



**Preparing an eSubmission based
on multiple trials, some of which
are ongoing**

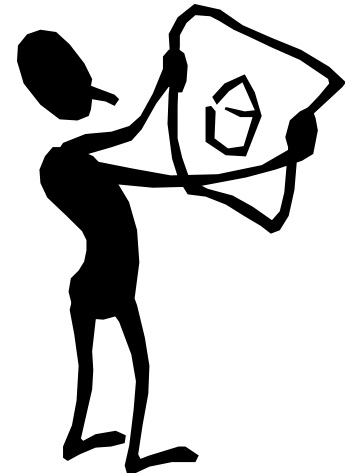
– challenges for statistical programming

Åsa Carlsheimer, Statistical Programming Director

PhUSE October 9-11, 2011

Outline

1. Introduction
2. Data standards
3. Data repository
4. Output programs
5. Planning and communication
6. Key message



Introduction

Drug FER123 was approved by FDA and EMEA in 2009

Different dose and longer treatment duration now investigated

1 pivotal phase III trial

17 completed phase II-IIIb trials

8 ongoing phase IIIb trials

} Scope of new eSubmission



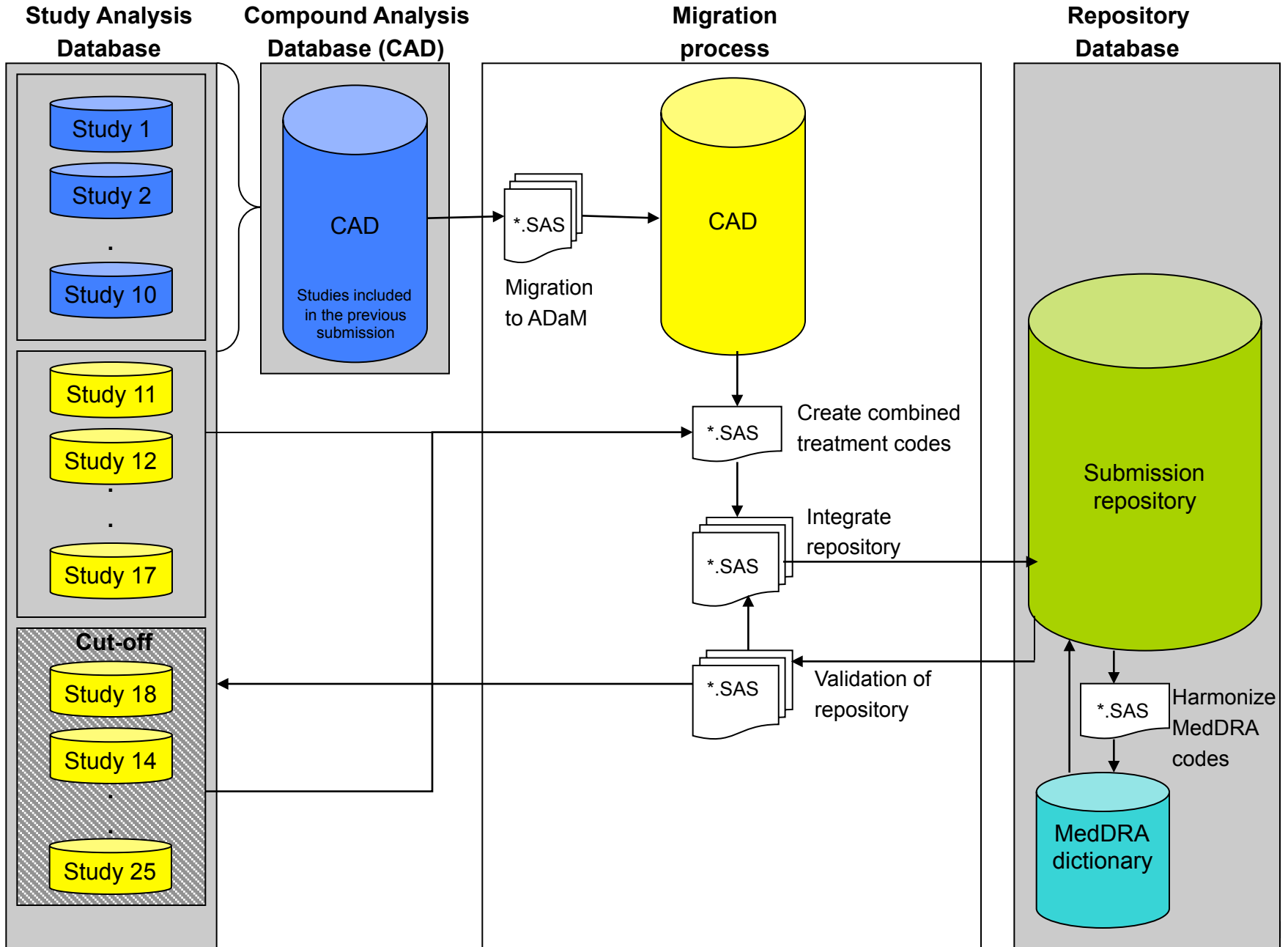
Combined safety & efficacy analysis for FER123

