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Medical Writing and the Parallel Processing Approach™

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Medical Writer

Premier Research Group Ltd.

The Premier Research logo consists of a white rounded rectangle with a white border. The left portion of the rectangle is dark blue and contains the words 'PREMIER' and 'RESEARCH' stacked vertically in white, bold, sans-serif capital letters. The right portion of the rectangle is solid red.

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RESEARCH**

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MW & the Parallel Processing Approach™

About Dr. Frijhoff:

- MS in medical biology
- PhD in medicine
- Researcher and writer at The UT M. D. Anderson Cancer Center for 8 years
- Since March 2007, medical writer at Premier Research, a contract research organization



MW & the Parallel Processing Approach™

- **Problem:** Generating the final deliverable, the clinical study report (CSR), often with reduced timelines, while accommodating data and analytical issues that occurred during the study
- **Solution:** Medical Writing is involved from study design to conclusion and able to proactively identify study issues (PPA)



Learning Objectives

After this session, you will be able to

1. Ensure that the statistical analysis plan (SAP) output adequately supports presentation of study results and conclusions in the clinical study report (CSR) by conducting a thorough SAP review.



Learning Objectives (*cont.*)

2. Identify critical variables and potential data errors during the blinded patient data listings review to make certain that patient safety is accurately presented in the CSR.
3. Propose 3 solutions to reduce biometric timelines.



What is the PPA?

- Parallel Processing Approach™ (PPA) is the process used by Premier Research (CRO) for executing clinical studies
- PPA:
 - Biometrics Project Manager (BPM) manages biometric timelines and deliverables
 - BPM works with the leads in Data Management, Biostatistics, and MW to ensure parallel conduct of critical processes



What is the PPA? (cont.)

Protocol and case report form (CRF) finalized

Data Management

Biostatistics

Medical Writing

Database
Editing checks

SAP
TLG shells

SAP Review (1)
Shell CSR (2)

Enter/clean data

Programming
Validation

Blinded listings
review (3)

Lock database

Draft & final
TLGs

TLG review (4)
Final CSR (5)



PPA task #1 for Medical Writing

Review SAP and TLG shells

- What is a SAP?
 - Comprehensive and detailed description of the methods and presentation of data analyses proposed for a clinical study
 - Text & shells for tables/listings/graphs (TLGs)
 - A SAP is written before database lock per ICH guidelines to minimize potential for bias and define scope



PPA task #1 for Medical Writing

Review SAP and TLG shells (*cont.*)

- What is a review of SAP and TLG shells?
 - Consistency with the protocol
 - Completeness of statistical methods
 - Accuracy of planned outputs
 - Consistency with the CRF



PPA task #1 for Medical Writing

Review SAP and TLG shells (*cont.*)

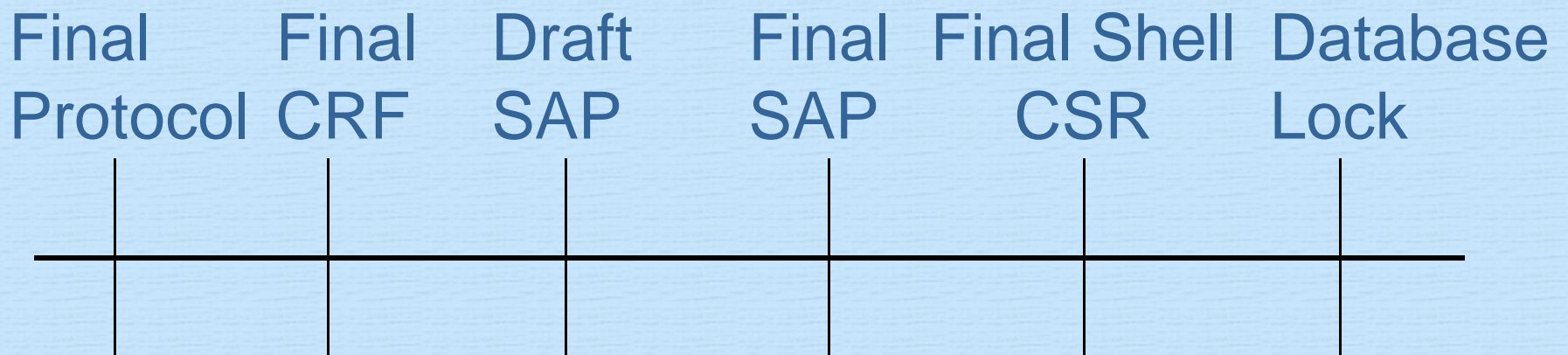
- Benefits for MW
 - Planned output (different for each sponsor) meets CSR requirements
 - Identify unnecessary summaries or absence of key tabulations
- Benefits for Biostats
 - Minimize programming changes later in study



