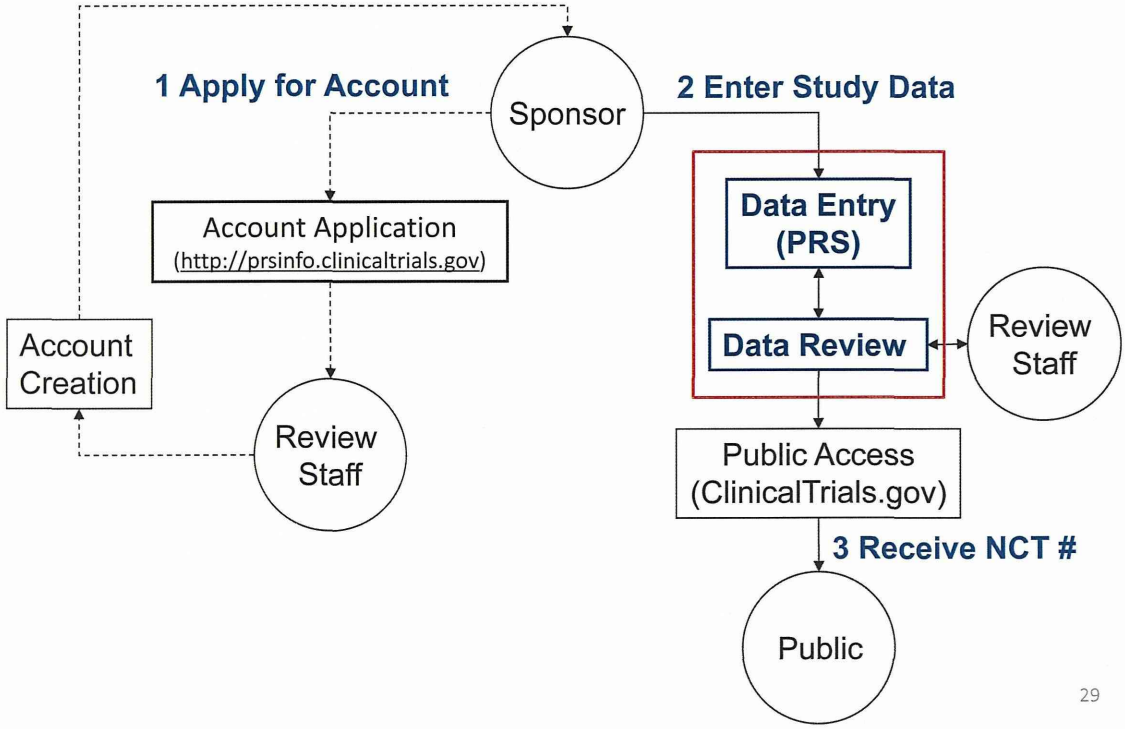
ClinicalTrials.gov Data Flow



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Data Submission Basics

- Web-based data entry system for summary protocol and results information
  - Requires organizational account, user name, password
- Structured data elements
  - Some required* and others optional
  - Pull-down menus and text
- Business rules/validation
  - ERROR- Study cannot be released; must be addressed
  - WARNING- Should be addressed
  - NOTE- Helpful hints; may or may not apply

