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Outcome Measures Module

Results Database Train-the-Trainer Workshop
September 2015

http://ClinicalTrials.gov

FDAAA 801 - Outcomes

"…a table of values for each of the primary and secondary outcome measures for each arm of the clinical trial…including the results of scientifically appropriate tests of the statistical significance of such outcome measures."

[Sec. 282(j)(3)(C)(ii)]

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FDAAA 801 = Section 801 of the Food and Drug Administration Amendments Act of 2007

Results: Outcome Measures

Publication

"At week 52, no difference was noted in major clinical responses or partial clinical responses between the placebo group (15.9% had a major clinical response …) and the rituximab group (12.4% had a major clinical response …)"

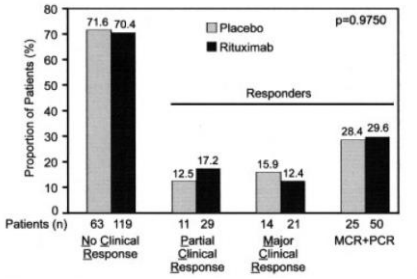

Figure 2A. Proportion of patients experiencing a major clinical response (MCR) … at 52 weeks

ClinicalTrials.gov

Primary Outcome

Measure Title	**Participants Achieving Either a Major Clinical Response (MCR) or Partial Clinical Response (PCR) Defined by British Isles Lupus Assessment Group (BILAG) Scores Over the 52-week Treatment Period**
Measure Description	The BILAG Index is used for measuring clinical disease activity in Systemic Lupus …
Time Frame	Baseline to 52 weeks

Measured Values

	Placebo + Prednisone	Rituximab + Prednisone
Number of Participants Analyzed	88	169
[*units: participants*]		
MCR (excluding PCR)	14	21
PCR	11	29
Nonclinical Response	63	119

Adapted from Merrill JT et al. *Arthrit Rheum* 2010 and NCT00137969

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Outcome Measure Template

http://prsinfo.clinicaltrials.gov/results_table_layout/ResultSimpleForms.html

* 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 ①						
* 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 ② Standard Deviation Standard Error Inter-Quartile Range Full Range ____ % Confidence Interval Geometric Coefficient of Variation					
[*] Category Title ④			③		③	③
[*] Category Title ④			③		③	③
* Unit of Measure						

* Required by ClinicalTrials.gov
[*] Conditionally required by ClinicalTrials.gov

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Outcome Measures Checklist

http://prsinfo.clinicaltrials.gov/results_table_layout/ResultSimpleForms.html

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[A] 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.	*[A]Outcome Measure Type
☐	• Title—Describe specifically what was measured and will be reported as data o 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). o 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 o 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.	*[A]Outcome Measure Title [A]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 o 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)	*[A]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: o Title—A descriptive label for the group (header for table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1"). o 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.	*[A]Arm/Group Title [A]Arm/Group Description
☐	• Number of participants, in each group, from whom data were collected and summarized. o 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].	*[A]Number of Participants Analyzed

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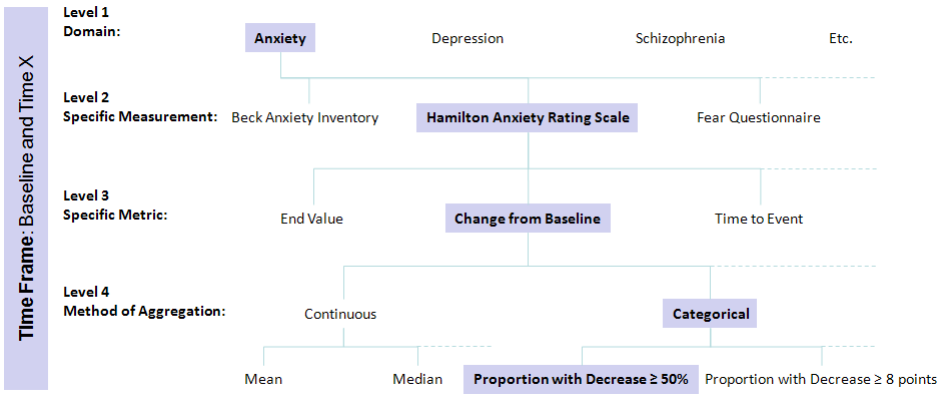
Outcome Measures
Conceptual Framework

Four Levels of Specification in Reporting Outcome Measures



Zarin DA, Tse T, Williams RJ, Califf RM, Ide NC. *N Engl J Med* 2011; 364:852-860.

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Specification of Outcome Measures in Protocol

Level	Primary OMs (% Total) n=100
1 – Domain (only)	36%
2 – Specific Measurement	25%
3 – Specific Metric	26%
4 – Method of Aggregation	13%
Included Specific Timeframe	63%

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Zarin DA, Tse T, Williams RJ, Califf RM, Ide NC. *N Engl J Med* 2011; 364:852-860.

