - 3 Quality
 - 4 Nonclinical Study Reports
 - 5 Clinical Study Reports
 - 5.2 Tabular Listing of all Clinical Studies
 - 5.3 Clinical Study Reports
 - 5.3.1 Reports of Biopharmaceutic Studies
 - 5.3.2 Reports of Studies Pertinent to Pharmacokinetics using Human Bi
 - 5.3.3 Reports of Human Pharmacokinetic (PK) Studies
 - 5.3.4 Reports of Human Pharmacodynamic (PD) Studies
 - 5.3.5 Reports of Efficacy and Safety Studies
 - 5.3.5.1 Study Reports of Controlled Clinical Studies Pertinent to the C
 - <Insert Study Title>
 - Synopsis
 - Report Body
 - 16.1 Appendices
 - 16.2 Appendices
 - CRFs
 - Datasets
 - Analysis Data Sets (Legacy)
 - Analysis Data Sets (ADAM)
 - Data Definitions
 - Program File
 - Datasets
 - Analysis datasets (ADAM)
 - Data Tabulation Datasets (Legacy)
 - Data Tabulation Datasets (SDTM)

Properties

General

Structure Number

Title

Program File

eSubmission Code

Analysis Datasets (ADaM) - Program File

Node Title Option

Configuration

Output Media

Properties Find Hyperlinks

Node Content

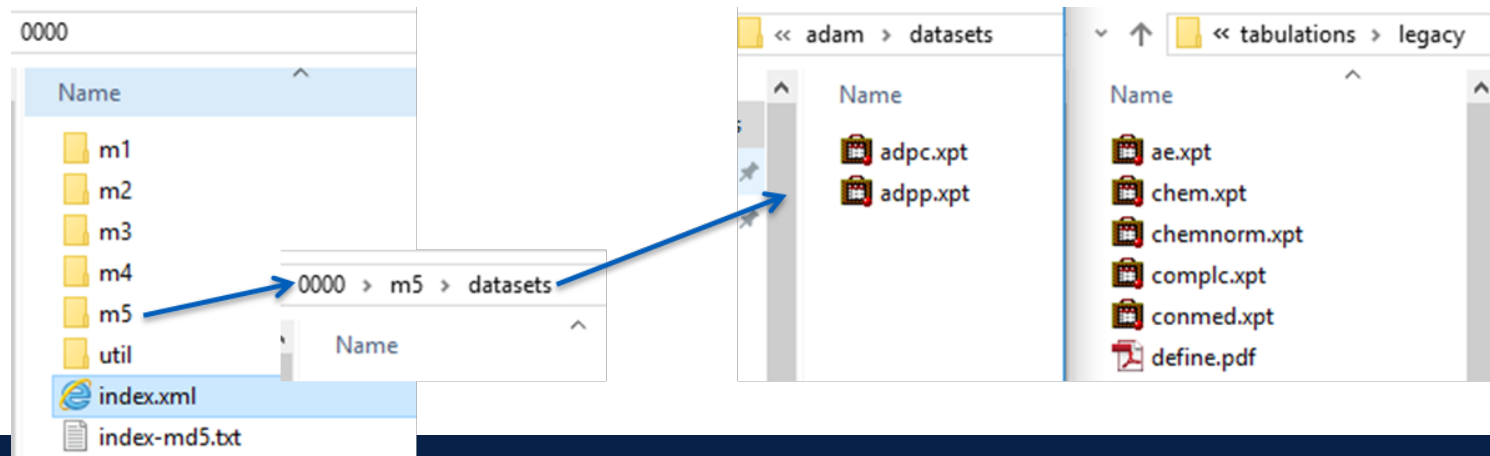
- Analysis Datasets (Legacy)
- Analysis Datasets (Legacy) - Split
- Analysis Datasets (Legacy) - Data Definition
- Analysis Datasets (Legacy) - Annotated CRF
- Analysis Datasets (Legacy) - Program File
- Analysis Datasets (ADaM)
- Analysis Datasets (ADaM) - Split
- Analysis Datasets (ADaM) - Data Definition
- Analysis Datasets (ADaM) - Annotated CRF
- Analysis Datasets (ADaM) - Program File
- Tabulation Datasets
- Tabulation Datasets (Legacy)
- Tabulation Datasets (Legacy) - Split
- Tabulation Datasets (Legacy) - Data Definition
- Tabulation Datasets (Legacy) - Annotated CRF
- Tabulation Datasets (SDTM)
- Tabulation Datasets (SDTM) - Split
- Tabulation Datasets (SDTM) - Data Definition
- Tabulation Datasets (SDTM) - Annotated CRF
- Tabulation Datasets (SEND)
- Tabulation Datasets (SEND) - Data Definition
- Miscellaneous Datasets
- Miscellaneous Datasets - Data Definition
- Miscellaneous Datasets - Annotated CRF
- Data Listing Datasets (BIMO)
- Data Listing Datasets (BIMO) - Data Definition



The Final Result

Quality Submission Output

- Programming team provided QC review of dataset output
- Confirmed all data outputs were 'coded' properly in the submission outline
- Confirmed data type, size, and contents were correct for each study



Measurement of Success

- Teams worked outside of comfort zones and silos to achieve a single goal of a successful NDA submission
- Developed the unique skillset of each functional group to best serve the submission team as a whole
- Gained insight into the daily workings of functional groups upstream and downstream in the submission process
- Produced a top-quality and on-time submission in the face of adversity

Questions?

****Special Thanks to Justin Sjogren and Kelly Williams for their cross-functional leadership on this project****