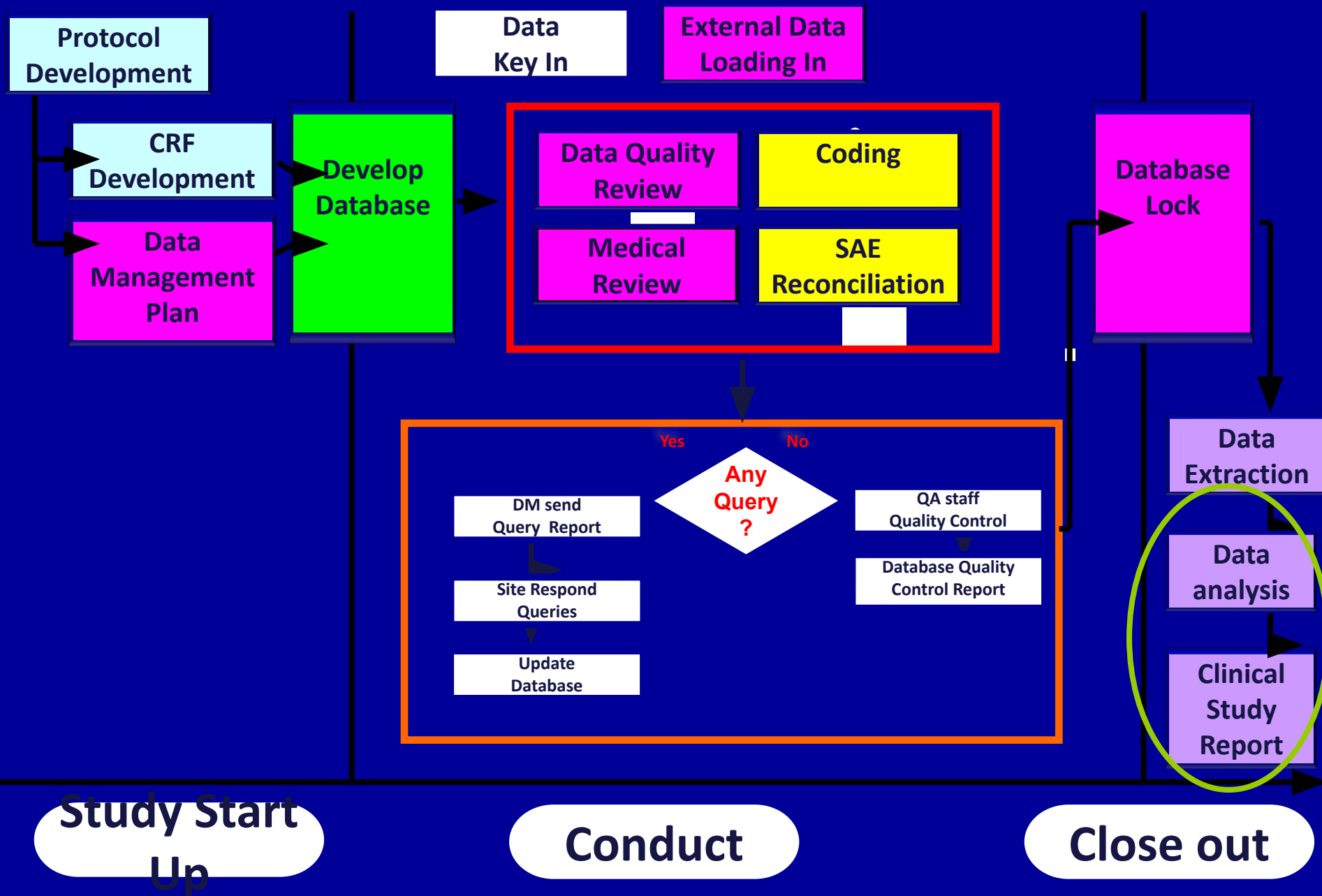


Before Presentation...

- This slide deck is based on Jain Chung's presentation for the 1st CDM training course in 2008.

DM Flow



ICH E9 Statistical Principles

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL
REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN
USE

