“Basic Results” Database

Deborah A. Zarin, M.D.
ClinicalTrials.gov
December 2008

ClinicalTrials.gov Overview and PL 110-85 Requirements

Module 1

Levels of "Transparency"

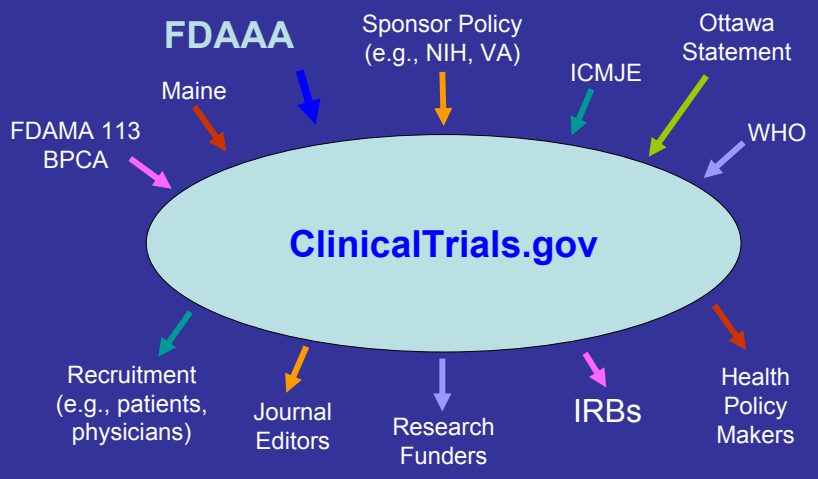
- Prospective Clinical Trials Registry
  - Captures key summary protocol information before or during the trial
- Results Database
  - Captures summary results of a completed trial

Zarin DA, Tse T. Medicine. Moving toward transparency of clinical trials. *Science*. 2008 Mar 7;319(5868):1340-2.

History of ClinicalTrials.gov

- FDAMA 113 (1997): Mandates Registry
  - IND trials for serious and life-threatening diseases or conditions
- ClinicalTrials.gov Launched in February 2000
- Calls for Increased Transparency of Clinical Trials
  - Maine State Law; State Attorneys General
  - Journal Editors (2004)
- ClinicalTrials.gov Accommodates Other Policies
- FDAAA 801 (2007): Expands Registry and Adds Results Database

Policies and Users



Public Law 110-85

Sec.801 Expanded Clinical Trial Registry

- Enacted on September 27, 2007
- Requires Trial Registration (Dec 2007)
  - Phase II-IV drug and device trials for all diseases
  - Data elements: ClinicalTrials.gov + ~ WHO/ICMJE
- Requires Results Reporting (Sept 2008)
  - Trials of FDA-approved or cleared drugs and devices
  - "Basic" Results: Baseline Characteristics, Primary & Secondary Outcomes, Statistical Analyses
  - Adverse Events (Sept 2009)
  - "Expansion" of results by rulemaking (Sept 2010)

Enforcement Mechanisms

- Public Notices of Non-Compliance
- Civil Monetary Penalties (up to $10,000 per day)
- Withholding of NIH funds
- FDA Sanctions

Key Terms

- Responsible Party
  - Sponsor
  - Designated Principal Investigator (PI)
- Applicable Clinical Trial
  - Drug
  - Device
- (Primary) Completion Date

Key Milestones

- December 26, 2007
  - Expanded registry requirements effective
  - Linking to existing results
- September 27, 2008
  - "Basic Results" reporting requirements effective
- March 2009 - Public Meeting
- September 27, 2009 – Adverse Events
- September 27, 2010 – Rulemaking Due

Basic Results Database: General Characteristics

- Results of "applicable clinical trials" of FDA-*approved/cleared* medical products
- Generally, submission within 12 months of the *earlier* of estimated or actual trial completion date (of primary outcome)
- Delayed Submission of Results
  - Seeking initial approval
  - Seeking approval of a new use
  - Extensions for "good cause"

Basic Results Information: Statutory Requirements

- Demographic & baseline characteristics
  - Table of values, overall and for each arm
  - # of patients dropped out & excluded from analysis
- Primary and secondary outcomes
  - Table of values for each primary & secondary outcome measure, by arm
  - Scientifically appropriate tests of statistical significance
- Point of contact (for scientific information)
- Certain agreements (restrictions on PI to discuss or publish results after trial completion date)

Adverse Events - Default

- If the Secretary fails to issue regulation by 24 months after the date of enactment [September 2009]
- SERIOUS ADVERSE EVENTS
  - Table of anticipated & unanticipated serious adverse events
  - Grouped by organ system
  - Number and frequency of event in each clinical trial arm
- FREQUENT (other) ADVERSE EVENTS
  - Table of anticipated & unanticipated adverse events
  - Exceed a frequency of 5 percent within any trial arm
  - Grouped by organ system
  - Number and frequency of event in each trial arm

Basic Results Modules

- Participant Flow
  - Number Started, Completed, Not Completed
  - Optional: Reasons for Not Completed
- Demographic and Baseline Characteristics
  - Measurement name and units (age & gender required)
  - Data: Overall and by trial arm
- Primary and Secondary Outcomes
  - Number Participants Analyzed
  - Measurement type, name, units and time frame
  - Data: By trial arm
  - Scientifically appropriate tests of statistical significance

"Basic Results" Data Entry

Module 2

Certain Agreements

"Whether there exists an agreement … between the sponsor or its agent and the principal investigator … that restricts in any manner the ability of the principal investigator, after the completion date 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."

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is:
☑ 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**. 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 embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.
☐ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Design Requirements

- Display consists of data tables with minimal text—must be self-explanatory
- System must accommodate range of study designs and facilitate comparison across studies
- NLM directed to:
  - Consider different methods of display based on principles of risk communication for different audiences
  - Ensure the data are searchable in many ways
- Structured data entry required to facilitate search and display needs

Design Features

- Tables are “constructed” by the data provider
  - Columns are pre-set as study arms, but can be changed by the data provider
  - Rows are measures—some are pre-set, others are customized for each study
  - Type of measure determines specific design of “cells”
- Attempt to balance fixed structure with flexibility

