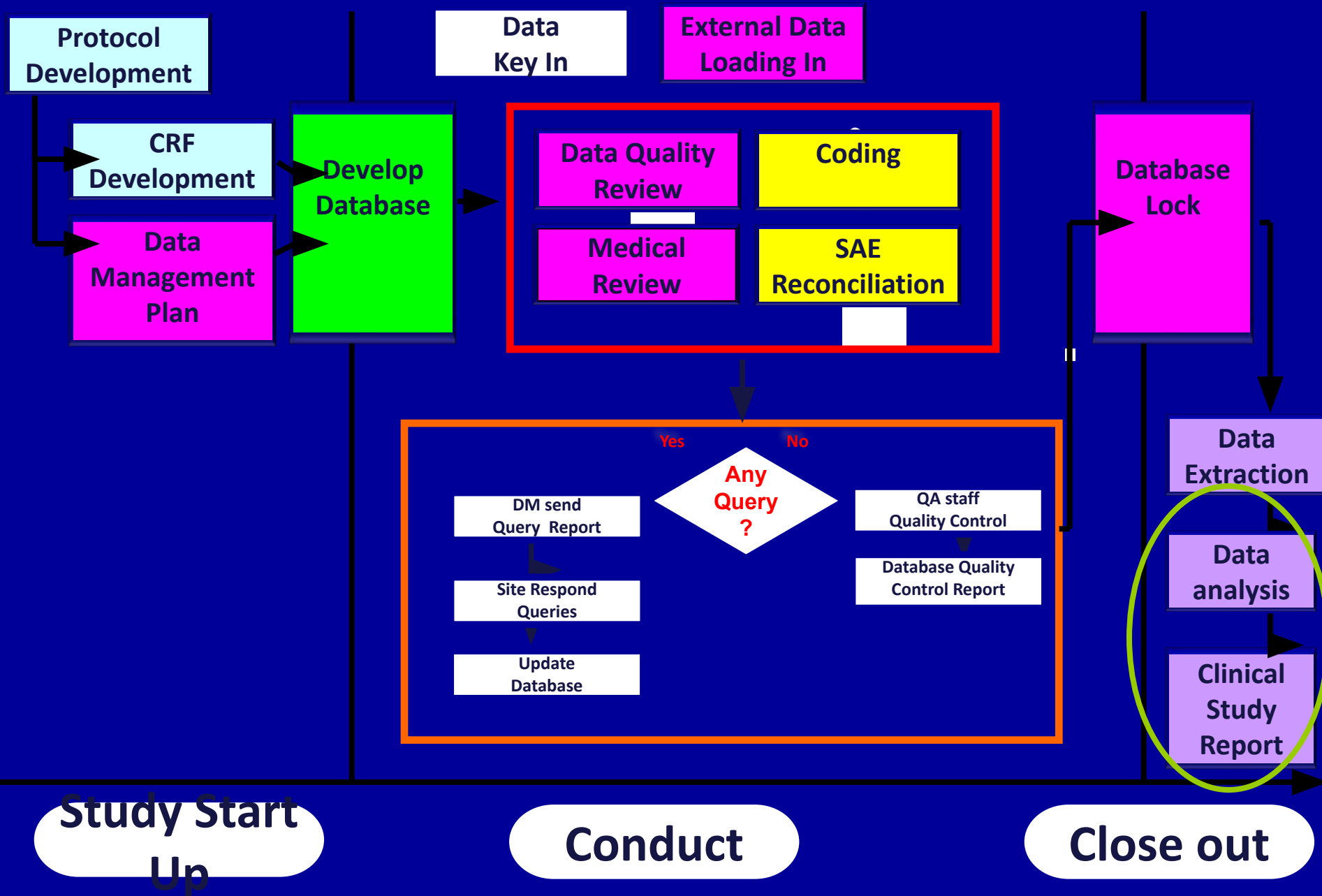


# Before Presentation...

- 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

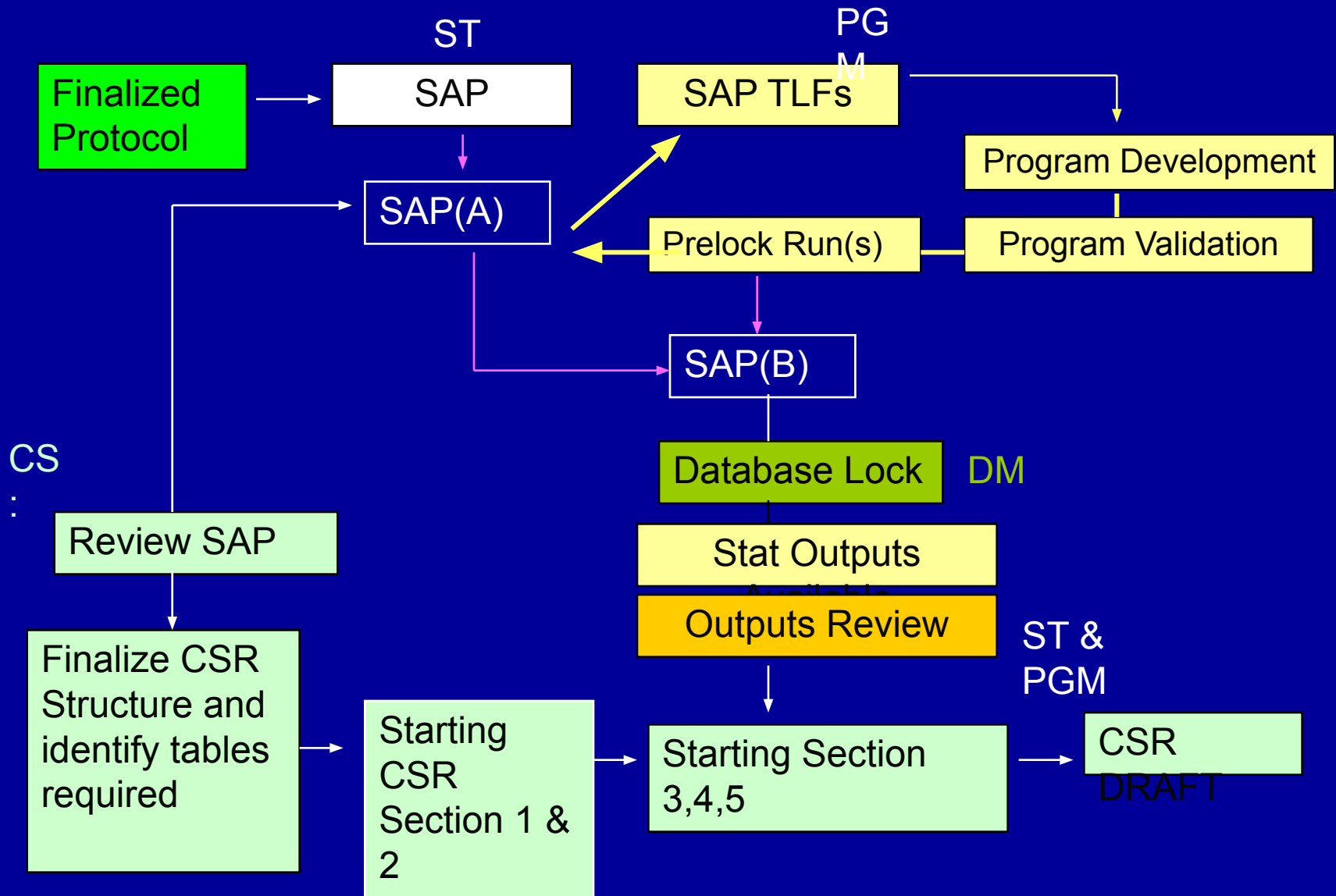
INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL  
REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN  
USE

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*

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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**3.1.2 Patients Withdrawn Prematurely from treatment**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
2. Synopsis
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4. List of abbreviations
5. Ethics
6. Investigators and study administrative structure
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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](http://www.ich.org)
  - E9 Statistical Principles for Clinical Trials
  - E3 Structure and Content of Clinical Study Reports