Best Practices

- If the Number of Participants Analyzed is not the same as a “row” in Participant Flow (Started, Completed, Other Milestone), describe the population in the Analysis Population Description
- Use multiple Outcome Measures to report results for the same measure at different time points
- If the reporting groups are different from Participant Flow, use Outcome Measure Arm/Group Title/Descriptions to explain and relate to Participant Flow Arm/Group Title/Descriptions

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Outcome Measures
Tutorial

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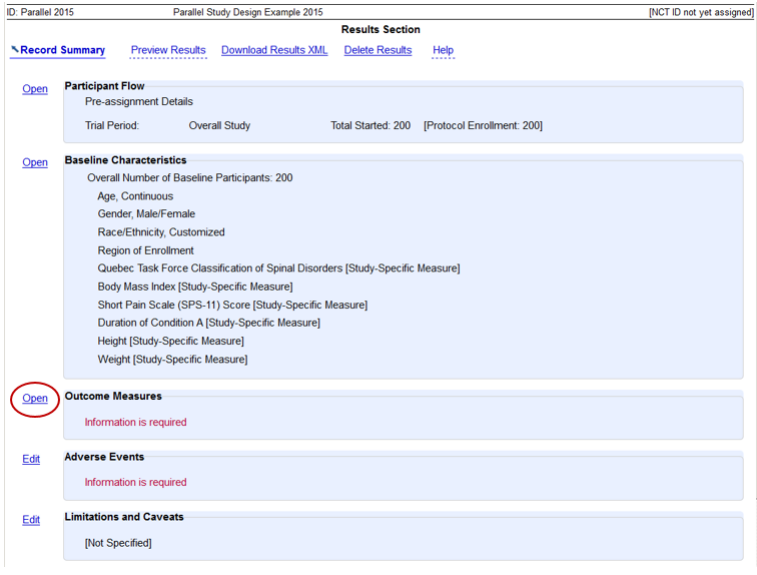
Results Section


ID: Parallel 2015 Parallel Study Design Example 2015 [NCT ID not yet assigned]

Results Section

Record Summary | Preview Results | Download Results XML | Delete Results | Help

Open **Participant Flow**
Pre-assignment Details
Trial Period: Overall Study Total Started: 200 [Protocol Enrollment: 200]

Open **Baseline Characteristics**
Overall Number of Baseline Participants: 200
Age, Continuous
Gender, Male/Female
Race/Ethnicity, Customized
Region of Enrollment
Quebec Task Force Classification of Spinal Disorders [Study-Specific Measure]
Body Mass Index [Study-Specific Measure]
Short Pain Scale (SPS-11) Score [Study-Specific Measure]
Duration of Condition A [Study-Specific Measure]
Height [Study-Specific Measure]
Weight [Study-Specific Measure]

Open **Outcome Measures**
Information is required

Edit **Adverse Events**
Information is required

Edit **Limitations and Caveats**
[Not Specified]

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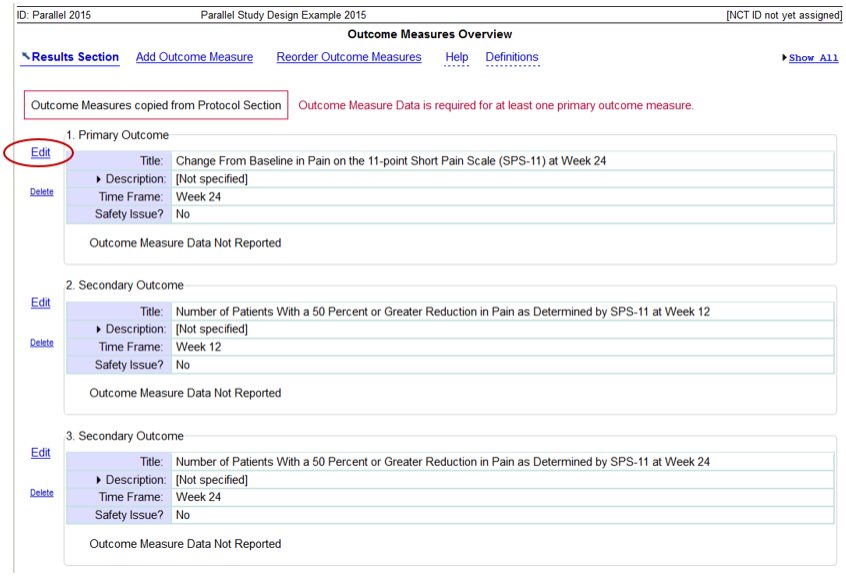
Outcome Measures Overview