Principles for Using the Basic Results Database

- Submitted data are used to develop basic tables for the public display
- Tables must be interpretable by people not familiar with each particular study
- Labels for rows, columns, and units of measure must be meaningful and precise

http://prsinfo.clinicaltrials.gov/fdaaa.html

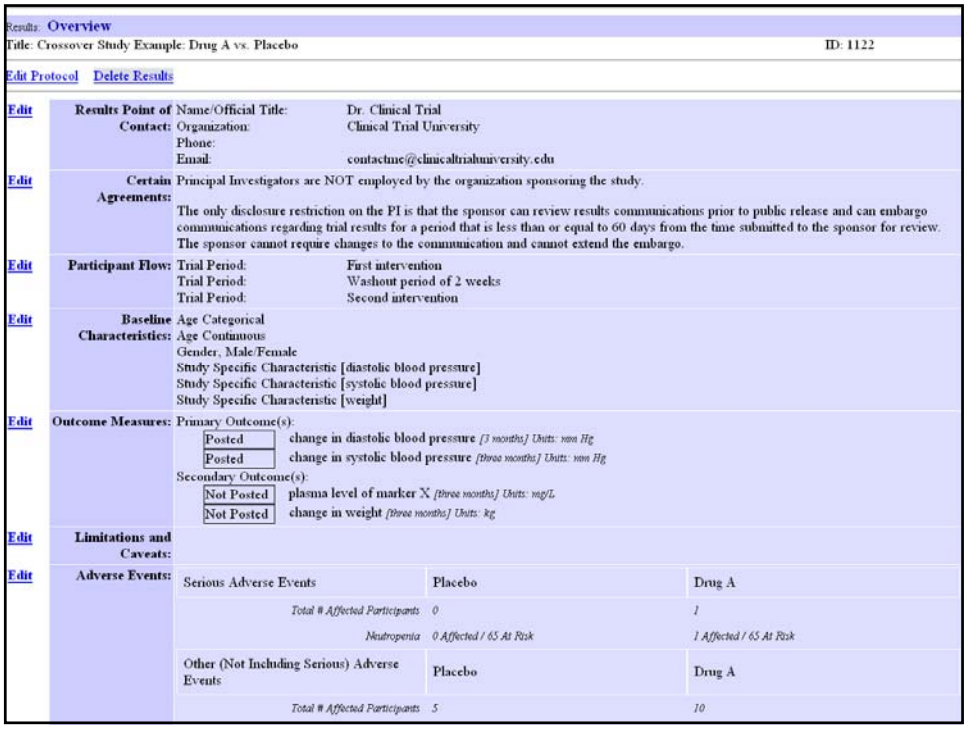
"Basic Results" Database

- Common errors (pdf) - overview of common types of errors identified in submitted records with "basic results"
- Helpful hints (pdf) - tips on entering results data, including three examples of common study models (parallel design, crossover design, and diagnostic accuracy studies), reporting measure types, including information on reporting outcomes measured with a scale.
- "Basic Results" Data Element Definitions (DRAFT) - details on the information that is entered about results via the PRS.
- May 21, 2008 Federal Register Notice - describes the public process for the expansion of ClinicalTrials.gov under FDAAA 801 (pdf).
- Basic Results Provisions - extracted from FDAAA 801.
- Delayed Submission of Results - information on submitting certifications or requests for extension

Expanded Registry

- Data Element Definitions (DRAFT) - details on the information that is entered via the PRS
- NIH Fact Sheet on registration at ClinicalTrials.gov under FDAAA 801
- Guidance from NIH Office of Extramural Research:
  - Clinical Trials Registration in ClinicalTrials.gov (Public Law 110-85): Competing Applications and Non-Competing Progress Reports (NOT-OD-08-023)
  - FAQs - Clinical Trials Registration in ClinicalTrials.gov
  - Guidance on New Law (Public Law 110-85) Enacted to Expand the Scope of ClinicalTrials.gov: Registration (NOT-OD-08-014)
- Certification of Compliance to FDA - to accompany Drug, Biological Product, and Device applications or submissions

For specific questions or comments as this relates to the PRS, contact us at register@clinicaltrials.gov.



Results: **Overview**

Title: Crossover Study Example: Drug A vs. Placebo — ID: 1122

Edit Protocol | Delete Results

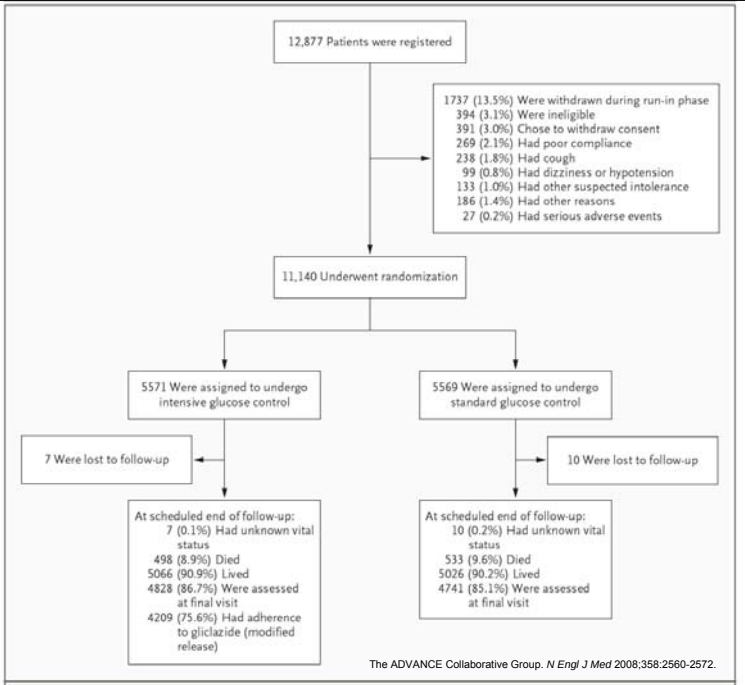
Edit	**Results Point of Contact:**	Name/Official Title: Dr. Clinical Trial Organization: Clinical Trial University Phone: Email: contactme@clinicaltrialuniversity.edu
Edit	**Certain Agreements:**	Principal Investigators are NOT employed by the organization sponsoring the study. The only disclosure restriction 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.
Edit	**Participant Flow:**	Trial Period: First intervention Trial Period: Washout period of 2 weeks Trial Period: Second intervention
Edit	**Baseline Characteristics:**	Age Categorical Age Continuous Gender, Male/Female Study Specific Characteristic [diastolic blood pressure] Study Specific Characteristic [systolic blood pressure] Study Specific Characteristic [weight]
Edit	**Outcome Measures:**	Primary Outcome(s): Posted — change in diastolic blood pressure *[3 months] Units: mm Hg* Posted — change in systolic blood pressure *[three months] Units: mm Hg* Secondary Outcome(s): Not Posted — plasma level of marker X *[three months] Units: ng/L* Not Posted — change in weight *[three months] Units: kg*
Edit	**Limitations and Caveats:**	
Edit	**Adverse Events:**	

Serious Adverse Events	Placebo	Drug A
Total # Affected Participants	*0*	*1*
Neutropenia	*0 Affected / 65 At Risk*	*1 Affected / 65 At Risk*

Other (Not Including Serious) Adverse Events	Placebo	Drug A
Total # Affected Participants	*5*	*10*

Data Elements: Participant Flow

- Number of Participants - *Required*
  - Started Study
  - Completed Study
  - [Not Completed: e.g., dropped out or excluded]
- Other Information
  - Recruitment Details
  - Pre-assignment Details
  - Reasons for Not Completed (e.g., adverse events)
  - Additional Periods or “Milestones”



The ADVANCE Collaborative Group. *N Engl J Med* 2008;358:2560-2572.

Figure 1. Enrollment, Randomization, and Follow-up of Study Participants.