ICH HARMONISED TRIPARTITE GUIDELINE

STATISTICAL PRINCIPLES FOR CLINICAL TRIALS
E9

Current *Step 4* version
dated 5 February 1998

ICH E3 Clinical Study Reports

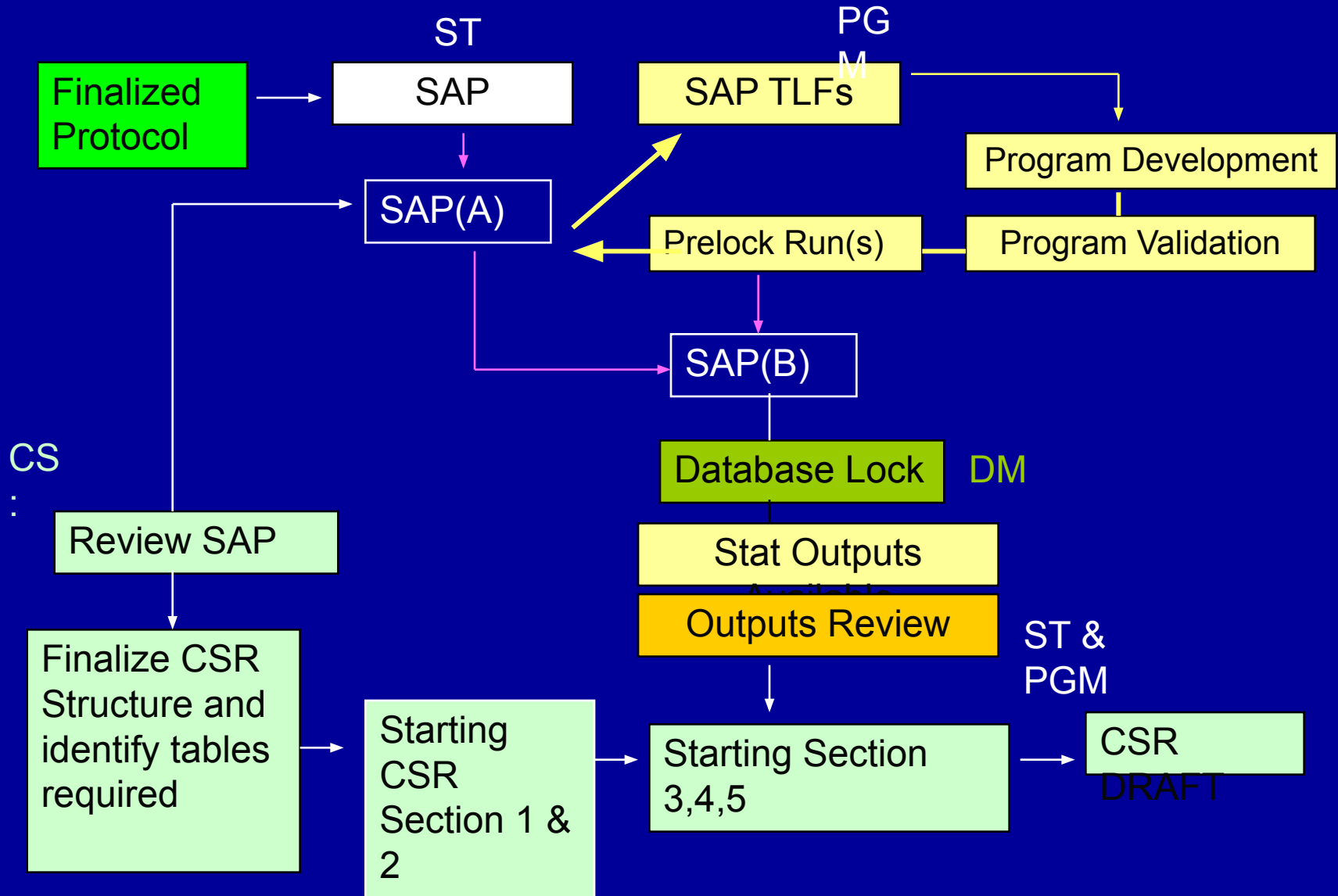
INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL
REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN
USE

ICH HARMONISED TRIPARTITE GUIDELINE

STRUCTURE AND CONTENT OF CLINICAL STUDY REPORTS E3

Current *Step 4* version
dated 30 November 1995

Process for Development Clinical Study Report



Sample of CSR Report Body

In the format of the Journal-Style scientific paper

1. Background, Rationale and Objectives

2. Materials And Methods

3. Results

3.1 Study Population

3.2 Efficacy Results

3.3 Pharmacodynamic, Pharmacokinetic and PK/PD Modeling

3.4 Safety Analysis

4. Discussion

5. Conclusion

6. References

Appendices

Sample of CSR Report Body

In the format of ICH E3 “Structure and Content of Clinical Study Reports”

- 1. Title page**
- 2. Synopsis**
- 3. Table of contents**
- 4. List of abbreviations**
- 5. Ethics**
- 6. Investigators and study administrative structure**
- 7. Introduction**
- 8. Study objectives**
- 9. Investigational plan**
- 10. Study patients**
- 11. Efficacy evaluation**
- 12. Safety evaluation**
- 13. Discussion and overall conclusions**
- 14. Tables, figures and graphs referred to but not included in the text**
- 15. Reference list**
- 16. Appendices**