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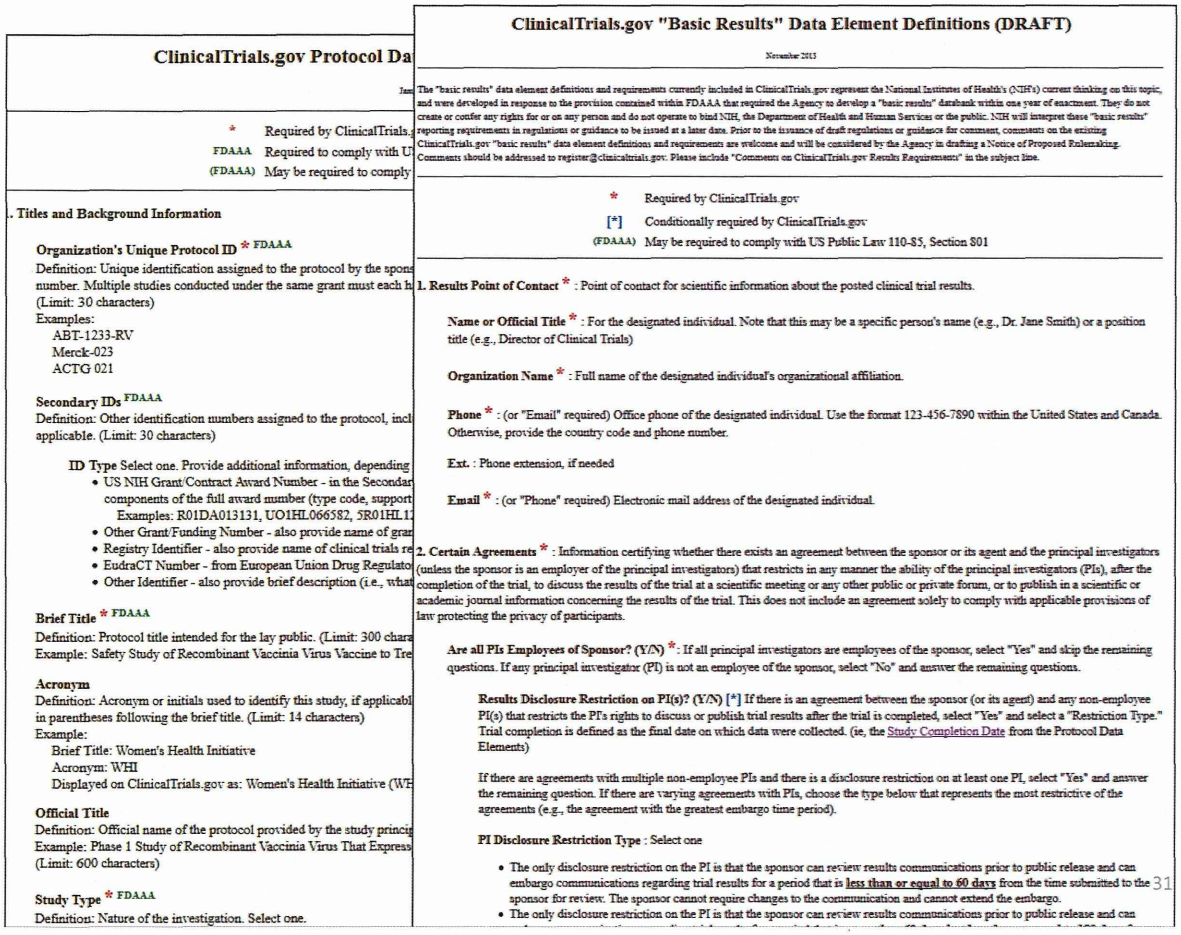

ClinicalTrials.gov Protocol Da

* Required by ClinicalTrials.
FDAAA Required to comply with U
(FDAAA) May be required to comply

. Titles and Background Information

Organization's Unique Protocol ID * FDAAA
Definition: Unique identification assigned to the protocol by the spons
number. Multiple studies conducted under the same grant must each h
(Limit: 30 characters)
Examples:
ABT-1233-RV
Merck-023
ACTG 021

Secondary IDs FDAAA
Definition: Other identification numbers assigned to the protocol, incl
applicable. (Limit: 30 characters)

ID Type Select one. Provide additional information, depending
- US NIH Grant/Contract Award Number - in the Secondar
components of the full award number (type code, support
Examples: R01DA013131, UO1HL066582, 5R01HL1
- Other Grant/Funding Number - also provide name of grar
- Registry Identifier - also provide name of clinical trials re
- EudraCT Number - from European Union Drug Regulato
- Other Identifier - also provide brief description (i.e., what

Brief Title * FDAAA
Definition: Protocol title intended for the lay public. (Limit: 300 chara
Example: Safety Study of Recombinant Vaccinia Virus Vaccine to Tre

Acronym
Definition: Acronym or initials used to identify this study, if applicabl
in parentheses following the brief title. (Limit: 14 characters)
Example:
Brief Title: Women's Health Initiative
Acronym: WHI
Displayed on ClinicalTrials.gov as: Women's Health Initiative (WH

Official Title
Definition: Official name of the protocol provided by the study princig
Example: Phase 1 Study of Recombinant Vaccinia Virus That Express
(Limit: 600 characters)

Study Type * FDAAA
Definition: Nature of the investigation. Select one.

