Involvement of Programming in Clinical Trials Disclosure on ClinicalTrials.gov – Conclusions and Outlook

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Boehringer Ingelheim

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- The ClinicalTrials.gov website
- Collecting and uploading results
- Involvement of Programming
- Conclusion

Introduction

- FDA Amendment Act (FDAAA) 2007
  - A “responsible party” has to register and report results of “applicable clinical trials”

- ClinicalTrials.gov “basic results” database launched in September 2008
  - Four sections
    - Participant flow
    - Baseline characteristics
    - Outcome measures
    - Statistical analyses

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

ClinicalTrials.gov – starting screen

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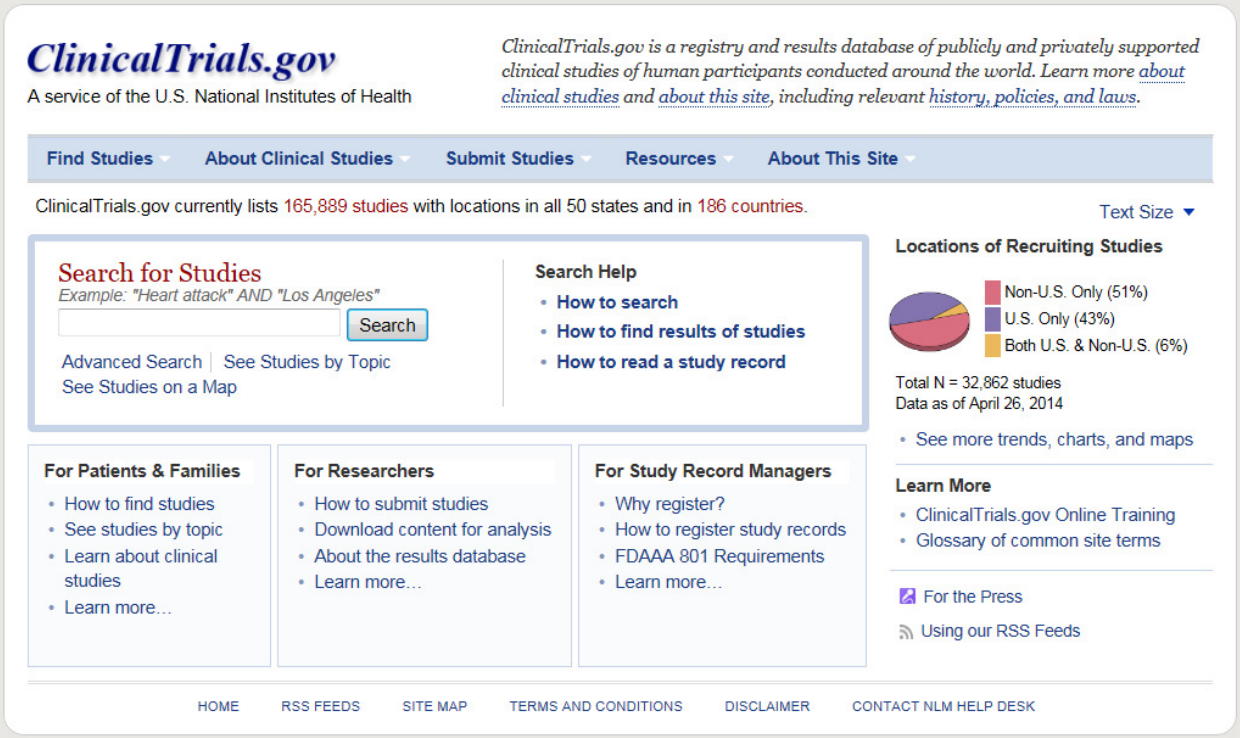