Results: **Participant Flow**

Title: Crossover Study Example: Drug A vs. Placebo ID: 1122

Results Overview

Edit	**Recruitment Details:**	Participants recruited from a specialty clinic at a hospital,in Fictional City, USA between October 2004 and January 2007.		
	Pre-assignment Details:	267 participants recruited; 186 screened, 56 excluded (36 did not meet inclusion criteria and 20 refused participation).		
	Create Period	**Add Arm/Group**		
	Periods		**Placebo first** *Placebo twice daily in first i...* Modify/Delete	**Drug A first** *Drug A 25 mg twice daily in fi...* Modify/Delete
Edit	**First intervention** Modify/Delete	**STARTED**	65	65
		Other Milestones:	Received at least one dose of drug	
		COMPLETED	65	63
		Not Completed: *(=Started - Completed)*	0 *(Calculated)*	2 *(Calculated)*
			Other [neutropenia] *(0, 1)*; Withdrawal by Subject *(0, 1)*;	
Edit	**Washout period of 2 weeks** Modify/Delete	**STARTED**	65	63
		COMPLETED	63	62
		Not Completed: *(=Started - Completed)*	2 *(Calculated)*	1 *(Calculated)*
			Other [Disease relapse] *(2, 1)*;	
Edit	**Second intervention** Modify/Delete	**STARTED**	63	62
		COMPLETED	60	62
		Not Completed: *(=Started -*	3 *(Calculated)*	0 *(Calculated)*
			Adverse Event *(2, 0)*; Lost to Follow-up *(1, 0)*;	

Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
Participants recruited from a specialty clinic at a hospital, in Fictional City, USA between October 2004 and January 2007.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
267 participants recruited; 186 screened, 56 excluded (36 did not meet inclusion criteria and 20 refused participation).

Reporting Groups

	Description
Placebo First	Placebo twice daily in first intervention period and Drug A 25 mg twice daily in second intervention period (after washout period).
Drug A First	Drug A 25 mg twice daily in first intervention period and Placebo twice daily in second intervention period (after washout period).

Period: First Intervention

	Placebo First	Drug A First
STARTED	65	65
Received at Least One Dose of Drug	65	64
COMPLETED	65	63
NOT COMPLETED	0	2
neutropenia	0	1
Withdrawal by Subject	0	1

Period: Washout Period of 2 Weeks

	Placebo First	Drug A First
STARTED	65	63
COMPLETED	63	62
NOT COMPLETED	2	1
Disease relapse	2	1

Period: Second Intervention

	Placebo First	Drug A First
STARTED	63	62
COMPLETED	60	62
NOT COMPLETED	3	0
Adverse Event	2	0
Lost to Follow-up	1	0

Data Elements:
Demographic and Baseline Characteristics

- Demographic Characteristics - *Required*
  - Number of Participants Analyzed
  - Age (continuous or categorical)
  - Gender
- Other Demographic Characteristics
  - Race, ethnicity, region of enrollment
- Study-Specific Baseline Measures – Certain sub-elements required if provided
  - Measurement Name and Units
  - Measurement Type (e.g., Number, Median)
  - Measure of Dispersion, if continuous (e.g., Standard Deviation)

Table 1. Baseline Characteristics According to Randomized Study Assignment*

Parameter	Placebo (n = 2885)	Pexelizumab (n = 2860)
Age, y		
Median (IQR)	61 (52-71)	61 (51-71)
≥75, %	479 (16.6)	498 (17.4)
Women, No. (%)	634 (22.0)	691 (24.2)
Weight, median (IQR), kg	80 (70-91)	80 (70-91)
Heart rate, median (IQR), beats/min	75 (64-86)	75 (65-86)
Systolic blood pressure, median (IQR), mm Hg:	133 (117-150)	133 (117-150)
Killip class, No. (%)†		
I	2580 (89.6)	2548 (89.2)
II	236 (8.2)	253 (8.9)
III	33 (1.2)	31 (1.1)
IV	32 (1.1)	26 (0.9)
Infarct location, No. (%)		
Inferior	1180 (40.9)	1167 (40.8)

JAMA. 2007;297:43-51.

	Add Baseline Measure	Add Arm/Group
		Entire study population *Includes groups randomized to ...* Modify/Delete
Edit	**Overall Number of Baseline Participants**	130

Edit	**Age Categorical** *Units: participants* Modify/Delete	
		Entire study population
	<=18 years — *Number participants*	*0*
	Between 18 and 65 years — *Number participants*	*130*
	>=65 years — *Number participants*	*0*

	Add Baseline Measure	
	Age Continuous *Units: years* Modify/Delete	
Edit		*Entire study population*
	Mean (Standard Deviation) years	*40.3 (5.6)*

	Add Baseline Measure	
	Gender, Male/Female *Units: participants* Modify/Delete	
Edit		*Entire study population*
	Female — *Number participants*	*60*
	Male — *Number participants*	*70*

	Add Baseline Measure	
	Study Specific Characteristic [diastolic blood pressure] *Units: mm Hg* Modify/Delete	
Edit		*Entire study population*
	At enrollment — *Mean (Standard Deviation) mm Hg*	*82 (9.3)*
	Beginning of Placebo treatment — *Mean (Standard Deviation) mm Hg*	*81 (9.1)*
	Beginning of Drug A treatment — *Mean (Standard Deviation) mm Hg*	*82 (9.2)*

	Add Baseline Measure	
	Study Specific Characteristic [systolic blood pressure] *Units: mm Hg* *Measurements were taken at baseline, at beginning of 1st and 2nd intervention periods, and end of 1s...* Modify/Delete	
Edit		*Entire study population*
	At enrollment — *Mean (Standard Deviation) mm Hg*	*138 (21.2)*
	Beginning of Placebo treatment — *Mean (Standard Deviation) mm Hg*	*138 (18.6)*
	Beginning of Drug A treatment — *Mean (Standard Deviation) mm Hg*	*136 (19.7)*

	Add Baseline Measure	
	Study Specific Characteristic [weight] *Units: kg* Modify/Delete	
Edit		*Entire study population*
	Mean (Standard Deviation) kg	*65 (11.2)*

Baseline Measures

	Entire Study Population
Number of Participants [units: participants]	130
Age [units: participants]	
<=18 years	0
Between 18 and 65 years	130
>=65 years	0
Age [units: years] Mean ± Standard Deviation	40.3 ± 5.6
Gender, [units: participants]	
Female	60
Male	70
diastolic blood pressure [units: mm Hg] Mean ± Standard Deviation	
At enrollment	82 ± 9.3
Beginning of Placebo treatment	81 ± 9.1
Beginning of Drug A treatment	82 ± 9.2
systolic blood pressure[1] [units: mm Hg] Mean ± Standard Deviation	
At enrollment	138 ± 21.2
Beginning of Placebo treatment	138 ± 18.6
Beginning of Drug A treatment	136 ± 19.7
weight [units: kg] Mean ± Standard Deviation	65 ± 11.2

[1] Measurements were taken at baseline, at beginning of 1st and 2nd intervention periods, and end of 1st and 2nd intervention periods. Yielding baseline measurements for treatment with Placebo and Drug A.

Data Elements: Outcome Measures

- Pre-specified Primary and Secondary Outcome Measures (from registry) - *Required*
  - Measure Title and Description
  - Unit of Measurement
  - Measure Time Frame
  - Measurement Type (e.g., Number, Median)
  - Measure of Dispersion, if continuous (e.g., Standard Deviation)
  - Data: For each arm of the trial
- "Other Pre-specified" and "Post-hoc" Outcomes

Data Elements: Outcome Measures (cont.)