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

November 2013

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 Health and Human Services or the public. NIH 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 guidance for comment, comments on the existing ClinicalTrials.gov "basic results" data element definitions and requirements are welcome and will be considered by the Agency in drafting a Notice of Proposed Rulemaking. Comments should be addressed to register@clinicaltrials.gov. Please include "Comments on ClinicalTrials.gov Results Requirements" in the subject line.

* Required by ClinicalTrials.gov
[*] Conditionally required by ClinicalTrials.gov
(FDAAA) May be required to comply with US Public Law 110-85, Section 801

1. Results Point of Contact * : Point of contact for scientific information about the posted clinical trial results.

Name or Official Title * : For the designated individual. Note that this may be a specific person's name (e.g., Dr. Jane Smith) or a position title (e.g., Director of Clinical Trials)

Organization Name * : Full name of the designated individual's organizational affiliation.

Phone * : (or "Email" required) Office phone of the designated individual. Use the format 123-456-7890 within the United States and Canada. Otherwise, provide the country code and phone number.

Ext. : Phone extension, if needed

Email * : (or "Phone" required) Electronic mail address of the designated individual.

2. Certain Agreements * : Information certifying whether there exists an agreement between the sponsor or its agent and the principal investigators (unless the sponsor is an employer of the principal investigators) that restricts in any manner the ability of the principal investigators (PIs), after the completion of the trial, to discuss the results of the trial at a scientific meeting or any other public or private forum, or to publish in a scientific or academic journal information concerning the results of the trial. This does not include an agreement solely to comply with applicable provisions of law protecting the privacy of participants.

Are all PIs Employees of Sponsor? (Y/N) *: If all principal investigators are employees of the sponsor, select "Yes" and skip the remaining questions. If any principal investigator (PI) is not an employee of the sponsor, select "No" and answer the remaining questions.

Results Disclosure Restriction on PI(s)? (Y/N) [*] If there is an agreement between the sponsor (or its agent) and any non-employee PI(s) that restricts the PI's rights to discuss or publish trial results after the trial is completed, select "Yes" and select a "Restriction Type." Trial completion is defined as the final date on which data were collected. (ie, the Study Completion Date from the Protocol Data Elements)

If there are agreements with multiple non-employee PIs and there is a disclosure restriction on at least one PI, select "Yes" and answer the remaining question. If there are varying agreements with PIs, choose the type below that represents the most restrictive of the agreements (e.g., the agreement with the greatest embargo time period).

PI Disclosure Restriction Type : Select one

- The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days** from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.
- The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can

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PRS Validation Messages

Module Status:

Study Identification: ✓
Study Status: 3 Errors 1 Warning 2 Notes
Sponsor/Collaborators: 1 Error 1 Note
Oversight: ✓ 1 Note
Study Description: Information is required
Conditions: Information is required
Study Design: 1 Error 3 Warnings
Arms

Edit Study Status

Help Definitions

* ‡ Record Verification Date: November Year: 2014
ERROR Verification Date is a required field.

* ‡ Overall Recruitment Status: Not yet recruiting
Tip: Before selecting Suspended, Terminated or Withdrawn see the Overall Recruitment Status definition.
NOTE: One or more locations is recruiting, but the Overall Status of the study is Not yet recruiting.
ERROR: Results may not be specified for a study which is not yet recruiting.

‡ Study Start Date: -Select- Year:
WARNING: Study Start Date has not been entered.

* ‡ Primary Completion Date: January Year: 2010 Type: Anticipated
Final data collection date for primary outcome measure.
ERROR Anticipated Primary Completion Date cannot be in the past.

Study Completion Date: -Select- Year: Type: -Select-
Final data collection date for study.
NOTE: Study Completion Date has not been entered.

Save Cancel

* Required by ClinicalTrials.gov
‡ = FDAAA Required to comply with US FDA Amendments Act
(‡) = (FDAAA) May be required to comply with US FDA Amendments Act

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General Review Criteria

- Protocol and results must be clear and informative
- Review focuses on:
  - Logic and internal consistency
  - Apparent validity
  - Meaningful entries
  - Formatting, including appropriate use of database structure
- Not equivalent to peer review; not verified against external sources (e.g., full protocol)

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Review Criteria: http://clinicaltrials.gov/ct2/manage-recs/resources

Protocol Registration and Results System (PRS)