PPA task #1 for Medical Writing

Review SAP and TLG shells (*cont.*)

- Timeline schematic



- SAP review by MW usually 1 week before SAP is due to sponsor
- Duration 1 to 4 days depending on difficulty



What is the PPA? (cont.)

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Final CSR (5)



PPA task #2 for Medical Writing

Write shell CSR (ICH E3 numbering)

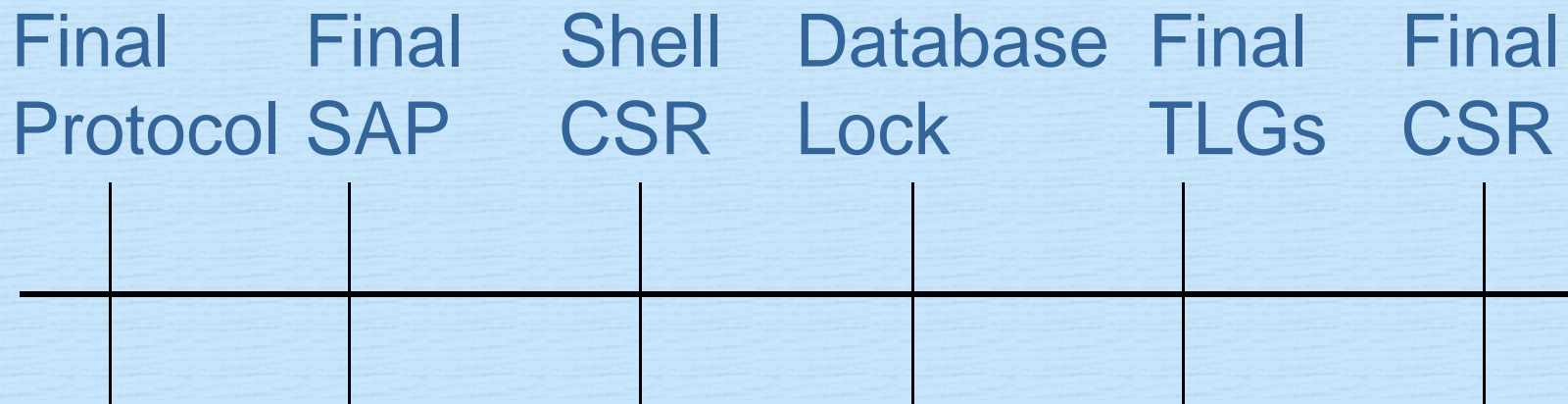
- Sections 1-9: complete using protocol and SAP
- Sections 10-13: Add sample text & mock tables



PPA task #2 for Medical Writing

Write shell CSR (ICH E3 numbering) (*cont.*)

- Timeline schematic



– Final SAP to Draft Shell CSR: 2 weeks



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PPA task #3 for Medical Writing

Review blinded listings

- What are blinded listings?
 - Patient listings from the SAP that are produced before database lock with random treatment codes assigned so that the study blind is maintained



PPA task #3 for Medical Writing

Review blinded listings (*cont.*)

- What is a blinded listings review?
 - Consistency with SAP and CRF
 - Identify programming and data errors, focusing on
 - Critical variables
 - Common errors
 - Review related listings for discrepancies



PPA task #3 for Medical Writing

Review blinded listings(*cont.*)