- Statistical Analyses
  - Which groups are being compared?
  - Test of non-inferiority? (Y/N)
    - If yes, other details
  - For each p-value provide
    - Name of test (e.g., Chi-squared, ANOVA)
    - Other details/comments
  - For each confidence interval provide
    - 95% confidence interval or other level
    - Name of estimate (e.g., OR, RR)
    - Value of estimate
    - Other details/comments

Table 4. Clinical Outcomes According to Randomized Study Assignment

	No. (%)			
	Placebo (n = 2885)	Pexelizumab (n = 2860)	HR (95% CI)	*P* Value*
Death				
30 days	113 (3.92)	116 (4.06)	1.04 (0.80-1.35)	.78
90 days	130 (4.51)	141 (4.93)	1.10 (0.86-1.39)	.45
Death, shock, or CHF				
30 days	265 (9.19)	257 (8.99)	0.98 (0.83-1.16)	.81
90 days	293 (10.16)	293 (10.24)	1.01 (0.86-1.19)	.91
CHF				
30 days	116 (4.02)	114 (3.99)	0.99 (0.77-1.29)	.96
90 days	139 (4.82)	136 (4.76)	0.99 (0.78-1.25)	.92
Cardiogenic shock				
30 days	98 (3.40)	95 (3.32)	0.98 (0.74-1.30)	.88
90 days	100 (3.47)	96 (3.36)	0.97 (0.73-1.28)	.82
Recurrent MI 90 days	69 (2.39)	87 (3.04)	1.28 (0.93-1.75)	.13

JAMA. 2007;297:43-51.

General Considerations: Precision

- Outcome Measure Title and Description
  - Name and description of measure must be informative to people not familiar with study
  - If categorized, need description of categories
- Units should directly reflect data in table
- Viewers of the table should be able to understand what the numbers represent

Add Outcome Measure

Posted **Primary Outcome: change in diastolic blood pressure** *; Units: mm Hg [3 months]*
Value at 3 months minus value at baseline.
Safety Issue? No
Modify/Delete

Edit

	Placebo	Drug A
Number of Participants Analyzed	*65*	*65*
Mean (95% Confidence Interval) mm Hg	*-2.3 (-5.0 to 1.0)*	*-4.9 (-8.2 to -3.0)*
Number of Statistical Analyses: 1		

Add Outcome Measure

Posted **Primary Outcome: change in systolic blood pressure** *; Units: mm Hg [three months]*
Value at 3 months minus value at baseline.
Safety Issue? No
Modify/Delete

Edit

	Placebo	Drug A
Number of Participants Analyzed	*62*	*60*
Mean (95% Confidence Interval) mm Hg	*-2.1 (-4.8 to 0.2)*	*-7.2 (-9.6 to -5.1)*
Number of Statistical Analyses: 1		

Add Outcome Measure

Not Posted **Secondary Outcome: plasma level of marker X** *; Units: mg/L [three months]*
Safety Issue? No
Modify/Delete

Add Outcome Measure

Not Posted **Secondary Outcome: change in weight** *; Units: kg [three months]*
Value at 3 months minus value at baseline.
Safety Issue? No
Modify/Delete

Posted

Primary Outcome: change in diastolic blood pressure *; Units: mm Hg [3 months]*

Add Arm/Group

		Placebo *Placebo administered twice dai...* Modify/Delete	Drug A *Drug A 25 mg administered twic...* Modify/Delete
Edit	Number of Participants Analyzed	65	65
	Analysis Population Description	Intent to treat analysis including only participants who had at least one post-baseline assessment.	

Create Categories — Create Categories if you wish to report categorical data (e.g., low, medium, or high).

		Placebo		Drug A	
	change in diastolic blood pressure	Mean	95% Confidence Interval	Mean	95% Confidence Interval
Edit	*Units: mm Hg*	-2.3	-5.0 to 1.0	-4.9	-8.2 to -3.0

Add Statistical Analysis

Edit	Statistical Analysis	Groups Compared: Placebo , Drug A Statistical Test of Hypothesis: P-Value: <0.04; Method: Other [Paired t-test] Method of Estimation:

Outcome Measures

1. Primary Outcome Measure: Change in Diastolic Blood Pressure

Measure Type	Primary
Measure Name	Change in Diastolic Blood Pressure
Measure Description	Intent to treat analysis including only participants who had at least one post-baseline assessment.
Time Frame	3 months
Safety Issue	No

Hide Details

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent to treat analysis including only participants who had at least one post-baseline assessment.

Reporting Groups

	Description
Placebo	Placebo administered twice daily in either first intervention period or second intervention period.
Drug A	Drug A 25 mg administered twice daily in either first intervention period or second intervention period.

Measured Values

	Placebo	Drug A
Number of Participants Analyzed	65	65
Change in Diastolic Blood Pressure *[units: mm Hg]* **Mean (95% Confidence Interval)**	-2.3 (-5.0 to 1.0)	-4.9 (-8.2 to -3.0)

Statistical Analysis 1 for Change in Diastolic Blood Pressure

Groups [1]	All groups
Method [2]	Paired t-test
P Value [3]	<0.04

[1] Additional details about the analysis, such as null hypothesis and power calculation:
125 patients required to detect 5 mm Hg difference in diastolic BP change, with 90% power. BP parameters not considered independent; 50% covariance assumed. Alpha level of 0.05.

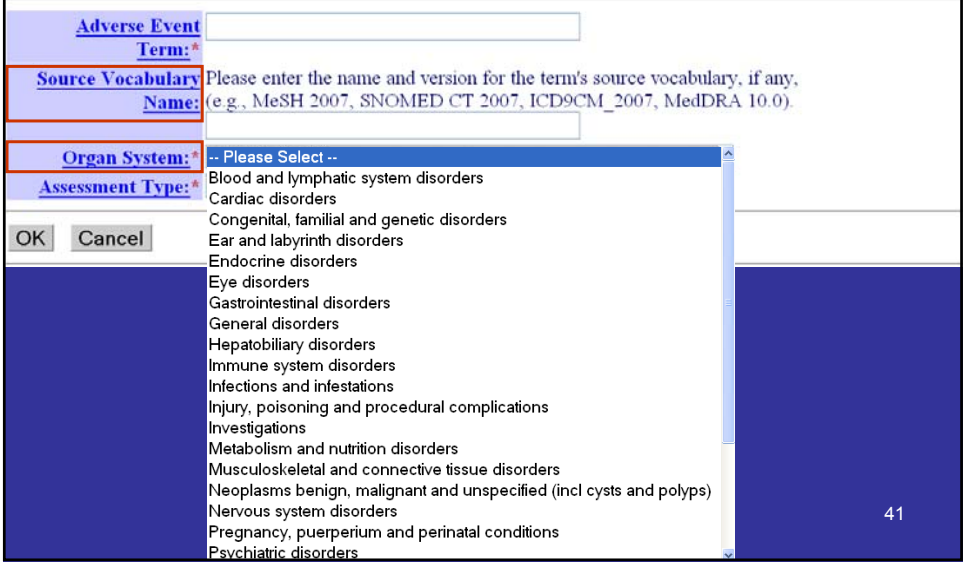
[2] Other relevant information, such as adjustments or degrees of freedom:
No text entered.

