



Bayer HealthCare
Bayer Schering Pharma

How to process data from clinical trials and their open label extensions

PhUSE, Berlin, October 2010

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Agenda

- **Introduction**
- **The “EDC Approach” – Pros and Cons**
- **The “SAS Approach” – Pros and Cons**
- **Implementation of the “SAS Approach”**
 - **Databases and Split of Study Datasets**
 - **Further Implementation**
 - **Problems and Solutions**
- **Summary**

Introduction

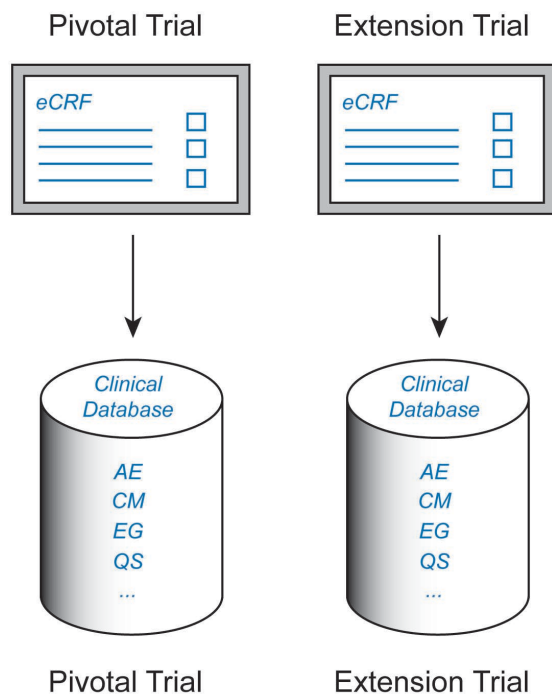
- **Definition: open label extension**
 - **clinical trial which follows double-blind, controlled trial crucial for submission**
- **Different kinds of study designs leading to open label extensions**
 - **one study protocol for both, pivotal and extension**
 - **two study protocols – one for each (our current scenario)**
 - **different study protocols for several double-blind, controlled trials, one open label extension as pool study**

Introduction

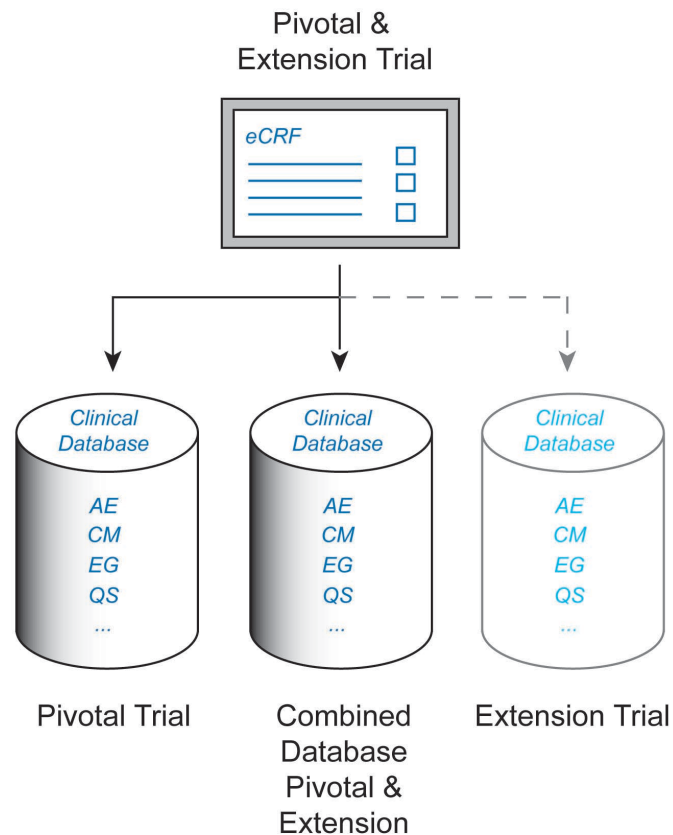
- **Pre-conditions:**
 - **Electronic Data Capture (EDC) as preferred data collection method**
 - **Transfer of data to clinical database using SAS**
 - **To be considered:**
 - **Set-up of EDC System/EDC Database**
 - **Set-up of SAS databases (clinical databases)**
- ➔ **Two main options for set-up**
 - **The “EDC Approach” and the “SAS Approach”**