ClinicalTrials.gov – advanced search interface

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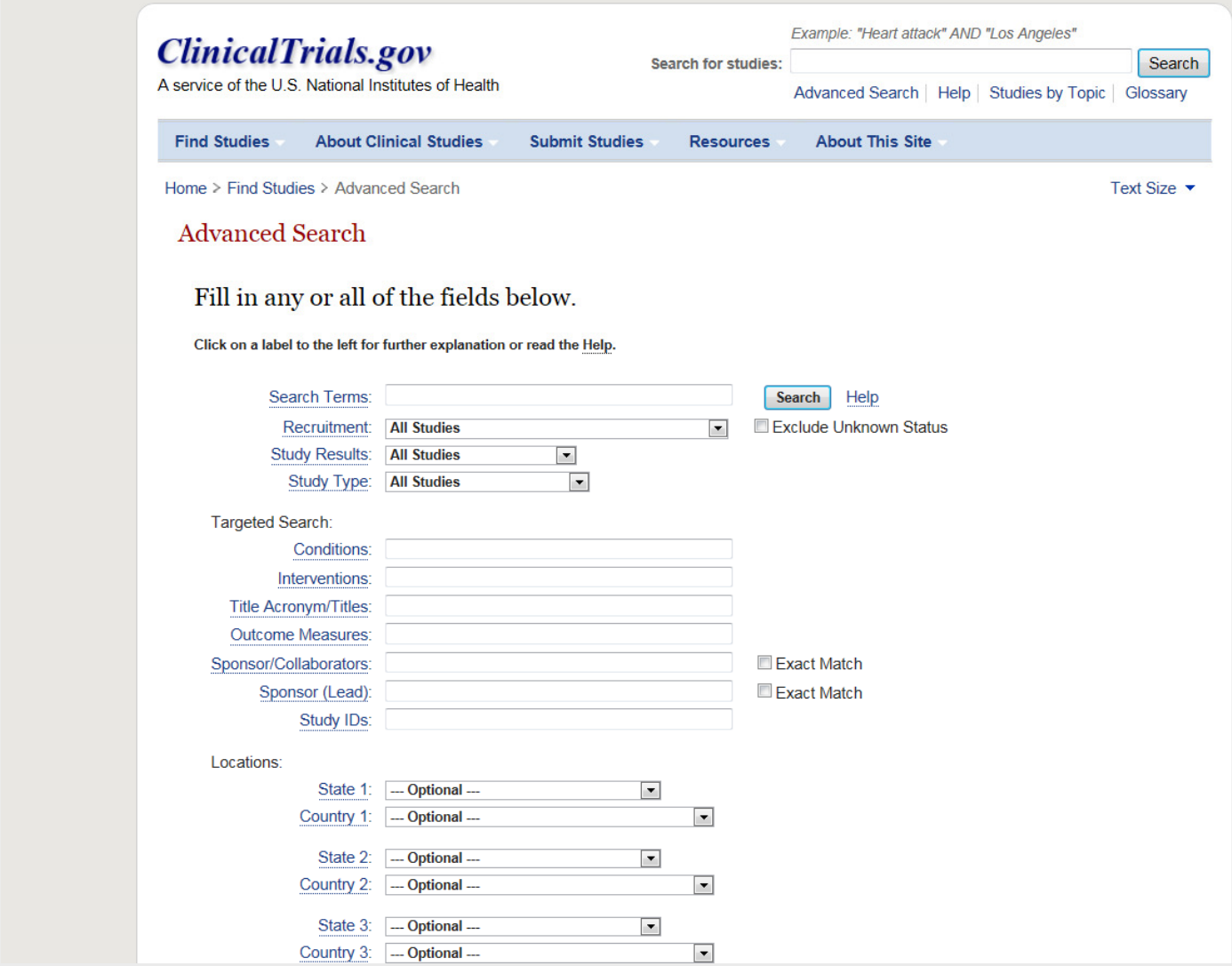
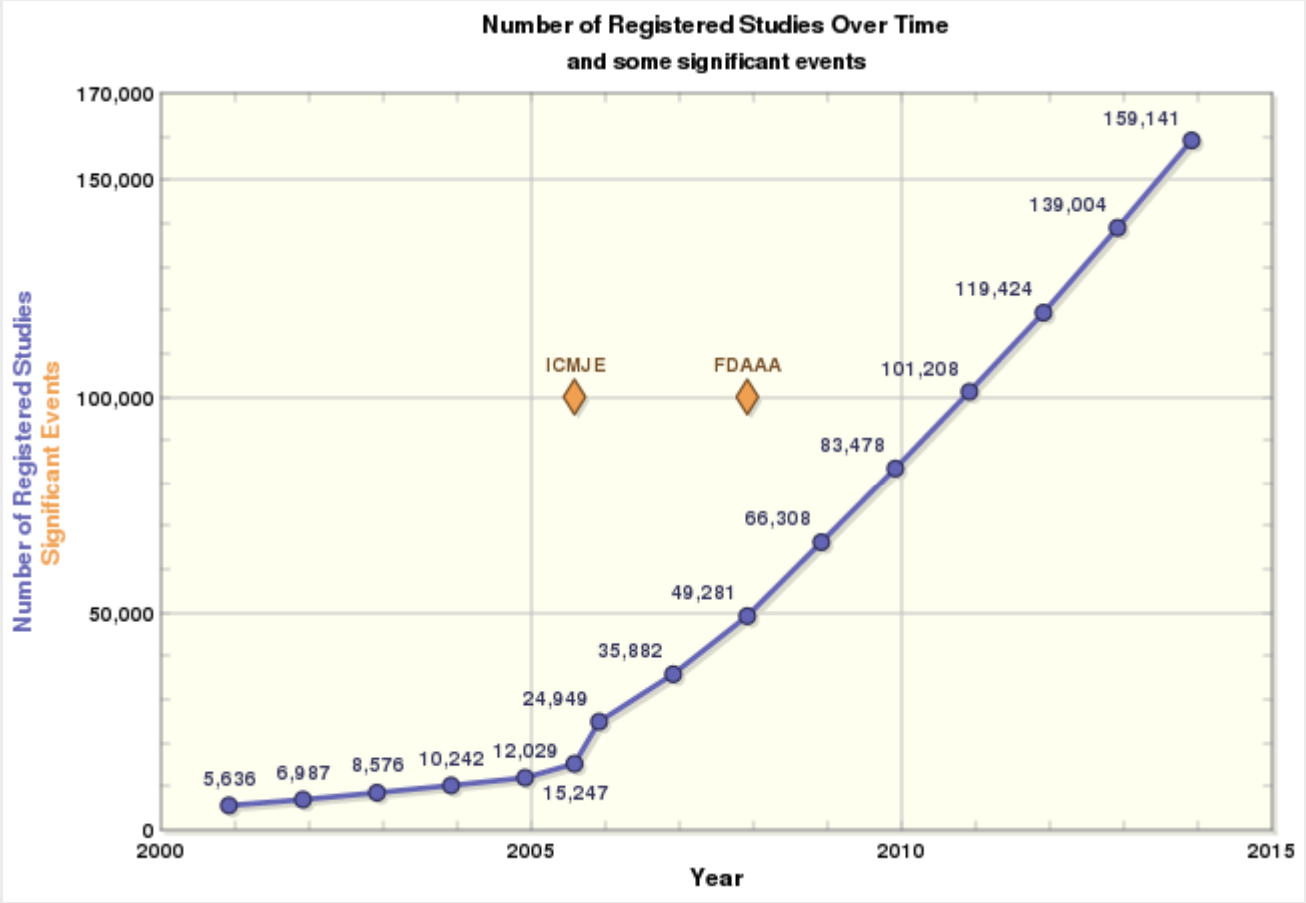