- Requires daily maintenance
- Improvements are made over time to adapt to user needs and keep current with technology
  - Data requirements are generally same over time
  - Experience, survey data, expert evaluation, and formal usability studies are used to support PRS modifications
- Recent updates (Sept 2014 – Dec 2015)
  - Easier and more efficient navigation within a record
  - Updated look for data entry and overview screens
  - New help resources
  - Improved overall workflow and portfolio management

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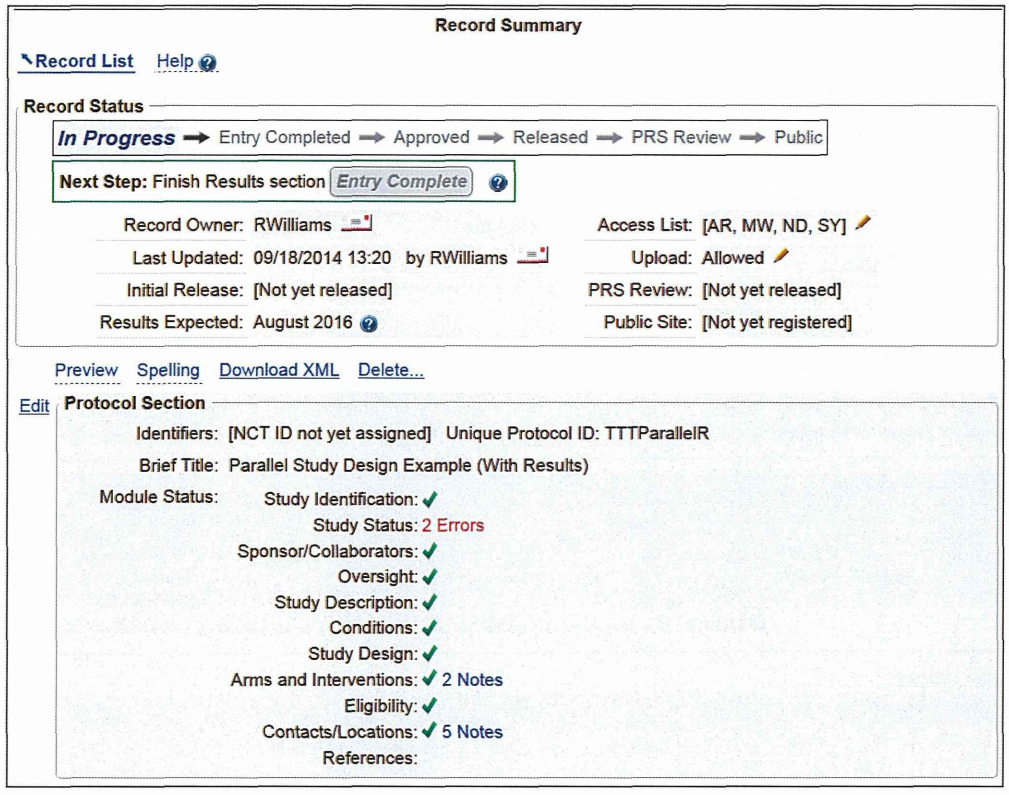
NEW Record Summary page



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NEW Protocol Section

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Results Baseline – Old

ClinicalTrials.gov
Protocol Registration System

Logout

Results

Results Point of Contact	Certain Agreements	Participant Flow	**Baseline** **Baseline Overview**	Outcome Measure	Limitations and Caveats	Adverse Events

Title: copy of NCT00327717 Org: NLM ID: 000-warning-bug

Results Overview Preview Baseline

Add Baseline Measure Add Arm/Group Recalculate Totals

		Placebo *Placebo : Patients in placebo ...* Modify/Delete	Zonisamide 100 mg Tablet *Zonisamide : Patients entered ...* Modify/Delete	Total
Edit	Overall Number of Baseline Participants	123	145	268 *(Calculated)*
	Baseline Analysis Population Description			

Age Categorical *[Units: participants]*
Modify/Delete

		Placebo	*Zonisamide 100 mg Tablet*	*Total*
Edit	*<=18 years*			*(Calculated)*
	Between 18 and 65 years			*(Calculated)*
	>=65 years			*(Calculated)*

ERROR : [9 occurrences] A Baseline Measure Number or Central Tendency Value has not been entered.