Data standards

- **Implementation**
 - Early 2009 based on draft CDISC ADaM 2.1
- **Maintenance**
 - All new trials across all projects and therapeutic areas
- **Benefits**
 - One common standard
 - Customization, recognition, facilitating communication with other functions
 - Easy to integrate in a repository
 - Submission ready



Data repository

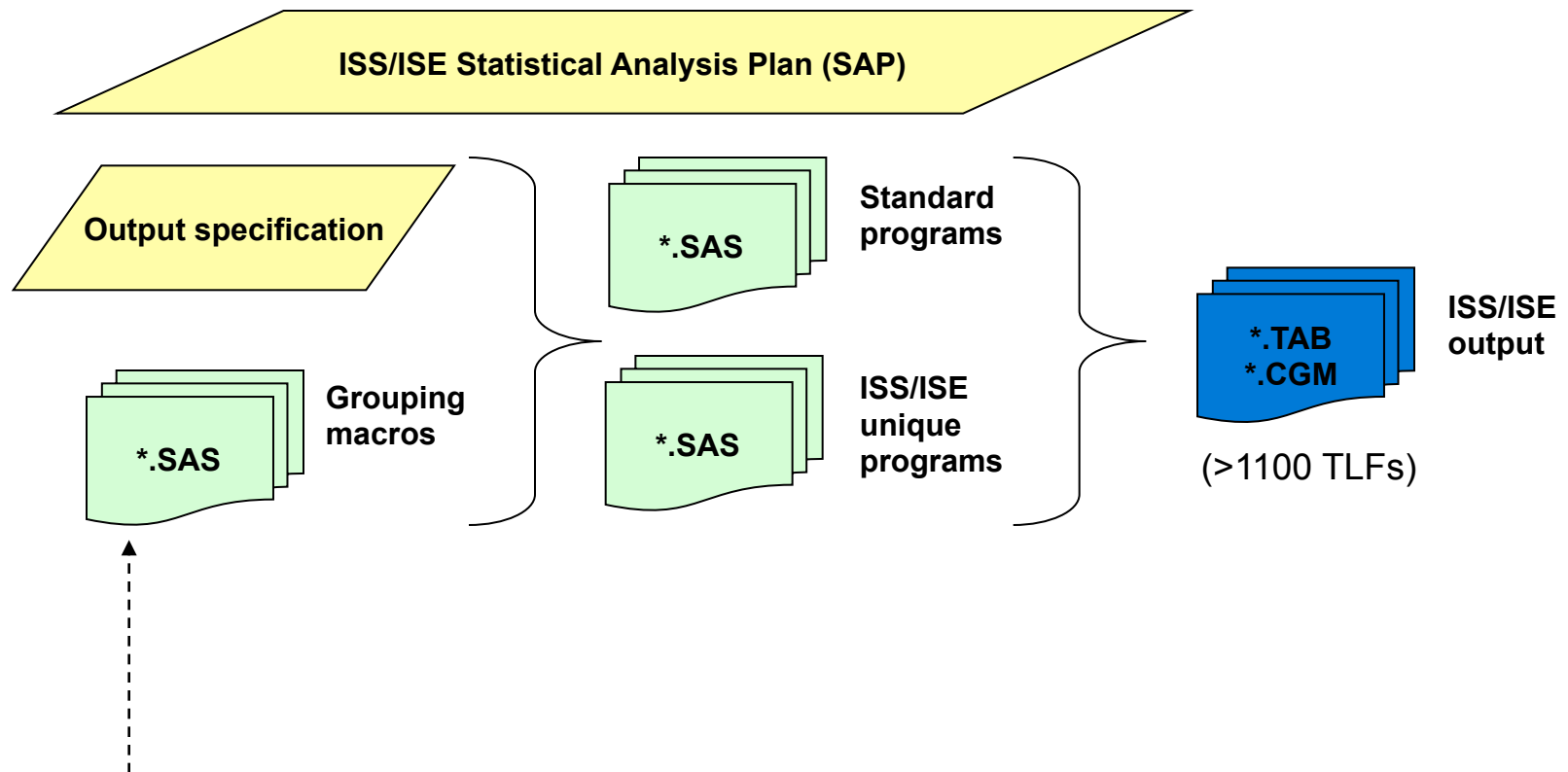


Repository learnings

- Discuss expectations on level of data cleaning for cut-off
- Include time for coding of ongoing trials after cut-off in timelines
- Agree on version of MedDRA dictionary for pivotal trial and Integrated Summary of Safety (ISS)
- Document outcome of repository validation together with actions and responsible programmer
- Easy to underestimate the resources & time needed for cleaning up the ongoing trials



Output program set-up

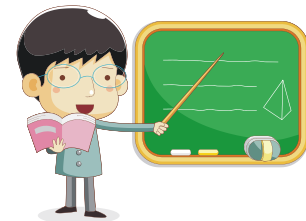


Subgroups (age, weight, race, geographic region, disease severity)

Pooled trials (phase 2/3, phase IIIb), dose/regimens, controlled/uncontrolled

Output program learnings

- Include an option to present data by multiple trials when developing standard programs (for ISS/ISE)
- >1100 TLFs need to split in to several documents (consider numbering)
- Test transfer to eCTD tool (pdf-size, templates, bookmarks, hyperlinks)