[3] Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
Two-sided

Data Elements: Adverse Events (Optional)

- All Serious Adverse Events (if provided)
- Other Adverse Events (above a specified frequency threshold, if provided)
- Adverse Event Information
  - Name of Adverse Event
  - Organ System
  - Type of Assessment (systematic vs. spontaneous)
  - Data: Total and by trial arm

Data Entry: Adverse Events



Serious Adverse Events

	Placebo	Drug A
Total over all serious adverse events		
number of participants affected	0	1
Blood and lymphatic system disorders		
Neutropenia		
number of participants at risk	65	65
number of events	0	1
number of participants affected	0	1

Frequency Threshold for Reporting Other Adverse Events: 5%

Other Adverse Events

	Placebo	Drug A
Total over all other adverse events		
number of participants affected	5	10
Gastrointestinal disorders		
Nausea †		
number of participants at risk	65	65
number of events	7	12
number of participants affected	5	10

† Indicates events were collected by systematic assessment. All other events were spontaneously reported.

Posted Results at ClinicalTrials.gov

Module 3

Quality Assurance Challenges

- Data tables will be the public representation of the study—must be clear and informative;
- NLM QA Focuses on:
  - Apparent Validity (when possible)
  - Meaningful Entries
  - Internal consistency/logic
  - Format

Problems with Early Entries

- Participant Flow
- Reporting Scales
- Defining Categories
- Reporting Time-to-Event Data
- Logical Errors in Table Construction and Illogical Units
- Lack of Detail in Outcome Measures
- Problems with Statistical Analyses

http://prsinfo.clinicaltrials.gov/fdaaa.html

"Basic Results" Database

- Common errors (pdf) - overview of common types of errors identified in submitted records with "basic results"
- Helpful hints (pdf) - tips on entering results data, including three examples of common study models (parallel design, crossover design, and diagnostic accuracy studies), reporting measure types, including information on reporting outcomes measured with a scale.
- "Basic Results" Data Element Definitions (DRAFT) - details on the information that is entered about results via the PRS.
- May 21, 2008 Federal Register Notice - describes the public process for the expansion of ClinicalTrials.gov under FDAAA 801 (pdf).
- Basic Results Provisions - extracted from FDAAA 801.
- Delayed Submission of Results - information on submitting certifications or requests for extension

Expanded Registry

- Data Element Definitions (DRAFT) - details on the information that is entered via the PRS
- NIH Fact Sheet on registration at ClinicalTrials.gov under FDAAA 801
- Guidance from NIH Office of Extramural Research:
  - Clinical Trials Registration in ClinicalTrials.gov (Public Law 110-85): Competing Applications and Non-Competing Progress Reports (NOT-OD-08-023)
  - FAQs - Clinical Trials Registration in ClinicalTrials.gov
  - Guidance on New Law (Public Law 110-85) Enacted to Expand the Scope of ClinicalTrials.gov: Registration (NOT-OD-08-014)
- Certification of Compliance to FDA - to accompany Drug, Biological Product, and Device applications or submissions

For specific questions or comments as this relates to the PRS, contact us at register@clinicaltrials.gov.

Participant Flow

- Number STARTED should be consistent with “Enrollment, Actual” in protocol section
  - Correct “Enrollment, Actual” (or explain inconsistencies in Pre-Assignment Details)
- If more than one Period, number COMPLETED for each Period must equal number STARTED for next Period (or comment must inserted to explain loss of participants)
- If “Milestones” are defined, number for each “Milestone” must be
  - Less than or equal to number STARTED Period (or number achieved previous Milestone)
  - Greater than or equal to number COMPLETED Period (or number achieved subsequent Milestone)

BEFORE Revision (Public View)

Summary Protocol Section:

Actual Enrollment: 229
Study Start Date: June 2006
Study Completion Date: October 2007
Primary Completion Date: October 2007 (Final data collection date for primary outcome measure)

Actual enrollment (229) displayed in the protocol section does not match total number started in the basic results section (220 + 211 = 431)

Basic Results Section:

Participant Flow: Initial Treatment

	Placebo	Drug X
STARTED	220	211
COMPLETED	218	210
NOT COMPLETED	2	1

BEFORE Revision (Public View)

Participant Flow: Overall Study

	Placebo	Drug X
STARTED	301	299
Received First Dose	300	280
COMPLETED	298	295
NOT COMPLETED	3	4

Number of participants in a milestone ("Received First Dose") within a period cannot be less than the number COMPLETED (or greater than the number STARTED)

BEFORE Revision (Public View)

Participant Flow: First Period

	Placebo	Drug X
STARTED	301	299
COMPLETED	291	285
NOT COMPLETED	10	14

Number of participants STARTED in second period of Participant Flow needs to be the same as numbers COMPLETED in the first period

Participant Flow: Second Period

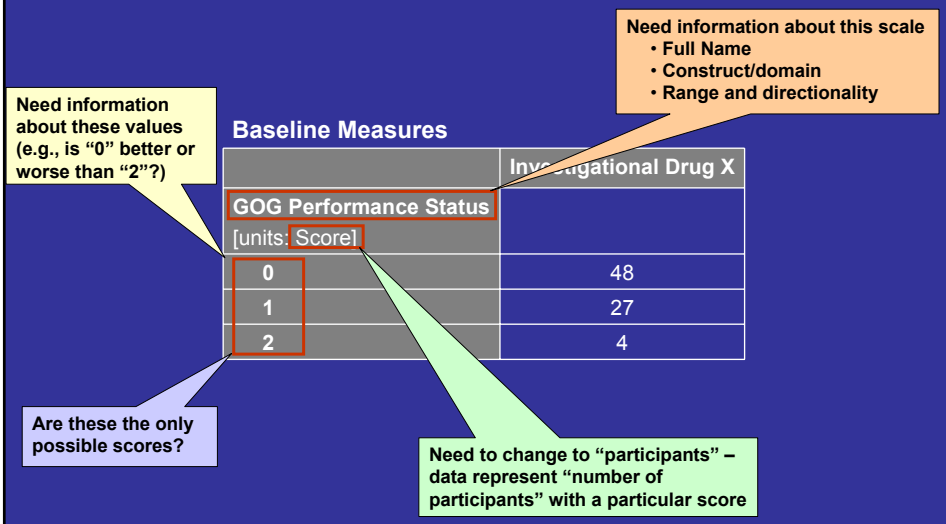
	Placebo	Drug X
STARTED	298	290
COMPLETED	288	278
NOT COMPLETED	10	12

Reporting Scales

How to Report a Scale

- Measure Title
  - Specific name of scale
    - Spell out acronyms
- Measure Description
  - Construct/Domain if not clear from Measure Title
    - e.g., pain, quality of life
  - Range and direction of scores (e.g., 0 is best; 10 is worst)
  - Optional: Type of scale
    - e.g., continuous, ordinal
- Unit of Measure
  - Use “participants,” if applicable (i.e., for categorical data)
  - Use “units on a scale” or “points on a scale,” if no other units (i.e., for continuous data)

BEFORE Revision (Public View)



Defining Categories

How to Define a Category

- Provide informative Category Titles
- Typical characteristics
  - Mutually exclusive (non-overlapping) categories
  - Comprehensive categories, covering the full range of possible results
- For categories based on continuous measures, provide thresholds when possible
  - Especially for 2 categories (i.e., dichotomous measures)

How to Define a Category (continued)

- If multichotomous or continuous data are converted to dichotomous, explain the algorithm
- Outcomes such as “improved” and “responders” are actually implied dichotomous categories that represent change over time
  - Best to report *both* possible outcomes (e.g., “improved” and “not improved”)
  - Necessary to explain the derivation of data
    - Provide time period of assessment
      e.g., baseline & 6 weeks
    - E.g., How was it determined who was “improved” and “not improved”?