Add Baseline Measure

Age Continuous *[Units: years]*
Modify/Delete

		Placebo	*Zonisamide 100 mg Tablet*	*Total*
Edit		±	±	±

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Results Baseline - New

ClinicalTrials.gov PRS
Protocol Registration and Results System

Org: PRS User: RJW

Home > Record List > Record Summary > Results Section > Baseline

Gtech ID: U2971g A Study to Evaluate the Efficacy and Safety of Rituximab in Patients With Severe Systemic Lupus Erythematosus NCT00137969

Baseline Measures Overview

Results Section Add Baseline Measure Help Definitions Show All

Edit	Arm/Group Title ▸ Arm/Group Description	Rituximab + Prednisone Rituximab intravenously at a dose o...	Placebo + Prednisone Placebo intravenously at a dose of ...	Total
Edit	**Overall Number of Baseline Participants** ▸ Baseline Analysis Population Description	169	88	**257**
Edit Delete	Age, Customized units: participants Measure Type: Number			
	< 20 years	2	2	4
	Between 20 and 64 years	166	83	249
	> 64 years	1	3	4
Edit Delete	Age, Continuous units: years Mean (Standard Deviation)	40.2 (11.4)	40.5 (12.8)	40.3 (11.9)
Edit Delete	Gender, Male/Female units: participants Measure Type: Number			
	Female	152	82	234
	Male	17	6	23

Help: Results Modules

ClinicalTrials.gov PRS
Protocol Registration and Results System

Help: Results Modules > Participant Flow

Help: Participant Flow

- ▸ Overview

Data Elements

- ▸ Recruitment & Pre-assignment
- ▸ Arm/Group
- ▸ Period
- ▸ Milestones
- ▸ Reason Not Completed

Study Design Examples

- ▸ Parallel
- ▸ Cross-over
- ▸ Dose Escalation
- ▸ Factorial
- ▸ Multiple Period

Close

U.S. National Library of Medicine | U.S. National Institutes of Health | U.S. Department of Health & Human Services

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Help: Participant Flow - Overview

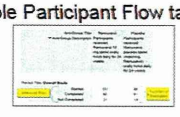
ClinicalTrials.gov PRS
Protocol Registration and Results System

Help: Results Modules > Participant Flow

Help: Participant Flow

▾ Overview

- Participant Flow shows how participants were assigned to intervention(s) and how they progressed through the study. It is a tabular version of a CONSORT flow diagram
- The table columns (Arm/Groups) describe participants' experiences as they progressed through the study.
- The table rows (Milestones) describe the number of participants starting and completing the study in addition to any other significant events.
- Additional tables (Periods) can be used to describe separate stages of the study.
- Example Participant Flow table.
  ▸ show



Resources:

Data you will need: Participant Flow Data Preparation Checklist (PDF)
1-page data organization tools: Participant Flow Template (PDF)
Video tutorial: Results: Participant Flow Module (17:32)
Review criteria: Results Review Criteria (PDF)

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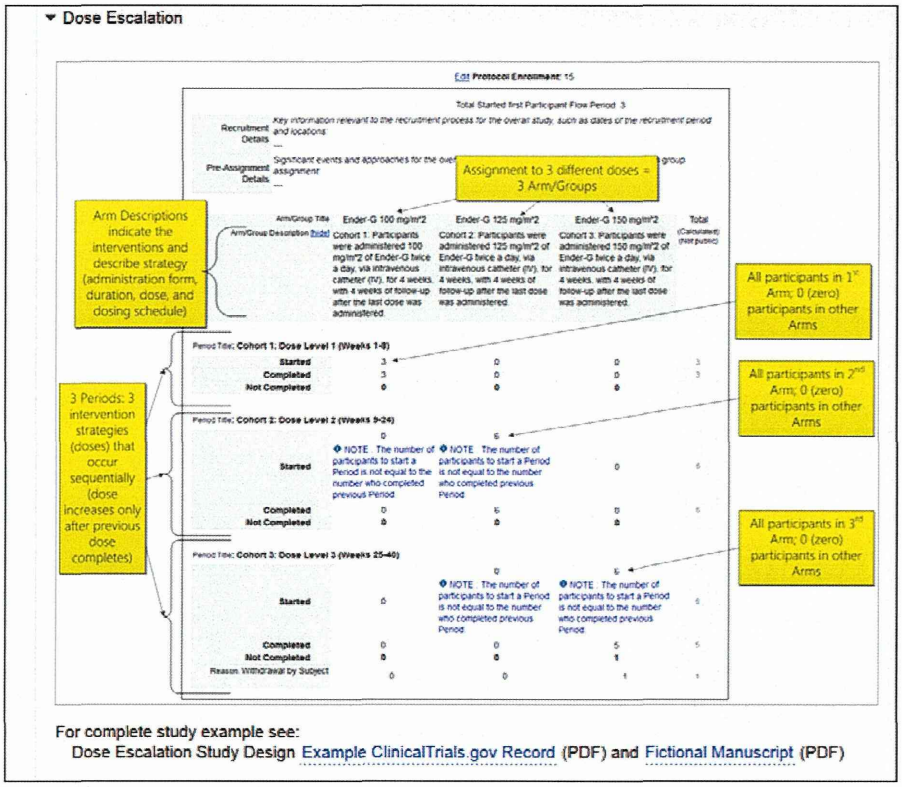
Help: Participant Flow – Study Design Examples