CSR Section 3 - Results

3.1 Study Population

3.1.1 Disposition of Patients

3.1.2 Patients Withdrawn Prematurely from treatment

3.1.3 Overall of Analysis Populations

3.1.4 Protocol Violations

3.1.5 Demographic Data and Baseline Characteristics

3.1.6 Previous Concomitant Medications and Diseases

CSR Section 3 - Results

3.2 Efficacy Results

3.2.1 Primary Efficacy Parameter

3.2.2 Secondary Efficacy Parameter (s)

3.1.3 Subgroup and Exploratory Analyses

3.3 Pharmacodynamic, Pharmacokinetic and PK/PD Modeling

CSR Section 3- Results

3.4 Safety Analysis

3.4.1 Extent of Exposure to Trial Medication

3.4.2 Overview of Safety

3.4.3 Adverse Events

3.4.3.1 Overview Adverse Events

3.4.3.2 Deaths

3.4.3.3 Serious Adverse Events

**3.4.3.4 Adverse Events and Laboratory
abnormalities Leading to Withdrawal from
treatment**

3.4.3.5 Dose Modifications for Safety Reasons

CSR Section 3 - Results

3.4.4 Laboratory Parameters

3.4.4.1 Mean (or Median) Change from Baseline

3.4.4.2 Shift from Baseline

3.4.5 Vital Signs

3.4.6 ECGs

Other CSR Sections: 4, 5, and 6

4. Discussion

5. Conclusion

6. References

Appendices

Review CSR, final TLFs

- **Validation**
- **Consistency**
- **Interpretations**
- **Discussions**

CSR Section 1: Background, Rationale and Objectives

1.1 Background

1.2 Rationale

1.3 Objective

CSR Section 2 - Materials and Methods

2.1 Overall Study Design

2.1.1 Protocol Amendments

2.2 Study Population

2.2.1 Overview

2.2.2 Inclusion Criteria

2.2.3 Exclusion Criteria

2.2.4 Criteria for Withdrawal from Treatment or Study and Replacement Policy

2.2.5 Concomitant Medication, Treatments and Procedures

2.3 Compliance with Good Clinical Practice

2.3.1 Ethics

2.3.2 Audits

2.3.3 Data Quality Assurance

2.4 Trial Medication

2.4.1 Rationale for Dosage Selection

2.4.2 Formulation and Packaging

2.4.3 Assignment to Treatment Group/Sequence

2.4.4 Blinding

2.4.5 Drug Administration

2.4.6 Dose Modification

2.4.7 Dose Accountability and Compliance

ICH E3 Structure and Content of Clinical Study Reports

1. Title page
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15. Reference list
16. Appendices

** Details for Sections 9 – 12 on next slides*

ICH E3 Structure and Content of Clinical Study Reports (cont.)

9. Investigational plan

9.1 Overall study design and plan description

9.2 Discussion of study design, including the choice of control groups

9.3 Selection of study population

9.3.1 Inclusion Criteria

9.3.2 Exclusion Criteria

9.3.3 Removal of Patients from Therapy or Assessment

9.4 Treatments

9.4.1 Treatments Administered

9.4.2 Identity of Investigational Product(s)

9.4.3 Method of Assigning Patients to Treatment Groups

9.4.4 Selection of Doses in the Study

9.4 Treatments (cont.)

9.4.5 Selection and Timing of Dose for each Patient

9.4.6 Blinding

9.4.7 Prior and Concomitant Therapy

9.4.8 Treatment Compliance

9.5 Efficacy and safety variables

9.5.1 Efficacy and Safety Measurements Assessed and Flow Chart

9.5.2 Appropriateness of Measurements

9.5.3 Primary Efficacy Variable(s)

9.5.4 Drug Concentration Measurements

9.6 Data quality assurance

9.7 Statistical methods planned in the protocol & determination of sample size

9.8 Changes in the conduct of the study or planned analyses

ICH E3 Structure and Content of Clinical Study Reports (cont.)

10 Study patients

- 10.1 Disposition of patients
- 10.2 Protocol deviations

11. Efficacy evaluation

- 11.1 Data sets analyzed
- 11.2 Demographic and other baseline characteristics
- 11.3 Measurements of treatment compliance
- 11.4 Efficacy results and tabulations of individual patient data

12. Safety evaluation

- 12.1 Extent of exposure
- 12.2 Adverse events (AEs)
- 12.3 Deaths, other SAEs, and other significant adverse events
- 12.4 Clinical laboratory evaluation
- 12.5 Vital signs, physical findings and other observations related to safety
- 12.6 Safety conclusions

References

- ICH Guidelines www.ich.org
 - E9 Statistical Principles for Clinical Trials
 - E3 Structure and Content of Clinical Study Reports