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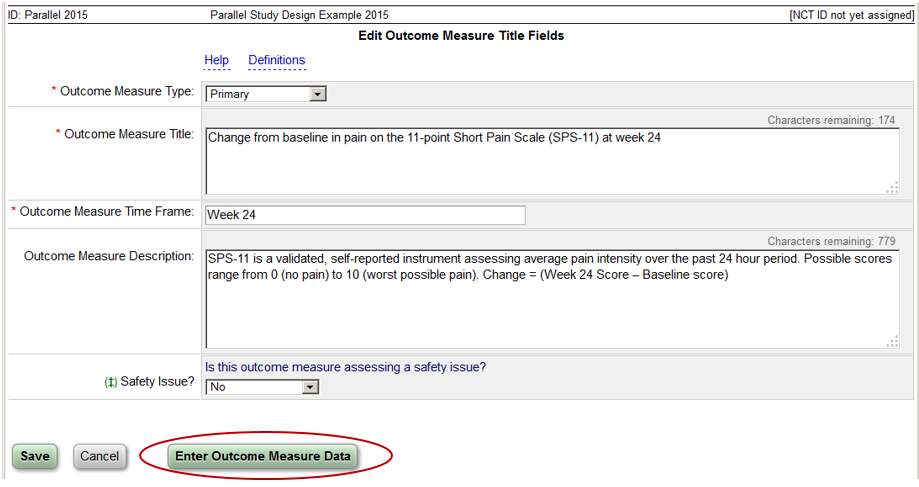
Edit Outcome Measure Title Fields



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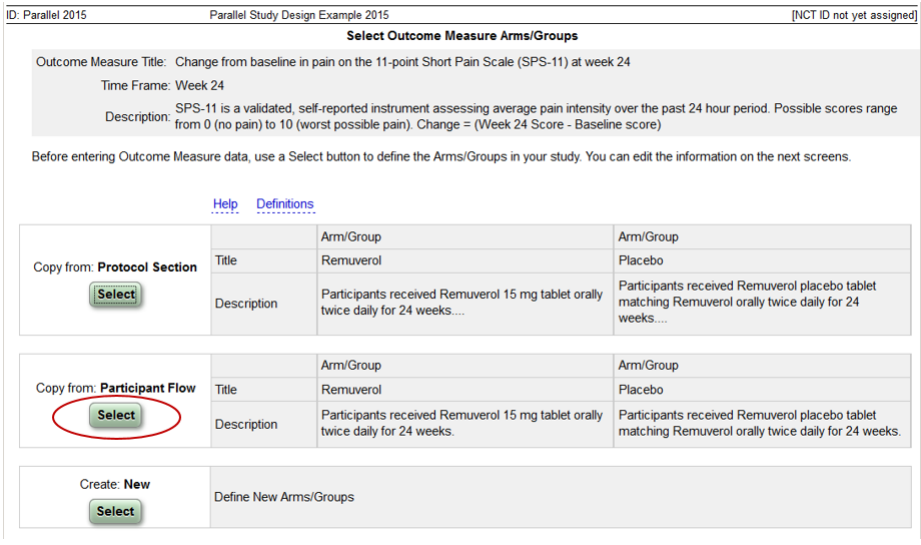
Select Outcome Measure Arms/Groups


ID: Parallel 2015 | Parallel Study Design Example 2015 | [NCT ID not yet assigned]

Select Outcome Measure Arms/Groups

Outcome Measure Title: Change from baseline in pain on the 11-point Short Pain Scale (SPS-11) at week 24

Time Frame: Week 24

Description: SPS-11 is a validated, self-reported instrument assessing average pain intensity over the past 24 hour period. Possible scores range from 0 (no pain) to 10 (worst possible pain). Change = (Week 24 Score - Baseline score)

Before entering Outcome Measure data, use a Select button to define the Arms/Groups in your study. You can edit the information on the next screens.

Help Definitions

		Arm/Group	Arm/Group
Copy from: **Protocol Section** Select	Title	Remuverol	Placebo
	Description	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks....	Participants received Remuverol placebo tablet matching Remuverol orally twice daily for 24 weeks....

		Arm/Group	Arm/Group
Copy from: **Participant Flow** Select	Title	Remuverol	Placebo
	Description	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.	Participants received Remuverol placebo tablet matching Remuverol orally twice daily for 24 weeks.