Planning and communication

Submission team 13 statistical programmers (including biostatisticians and off-shore)

Weekly internal programming/biostat meetings (status, issues, validation strategies, assign tasks to person)

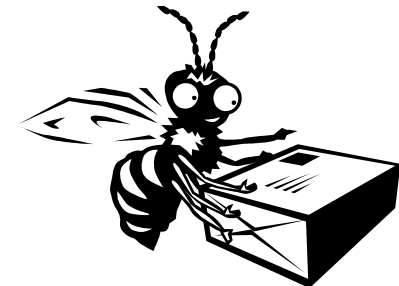
One representative in the regulatory led cross-functional team

Structured programming approach using planning tools



Delivery times after database lock

- ✓ Pivotal phase III trial (500 TLF) within 1 week
- ✓ ISE (200 TLF) within 2 weeks
- ✓ ISS (900 TLF) within 3 weeks



Key message

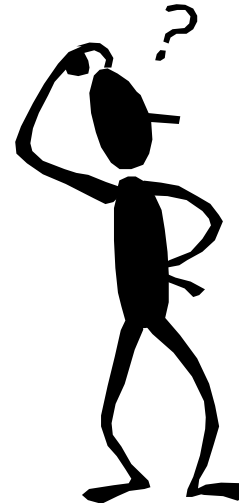
To prepare for a submission based on multiple trials, some of which are ongoing is a complex and challenging task!

Utilizing the following will facilitate the work and ensure timely deliveries:

- Implemented ADaM standards
- Maintaining data repository
- Clear programming and validation strategy
- Good communication & planning



Questions/comments?



Contact information: asa.carlsheimer@ferring.com



Data format considerations

Read eCTD to FDA “[Study Data Specifications 1.5](#)”

Define file (metadata and logic) generated from ADaM specifications in Word

Format SAS transport files *.xpt maximum 400 MB

Ferring eCTD system limitation of 100 MB

ADLB > 830 MB = ADLB1, ADLB2,----,ADLB10

Split by subject, site, X number of observations?