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Additional Help Resources

- General
  - Data element definitions
  - Review criteria
- Results Submission
  - Simple results templates
  - Results data preparation checklists
  - Example records using common study designs (e.g., parallel, cross-over, factorial, dose escalation)
- Help [PRS Main Menu and on data entry screens]
- ClinicalTrials.gov staff: register@clinicaltrials.gov

Support Materials: http://www.clinicaltrials.gov/ct2/manage-recs/resources

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Simple Results Templates:

Basic Information Needed

* Outcome Measure Type	*(Circle One)* Primary	Secondary	Other Pre-specified	Post-Hoc	**Safety Issue?**	*(Circle One)* Yes	No
* Outcome Measure Title								
Outcome Measure Description								
* Outcome Measure Time Frame								

	* Arm/Group Title							
	Arm/Group Description							
	* Number of Participants Analyzed							
	Analysis Population Description							
* Measure Type	* Measure of Dispersion/Precision							
(Circle One) Number Mean Median Least Squares Mean Geometric Mean Log Mean	*(Circle One)* Not Applicable Standard Deviation Inter-Quartile Range Full Range Standard Error 95% Confidence Interval 90% Confidence Interval Geometric Coefficient of Variation							
[*] Category Title								
[*] Category Title								
* Unit of Measure								

Results Data Preparation Checklists

ClinicalTrials.gov
A service of the National Institutes of Health

Edited: 19 August 2014

Outcome Measure Data Preparation Checklist

Overview: A tabular summary of outcome measure results by comparison group. You must report tables for each pre-specified primary and secondary outcome and any appropriate statistical analyses. The outcomes that were pre-specified in the Protocol Section of the record will be available to use and edit during results data entry. You may also include other pre-specified and *post hoc* outcomes. Use this checklist with the Outcome Measure Simple Results Template and Results Data Element Definitions.

	Information to have available for each Outcome Measure	Term
☐	• Label the measure as Primary, Secondary, Other Pre-specified, or Post hoc.	*‡Outcome Measure Type
☐	• Title—Describe specifically what was measured and will be reported as data ○ For example, "Change from baseline in systolic blood pressure at 6 months" specifically describes what was measured and how the outcome data will be reported; "Principle Vital Signs" does not. • Description—Any elaboration needed to understand the measure and the reported data. Information should be written for a public audience (i.e., not specialists in your field, but general readers of the medical literature). ○ For example, a description of how the measure was taken, relevant definitions (e.g., explain "response"), any methods of assessment, and/or calculations that were performed to summarize the data ○ If the measure was based on a scale, explain any numerical categories or provide the range and direction of possible scores (0=no pain; 10=worst possible pain) to allow a reader to properly interpret any reported values.	*‡Outcome Measure Title ‡Outcome Measure Description
☐	• The time point(s) or duration over which a participant was assessed for the measure, and for which data are being reported ○ For a time-to-event measure—A definition of the stopping rule and the longest duration over which a participant was observed (e.g., from randomization until death, up to 3 years)	*‡Outcome Measure Time Frame
☐	• The number of separate groups for which summary data will be provided • Tip: Generally equal to the number of intervention strategies or groups compared	Arm/Groups
☐	• For each group: ○ Title—A descriptive label for the group (header for table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1"). ○ Description—A detailed explanation of the participants included in the group and the interventions received. This may include a description of how groups of participants were recombined for analysis purposes.	*‡Arm/Group Title ‡Arm/Group Description
☐	• Number of participants, in each group, from whom data were collected and summarized. ○ If the unit of analysis is not participants, also provide the name of the unit (e.g., eyes, lesions) and the number of units [Type/Number Units Analyzed].	*‡Number of Participants Analyzed