Introduction

EDC Approach



SAS Approach



EDC Approach – Pros

- **EDC Approach: Set-up of double-blind, controlled trial and its open label extension as *two separate studies in the EDC system***
- **Pros**
 - **Clear differentiation of the two studies**
 - **Easy database closure/freeze**
 - **Other systems access the data in EDC system as usual**

EDC Approach – Cons

- **Cons**

- **Transfer of data from pivotal trial to extension eCRF (electronic Case Report Form)**
 - **e.g. demographics, ongoing adverse events, ongoing concomitant medication**
- **Reconciliation of data at site, by monitors and in data management after transfer**
- **Ongoing reconciliation of transfer (Queries)**
- **Problems with duplicate AEs (if studies pooled)**

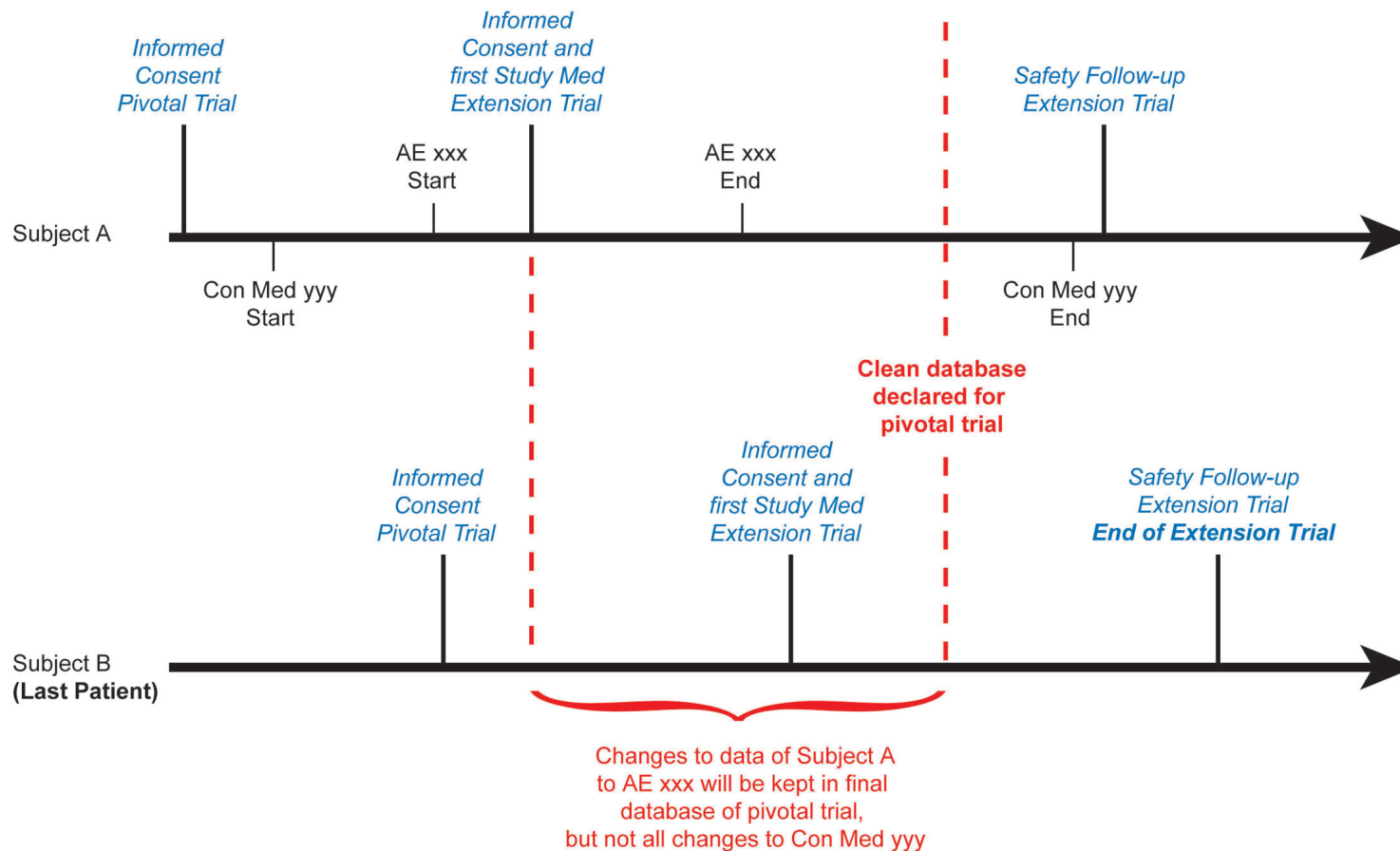
SAS Approach – Pros

- **SAS Approach: Set-up of double-blind, controlled trial and its open label extension as *one study in the EDC system and split with SAS***
- **Pros**
 - Much easier to use for sites and monitors
 - No data transfer
 - No reconciliation
 - More flexible in generating databases (pivotal only, combined database, or extension only)

SAS Approach – Cons

- **Cons**
 - **Clear differentiation of both trials lost**
 - **status of some ongoing AEs/Con Meds at end of pivotal trial might be lost (if patient-wise closure of eCRF not possible)**
 - ➔ **dependent on capabilities of used EDC system**

SAS Approach – Cons (cont.)



SAS Approach – Cons (cont.)

- **Cons (cont.)**
 - **Connection of extension to other systems
(applicable for extensions with separate protocol)**
 - **DB closure of main phase/pivotal trial
➔ dependent on capabilities of used EDC system**

Databases

- **Decision to use SAS approach**
- **2 databases required by statistics:**
 - **Pivotal trial database only**
 - **Combined database with pivotal and extension trial**
- **Database including only extension trial requested by Data Management function**

Split of Datasets

- **3 kinds of datasets with different “splitting rules”:**
 - **Visit independent datasets like Adverse Events**
 - **Visit dependent datasets like ECG**
 - **Datasets without visits or start dates e.g. Demography**

Visit Independent Datasets

- **Cut-off point for visit independent forms is the date of first study medication intake of extension trial**