Number of Registered Studies on CT.gov

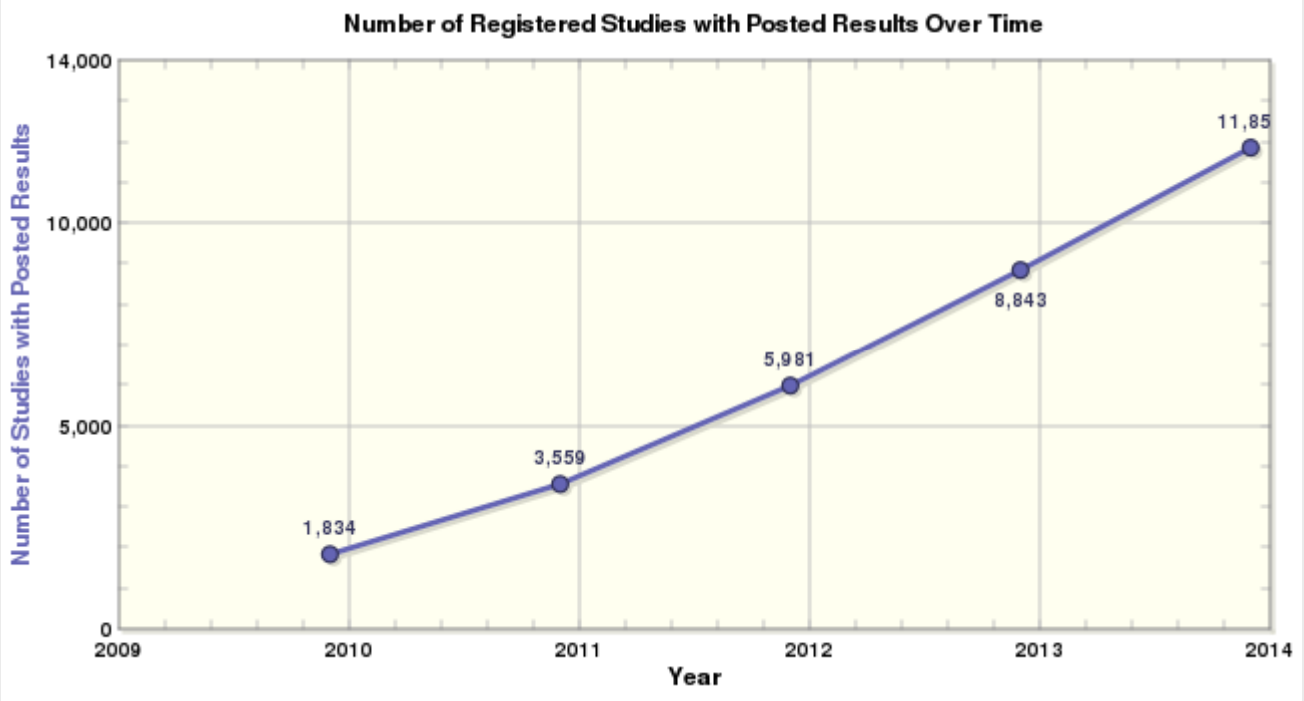


Source: http://www.clinicaltrials.gov/ct2/resources/trends (as of April 28, 2014)

ICMJE International Committee of Medical Journal Editors began requiring trial registration as a condition of publication (Sep 2005)

FDAAA expanded registration requirements of FDAAA began and were implemented (Dec 2007)

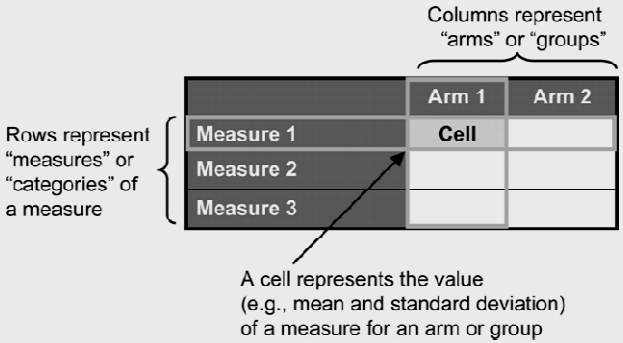
Number of Studies with Results on CT.gov



Source: http://www.clinicaltrials.gov/ct2/resources/trends (as of April 28, 2014)

Sections of “basic results” part

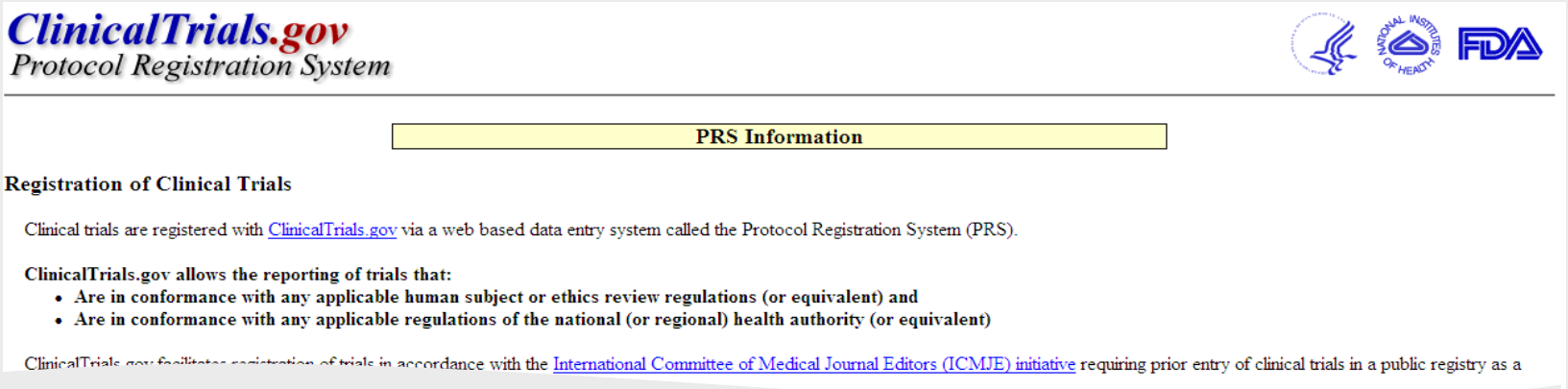
1. Participant flow
   - Patients dropped out the trial
   - Number of completed and not completed for every milestone
2. Baseline measures
   - Demographic and other baseline data overall and for each arm
   - Age, gender, and user-specified measures
3. Outcome measures and statistical analyses
   - Primary and secondary outcome measures
   - Statistical analysis description and results
4. Serious and frequent adverse events
   - Serious adverse events grouped by organ system
   - Adverse events above a 5 % threshold by organ system