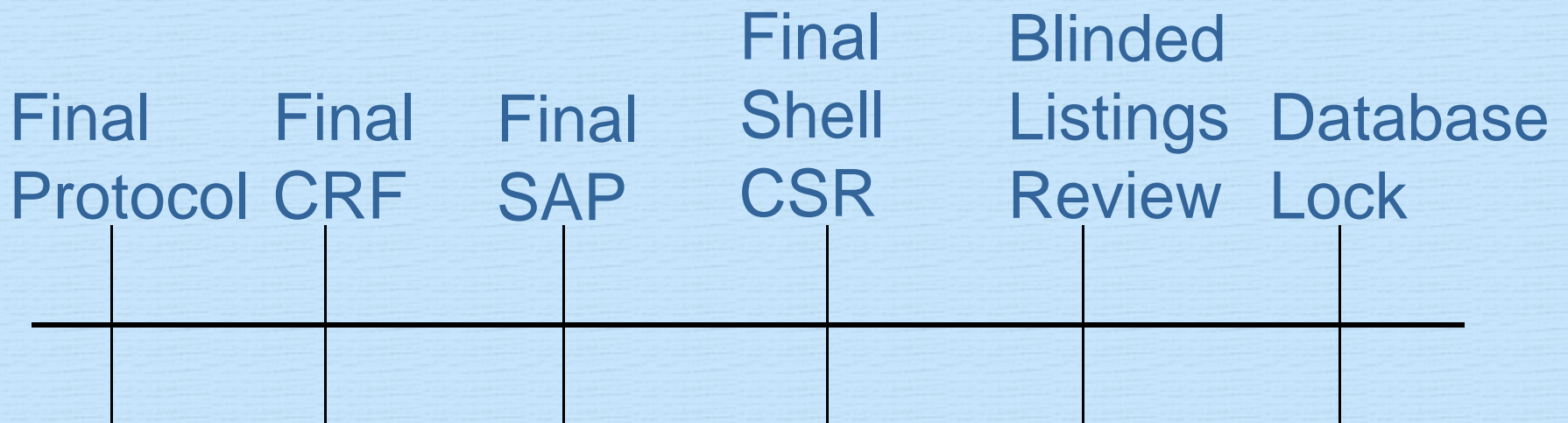
- Benefits for MW
 - Identify needed changes (ie, footnote)
 - Review trends across subjects and across sites
- Benefits for DM
 - Reduce or eliminate errors in database



PPA task #3 for Medical Writing

Review blinded listings (*cont.*)

- Timeline schematic



- Blinded listings review by MW usually the week before database lock
- Duration 1 to 2 days depending on difficulty



What is the PPA? (cont.)

Protocol and case report form (CRF) finalized

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TLG review (4)
Final CSR (5)



PPA task #4 for Medical Writing

Review draft TLGs

- Benefits for MW
 - Check draft TLGs for content and formatting
 - Prevent rewriting CSR sections
- Benefit for Biostats
 - Correct errors before finalizing TLGs



What is the PPA? (cont.)

Protocol and case report form (CRF) finalized

Data Management

Biostatistics

Medical Writing

Database
Editing checks

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TLG shells

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Enter/clean data

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Lock database

Draft & final
TLGs

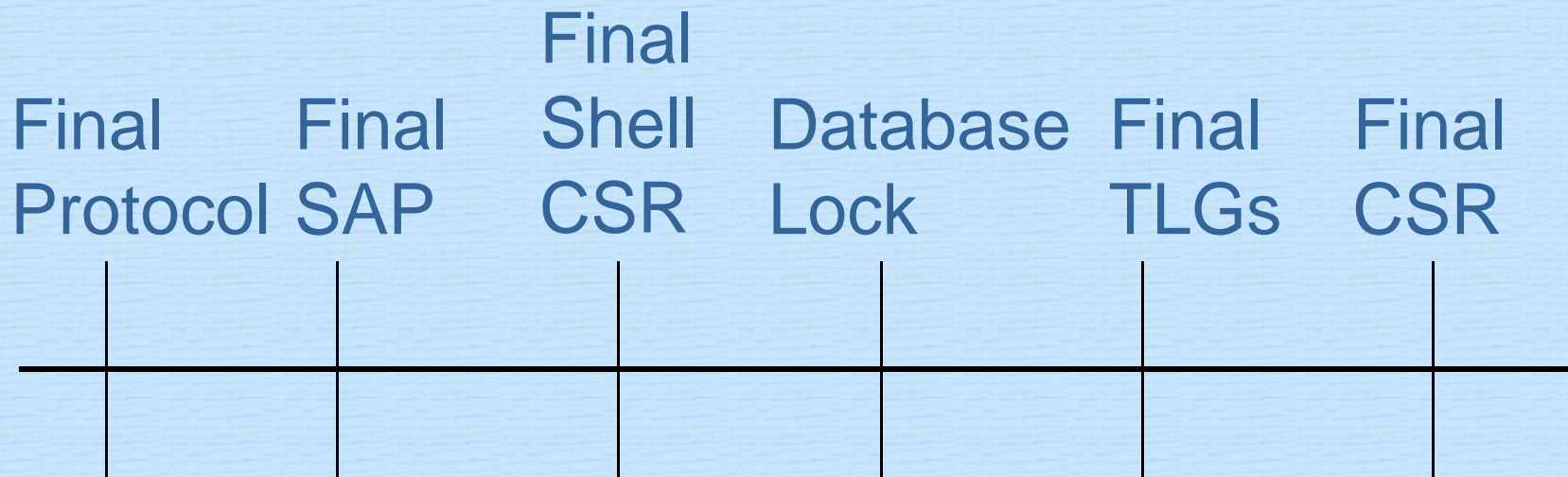
TLG review (4)
Final CSR (5)