BEFORE Revision (Public View)

Need to explain the scale:
- Range
- Directionality

Secondary Outcome Measure: Nausea

Measure Type	Primary
Measure Name	Nausea
Measure Description	Nausea scale
Time Frame	8 Weeks
Safety Issue	No

"Improved" is not a measurable unit

Measured Values

	Placebo	Investigational Drug X
Number of Participants	100	100
Nausea [units: Improved]	40	70

Report both possible outcomes as dichotomous categories: "improved" and "not improved"

Reporting Time-to-Event Data

How to Report Time-to-Event Data

- Data can be reported as continuous (e.g., median survival) or as categorical (e.g., 5-year survival)
- If data collection is incomplete, a possible approach:
  - At a minimum, report number who reached the "event"
  - Report time of last measurement (use the Outcome Measure Time Frame data element)
    - E.g., Median length of follow up with range
  - Report preferred descriptive statistic for those who achieved the "event" (e.g., median time to event)
    - Do not use a statistic that cannot be computed (e.g., if median cannot be computed, report a different percentile or choose another metric)

BEFORE Revision (Public View)

Secondary Outcome Measure: Time to Relapse of a Mood Episode

Measure Type	Secondary
Measure Name	Time to Relapse of a Mood Episode
Measure Description	
Time Frame	24 months
Safety Issue	No

Needs description

Measured Values

	Placebo	Investigational Drug X
Number of Participants	148	153
Time to Relapse of a Mood Episode [units: Days] Median (Inter-Quartile Range)	219 (83 to NA)	NA (73 to NA)

Invalid entry

Logical Errors in Table Construction and Illogical Units

Logic of Outcome Measure Tables

- Define rows (measures or counts) and columns (arms or comparison groups) to be logically consistent
- Cells (data) represent measures or counts derived from participants within arms or groups
  - Measure Type (and Measure of Dispersion) needs to be consistent with data being reported
  - Unit of Measure must be consistent with values

BEFORE Revision (Public View)

Measured Values

	Drug X, Week 10	Drug X, Change from Week 10 to 18
Number of Participants	88	80
Treatment Satisfaction Questionnaire After 18 Weeks of Treatment [units: Score] Mean ± Standard Deviation	81 ± 17.46	7.9 ± 12.16

Inconsistency between columns and rows: Measure "at week 10" and Measure "after 18 weeks of treatment"

63

BEFORE Revision (Public View)

Not informative

Primary Outcome Measure: Pharmacokinetics

Measure Type	Primary
Measure Name	Pharmacokinetics
Measure Description	
Time Frame	6 Weeks
Safety Issue	No

Not clear how to interpret this Outcome Measure table
- **Time Frame: 6 Weeks**
- **Units: Weeks**
- **Outcome Data: 6**

Measured Values

	Investigator	Drug X
Number of Participants	21	
Pharmacokinetics [units: Weeks]	6	

64

BEFORE Revision (Public View)

Measured Values

	Intervention X	Control
Number of Participants	28	27
Hours Per Day of Sleep [units: Average Hours per Day] Mean ± Standard Deviation	823 ± 92	864 ± 106

Inconsistency between Units of Measure, "average hours per day," and Measure Data: value provided is greater than the total number of hours in a day

Lack of Detail in Outcome Measures

Precision of Outcome Measure Information

- Outcome Measure Name, Description
  - Name and description of measure must be informative to people not familiar with study
  - If categorized, need description of categories
- Units should directly reflect data in the table
- Viewers of the table should be able to understand what the numbers represent

BEFORE Revision (Public View)

Secondary Outcome Measure: Potentially Clinically Significant Heart Rate

Measure Type	Secondary
Measure Name	New 24-Hour Holter Monitoring Alerts
Measure Description	New Holter monitoring alerts are defined as those alerts that occurred post-randomization and were not present at baseline
Time Frame	Visit 3 (Week 15)
Safety Issue	Yes

Indicates measure is "number of alerts"

Measured Values

	Drug X	Drug Y, Low Dose	Drug Y, High Dose
Number of Participants	174	194	174
New 24-Hour Holter Monitoring Alerts [units: Participants]	22	19	16

22 of what?
- **Alerts -or-**
- **Participants**

Indicates "number of participants"

BEFORE Revision (Public View)

Secondary Outcome Measure: Use of Community Health Resources

Measure Type	Secondary
Measure Name	Use of Community Health Resources
Measure Description	Evaluation of visits to primary care pediatrician, hospital emergency and re-hospitalization
Time Fr[illegible]e	Up to 3 months after discharge
S[illegible]y Issue	No

[illegible]red Values

	Early Discharge	Standard Discharge
Nu[illegible]ber of Participants	90	86
Use[illegible]f Community Health Resources [units: Number]	4.4%	10.5%

Implies number of health resources used – how was it measured?

- **Data are inconsistent: percentages of what?**
- **Invalid entry: needs to be numerical (cannot include "%")**

69

BEFORE Revision (Public View)

Secondary Outcome Measure: Frequency and Magnitude of Antibody Response

Measure Type	Primary
Measure Name	Frequency and Magnitude of Antibody Response
Measure Descripti[illegible]	Nasal secretions to Virus A/12 and B/14. Antibody Response: Three-fold increase after immunization
Time F[illegible]e	Visit 3 (Week 15)
[illegible]e	Yes

M[illegible]ured Values

	Vaccine, Low Dose	Vaccine, High Dose
Nu[illegible]er of Participants	35	34
Freq[illegible]ency and Magnitude of Antibody Respons[illegible] [units: Participants]	17	21

Same unit cannot represent measures of "frequency" *and* "magnitude"

May mean "three-fold or greater increase"

"Participants" is not a unit of measure for "frequency" or "magnitude"

Best to provide both categories for a dichotomous measure:
- < 3x increase
- ≥ 3x increase

70

Problems with Statistical Analyses

BEFORE Revision (Public View)

Measured Values

	Investigational Drug X
Number of Participants	96
Response to Drug X [units: Participants]	
Complete Response	2
Partial Response	18
Stable Disease	34
Increasing Disease	36
Unevaluable	6

Statistical Analysis 1 for Response to Drug X

Groups	Investigational Drug X
Overall Response Rate	0.21
95% Confidence Interval	0.12 to 0.33

Outcome Measure reported as categorical data (five categories of "response") but Statistical Analysis provided as dichotomous data ("Overall Response Rate = Number Responded / Total Participants")

Need information on how the 5 categories were "collapsed" into 2 (i.e., Which of 5 response categories were used in calculating the "Overall Response Rate"?).