Tse T et al. Chest 2009;136:295-303

Upload to ClinicalTrials.gov

- Manual data entry via a web-based Protocol Registration System (PRS)



ClinicalTrials.gov
Protocol Registration System

PRS Information

Registration of Clinical Trials

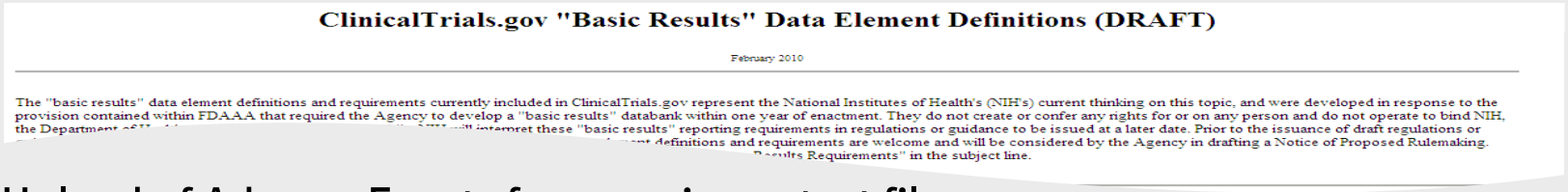
Clinical trials are registered with ClinicalTrials.gov via a web based data entry system called the Protocol Registration System (PRS).

ClinicalTrials.gov allows the reporting of trials that:

- **Are in conformance with any applicable human subject or ethics review regulations (or equivalent) and**
- **Are in conformance with any applicable regulations of the national (or regional) health authority (or equivalent)**

ClinicalTrials.gov facilitates registration of trials in accordance with the International Committee of Medical Journal Editors (ICMJE) initiative requiring prior entry of clinical trials in a public registry as a

- Upload part of/complete results as XML file
  - Contents by data element definition
  - XML schema available



ClinicalTrials.gov "Basic Results" Data Element Definitions (DRAFT)

February 2010

The "basic results" data element definitions and requirements currently included in ClinicalTrials.gov represent the National Institutes of Health's (NIH's) current thinking on this topic, and were developed in response to the provision contained within FDAAA that required the Agency to develop a "basic results" databank within one year of enactment. They do not create or confer any rights for or on any person and do not operate to bind NIH, the Department of [illegible] will interpret these "basic results" reporting requirements in regulations or guidance to be issued at a later date. Prior to the issuance of draft regulations or [illegible] definitions and requirements are welcome and will be considered by the Agency in drafting a Notice of Proposed Rulemaking. [illegible] Results Requirements" in the subject line.

- Upload of Adverse Events frequencies as text file
  - Template text file with mandatory header information available for download
- Changes of contents and layout possible

Challenges for ClinicalTrials.gov Reporting

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- Consistency of CTR results and CT.gov disclosure
- Non-standard outputs required for CT.gov disclosure (e.g., non-serious Adverse Events)
- Adherence to Timelines (1 year after LPO, 30 days after first submission)
- Consider interim analyses
- Complex (non-standard) study design or endpoint collection
- Involvement of very different functions in review and approval