PPA task #5 for Medical Writing

Update CSR Sections 10-13 with appropriate in-text tables and text

- Timeline schematic



– Final TLGs to Draft Final CSR: 1-2 weeks



MW's experience with the PPA

- PPA, including BPM's management of timelines, helpful for CSRs
- PPA requires full understanding of biometrics processes
 - Train inexperienced team members on PPA milestones
 - Focus PPA data reviews on analysis of study outcomes, not editorial corrections



MW's experience with the PPA (*cont.*)

- PPA-mandated extensive study involvement:
 - Medical writers aware of preceding milestones and manage their timelines proactively
 - Medical writers know specific study nuances and are able to improve quality of their deliverables



MW's experience with the PPA (*cont.*)

- For phase 1 studies:
 - PPA data reviews essential
 - Often no time for shell CSRs
- For phase 2-4 studies:
 - Sufficient time for completion of all PPA tasks
- PPA data reviews by MW requested for studies for which MW is not contracted



Learning Objective #1

After this session, you will be able to

1. Ensure that the statistical analysis plan (SAP) output adequately supports presentation of study results and conclusions in the clinical study report (CSR) by conducting a thorough SAP review.



Learning Objective #1 (*cont.*)

How can a SAP review help prevent problems with actual data and data presentation in CSR?

- ✓ Proposed analyses cover the objectives in the protocol
- ✓ Data collected for all enrolled/randomized patients are presented in data listings
- ✓ Fields in TLG shells match those on CRFs



Learning Objective #2

After this session, you will be able to

2. Identify critical variables and potential data errors during the blinded patient data listings review to make certain that patient safety is accurately presented in the CSR.



Learning Objective #2 (cont.)

How can a blinded listings review address data and programming issues?

- ✓ Listings do not contain unexpected blanks, zeros, implausible values; nor miss data fields or subjects
- ✓ Data in related listings match (eg, disposition, adverse events, concomitant medications, study completion, study drug administration)



Learning Objective #3

After this session, you will be able to

3. Propose 3 solutions to reduce biometric timelines.



Learning Objective #3 (cont.)

How can the PPA be used to reduce biometric timelines?

- ✓ PPA review of SAP & TLG shells allows MW to request customized tables for in-text presentation in CSR
- ✓ Through PPA review of blinded listings MW can identify data issues (eg, mistake in transfer of laboratory data) **before** database lock



Learning Objective #3 (cont.)

PPA data reviews are time-consuming.
So how can the PPA be used to reduce
biometric timelines?

- ✓ Help prevent problems that may delay timelines “downstream”
- ✓ Manage PPA data reviews by
 - Focusing on analyses of critical data
 - Limiting editorial corrections (eg, use of subject vs patient)



Conclusions

PPA-mandated study involvement allows MW to

- Proactively identify data and analytical issues
- Increase quality of CSRs
- Be part of an internal team with direct access to members for questions/issues
- Reduce biometric timelines



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