- **Events occurring on cut-off date are split in the context of start time of study medication and event**
- **Start information missing: start time is queried**
- **Impossible to track changes during study conduct**
- **Status at closure of pivotal trial will be saved in database**

Visit Dependent/Special Datasets

- **Visit dependent datasets contain visit information for each record**
- **Cut-off point is the first visit of the long term extension trial**
- **Clear differentiation between pivotal and extension data possible**
- **Special datasets: no visit or date information**
- **Splitting by single programs**

Further Implementation

- **Depending on structure of the extension set up:**
 - **One study number for pivotal and extension trial:**
 - **Relative days are calculated to start of pivotal and end of extension part in combined database**
 - **Two study numbers**
 - **Relative days are calculated to start of each study and end of each study in combined database**
- **All further relative days which are needed for statistical analyses are implemented in the analyses database created by statistical department**

Problems and Solutions

- **Implementation of split by SAS macro**
- **Macro is called with every transfer of EDC database into the final database structure provided for statistics**
- **Output provided by split program:**
 - **Query management:**
 - **List of missing start dates/time at visit independent events and study medication**

Problems and Solutions

- **Validation purposes:**
 - **List how every dataset is split**
 - **Comparison of records before and after splitting**
 - **Check that subjects who did not enter the extension have no records in extension database and vice versa**
- **Additional listings are provided by Data Management to insert information of extension trial (like First Patient/First Visit of extension) into study tracking systems**

Summary

- **Decided to use SAS approach**
- **Primary reasons:**
 - **avoiding reconciliation**
 - **“investigator friendly”**
- **Lost advantages of the EDC approach were outweighed by flexibility of SAS**
- **Data are already in use by statistics for Data Monitoring Committee listings and tables**

Questions and Answers

Your questions, please