BEFORE Revision (Public View)

Groups compared ("week 10" vs. "change from week 10 to 18") not a logical t-test

Measured Values

	Drug X, Week 10	Drug X, Change from Week 10 to 18
Number of Participants	88	80
Treatment Satisfaction Questionnaire After 18 Weeks of Treatment [units: Score] Mean ± Standard Deviation	± 17.46	7.9 ± 12.16

Statistical Analysis 1 for Treatment Satisfaction Questionnaire After 18 Weeks

Groups	Drug X, Week 10 vs. Drug X, Change from Week 10 to 18
Method	Paired t-test
P-Value	0.0018
na	4.684
95% Confidence Interval	to 7.730

Confidence Interval is not meaningful without an Estimation Parameter (e.g., mean difference, hazard ratio)

73

BEFORE Revision (Public View)

Measured Values

	Early Discharge	Standard Discharge
Number of Participants	100	100
Parental Stress [units: Points on a Likert Scale] Mean ± Standard Deviation	9.3 ± 1.2	7.8 ± 2.1

Inconsistency between Measure Data and Method of Estimation
- **Reported Mean Difference: "9"**
- **By Inspection: 9.3 – 7.8 = 1.5**

Statistical Analysis arental Stress

Groups	Ea charge vs. Standard Discharge
Method	ANOVA
P-Value	0.05
Mean Difference (Net)	9

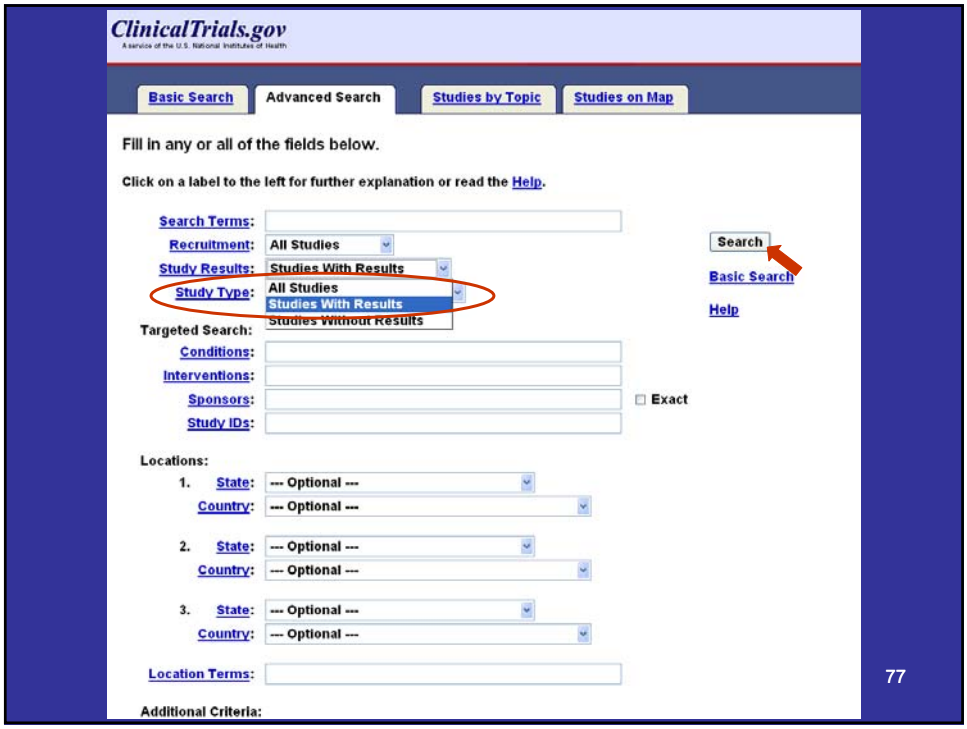
74

Lessons Learned from Early Submissions of Basic Results

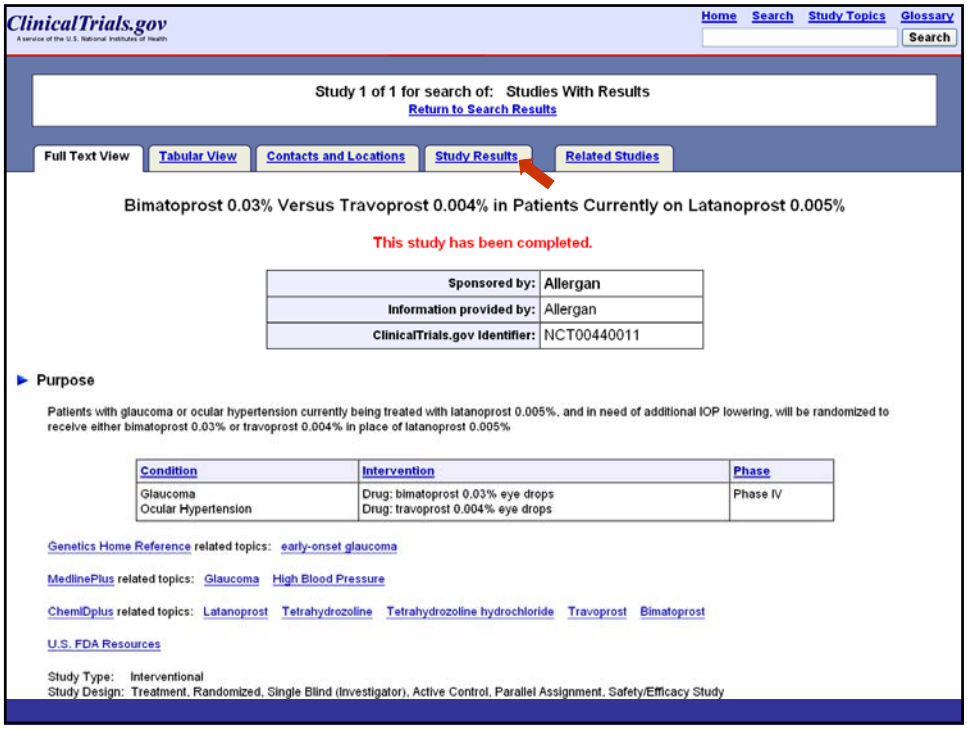
- Many iterations with the QA staff are necessary to reach minimal quality standards and to correct serious flaws
- **Data Providers must be able to understand the study design and data analysis**
  - **Typically, the investigator and a statistician will need to be involved**