Example Process Flow

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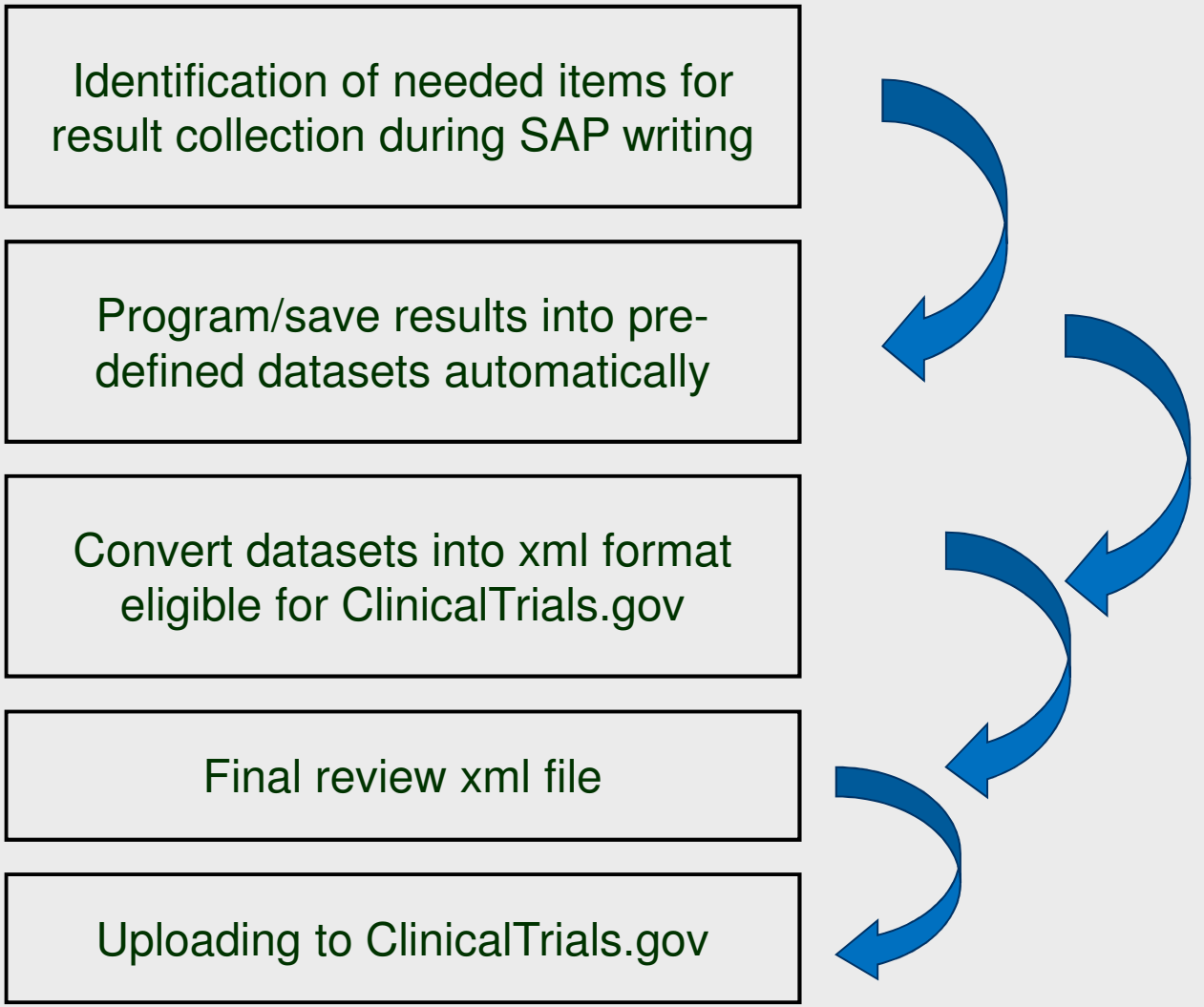

Involvement of Programming – pros and cons

Specification and creation of CT.gov items for disclosure done during SAP writing and table programming for CTR

+ Process fully embedded in established processes
+ CT.gov results available when CTR is finalized
+ Consistency between CT.gov and CTR results
+ Easy expandable to other results disclosure requirements in future
+ Highly standardized process

- Additional workload (specs and programming)
- Different outcome formats
- Updates to required contents and formats
- Separate review circle for CT.gov

Conclusions

- Developing a standardized process to handle the legal requirements
- No manual data entry – very error-prone, additional validation are needed
- New process fully integrated in existing workflow for CTR creating
- Main responsibilities by Statisticians and Programmers (and ?)
- Final disclosure information prepared at same time as CTR tables are finalized

Involvement of Programming:
Minor additional workload – meet legal requirements – standardized process