Recorded Presentations

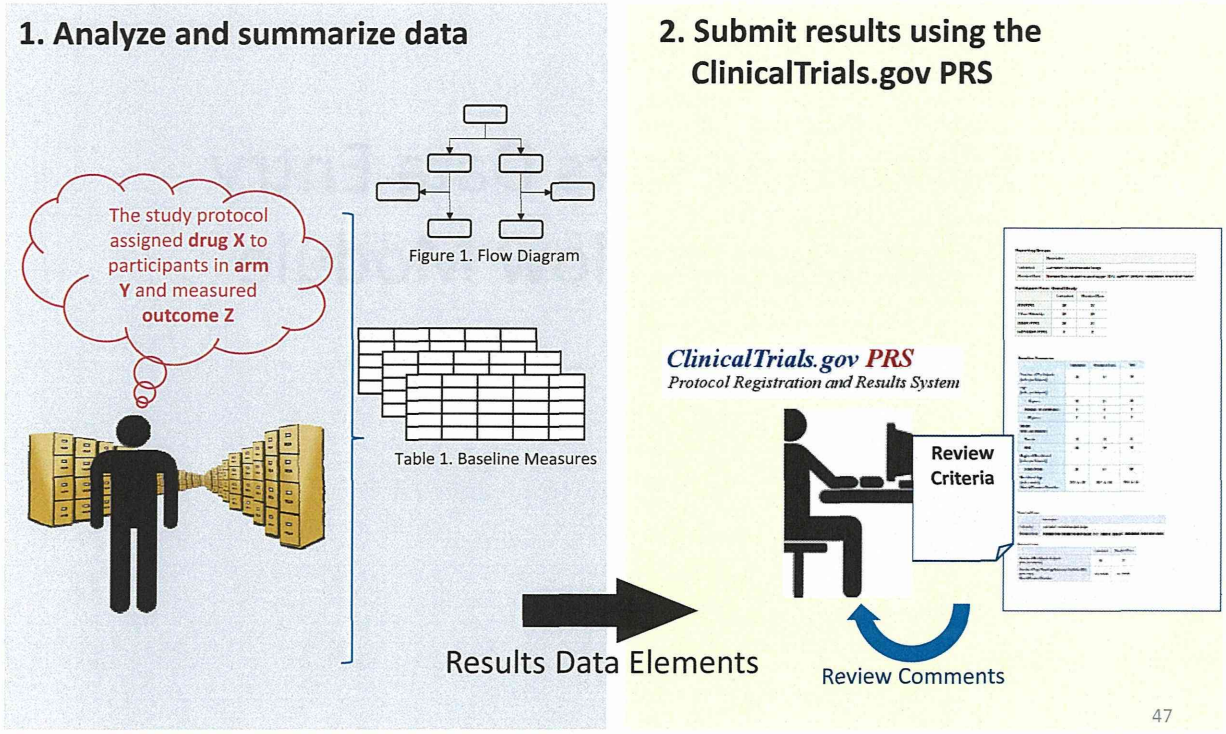
- Available at: http://clinicaltrials.gov/ct2/manage-recs/present
- Six presentations with audio and slides

1. Overview of ClinicalTrials.gov
2. Key FDAAA Issues
3. Results: Participant Flow Module
4. Results: Baseline Characteristics Module
5. Results: Outcome Measures and Statistical Analysis Module
6. Results: Adverse Events Module

ClinicalTrials.gov Results Statistics
(as of 1/27/2016)

- 19,800 studies with results posted
  - Approximately 33% of records are posted on initial submission (others require revisions)
- 1,017 Industry sponsors have submitted 58% of the studies with results
- 1,639 Non-Industry sponsors have submitted 42% of the studies with results
- PRS Review time about 30 days

Two Basic Steps for Submitting Results



Experience with Results Database

- Entering results is similar to the process of preparing a journal article
- Data provider must be familiar with the study design and data analysis
  - Typically, the investigator and/or a statistician will need to be involved