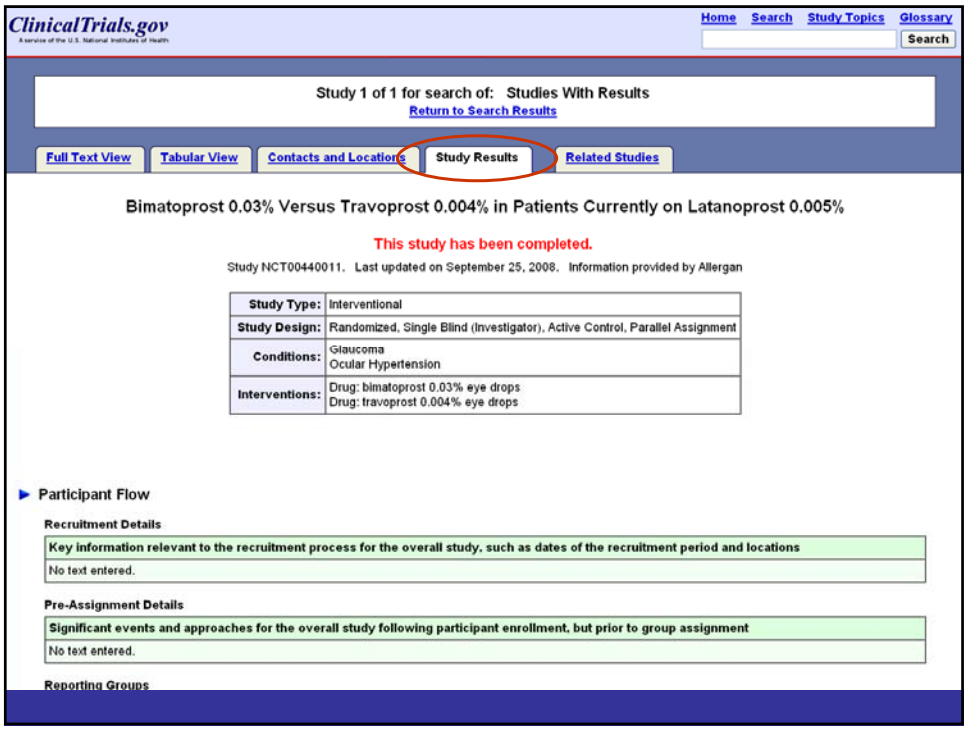
Finding Results at ClinicalTrials.gov

- From Homepage
  - Go to “Search for Clinical Trials”
  - Select “Advanced Search”
  - Select “Studies with Results” from the menu for the Study Results field
  - Select study record from results list
  - Click “Study Results” tab


ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Basic Search
Advanced Search
Studies by Topic
Studies on Map
Fill in any or all of the fields below.
Click on a label to the left for further explanation or read the Help.
Search Terms:
Recruitment: All Studies
Study Results: Studies With Results
Study Type: All Studies
Studies With Results
Studies Without Results
Search
Basic Search
Help
Targeted Search:
Conditions:
Interventions:
Sponsors:
Exact
Study IDs:
Locations:
1. State: --- Optional ---
Country: --- Optional ---
2. State: --- Optional ---
Country: --- Optional ---
3. State: --- Optional ---
Country: --- Optional ---
Location Terms:
Additional Criteria:


ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Home
Search
Study Topics
Glossary
Search
List Results
Refine Search
Results by Topic
Results on Map
Search Details
Found 16 studies with search of: Studies With Results
Hide studies that are not seeking new volunteers.
Display Options
1 Completed
Has Results
Ezetimibe (+) Simvastatin Versus Atorvastatin Comparative Study
Condition: Hypercholesterolemia
Interventions: Drug: ezetimibe (+) simvastatin; Drug: atorvastatin
Sponsor: Merck
2 Completed
Has Results
Bimatoprost 0.03% Versus Travoprost 0.004% in Patients Currently on Latanoprost 0.005%
Conditions: Glaucoma; Ocular Hypertension
Interventions: Drug: bimatoprost 0.03% eye drops; Drug: travoprost 0.004% eye drops
Sponsor: Allergan
3 Completed
Has Results
Reducing Depression in Dementia Caregivers
Condition: Depression
Interventions: Behavioral: Basic Education; Behavioral: Behavioral Skills Training: Experimental
Sponsor: National Institute of Mental Health (NIMH)
4 Completed
Has Results
The Effects of Gum Chewing on Math Scores in Adolescents
Condition: Academic Achievement in Math
Intervention: Behavioral: Gum Chewing
Sponsors: Baylor College of Medicine; Children's Nutrition Research Center
5 Completed
Has Results
The Beta Cell Responsiveness to Glucose-Dependent Insulinotropic Polypeptide (GIP) With and Without Sulfonylurea in Patients With Type 2 Diabetes
Condition: Diabetes Mellitus, Type 2
Intervention: Drug: Sulfonylurea
Sponsor: University Hospital, Gentofte, Copenhagen
6 Completed
Has Results
Probiotics and Hospital Outcome in the Elderly
Conditions: Diarrhea; Constipation
Interventions: Dietary Supplement: VSL#3; Dietary Supplement: placebo
Sponsor: Kaplan-Harzfeld Medical Center


ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Home Search Study Topics Glossary
Search
Study 1 of 1 for search of: Studies With Results
Return to Search Results
Full Text View
Tabular View
Contacts and Locations
Study Results
Related Studies
Bimatoprost 0.03% Versus Travoprost 0.004% in Patients Currently on Latanoprost 0.005%
This study has been completed.
Sponsored by: Allergan
Information provided by: Allergan
ClinicalTrials.gov Identifier: NCT00440011
Purpose
Patients with glaucoma or ocular hypertension currently being treated with latanoprost 0.005%, and in need of additional IOP lowering, will be randomized to receive either bimatoprost 0.03% or travoprost 0.004% in place of latanoprost 0.005%
Condition
Intervention
Phase
Glaucoma
Ocular Hypertension
Drug: bimatoprost 0.03% eye drops
Drug: travoprost 0.004% eye drops
Phase IV
Genetics Home Reference related topics: early-onset glaucoma
MedlinePlus related topics: Glaucoma High Blood Pressure
ChemIDplus related topics: Latanoprost Tetrahydrozoline Tetrahydrozoline hydrochloride Travoprost Bimatoprost
U.S. FDA Resources
Study Type: Interventional
Study Design: Treatment, Randomized, Single Blind (Investigator), Active Control, Parallel Assignment, Safety/Efficacy Study


ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Home Search Study Topics Glossary
Search
Study 1 of 1 for search of: Studies With Results
Return to Search Results
Full Text View
Tabular View
Contacts and Locations
Study Results
Related Studies
Bimatoprost 0.03% Versus Travoprost 0.004% in Patients Currently on Latanoprost 0.005%
This study has been completed.
Study NCT00440011. Last updated on September 25, 2008. Information provided by Allergan
Study Type: Interventional
Study Design: Randomized, Single Blind (Investigator), Active Control, Parallel Assignment
Conditions: Glaucoma
Ocular Hypertension
Interventions: Drug: bimatoprost 0.03% eye drops
Drug: travoprost 0.004% eye drops
Participant Flow
Recruitment Details
Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.
Pre-Assignment Details
Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.
Reporting Groups

Additional Information

- Email LISTSERV and other FDAAA information:
  - http://prsinfo.clinicaltrials.gov/fdaaa.html
- Other general information:
  - http://prsinfo.clinicaltrials.gov
- Questions?
  - prsinfo@clinicaltrials.gov