Create: **New** Select — Define New Arms/Groups

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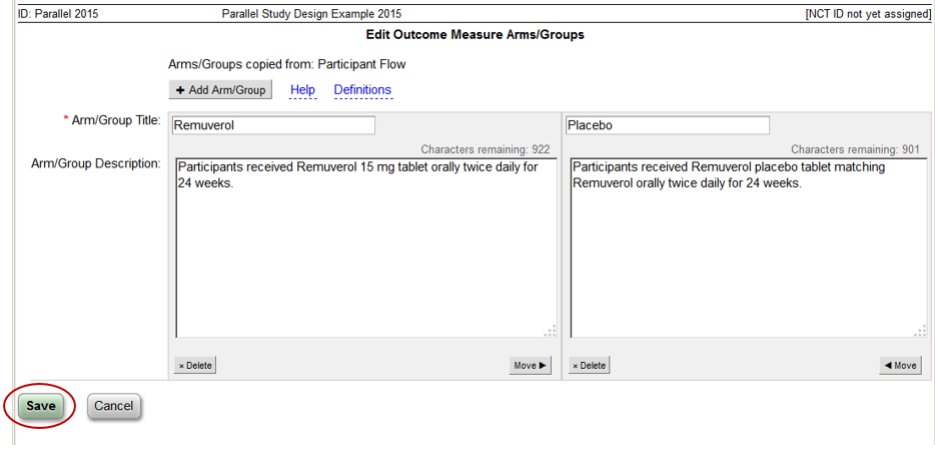
Edit Outcome Measure Arms/Groups


ID: Parallel 2015 | Parallel Study Design Example 2015 | [NCT ID not yet assigned]

Edit Outcome Measure Arms/Groups

Arms/Groups copied from: Participant Flow

+ Add Arm/Group Help Definitions

* Arm/Group Title:	Remuverol	Placebo
	Characters remaining: 922	Characters remaining: 901
Arm/Group Description:	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.	Participants received Remuverol placebo tablet matching Remuverol orally twice daily for 24 weeks.
	× Delete Move ►	× Delete ◄ Move

Save Cancel

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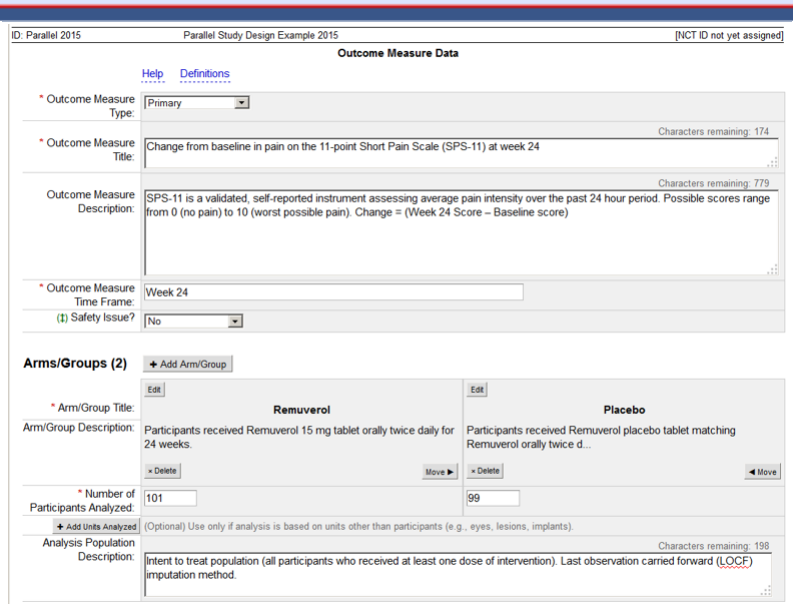
Outcome Measure Data



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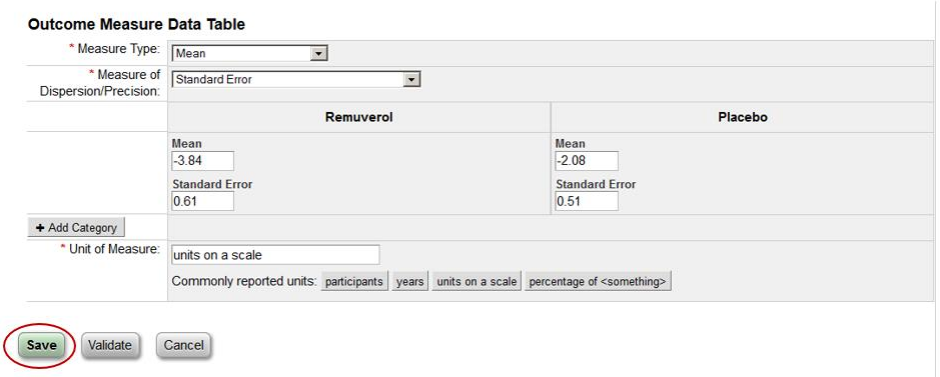
Outcome Measure Data (cont.)



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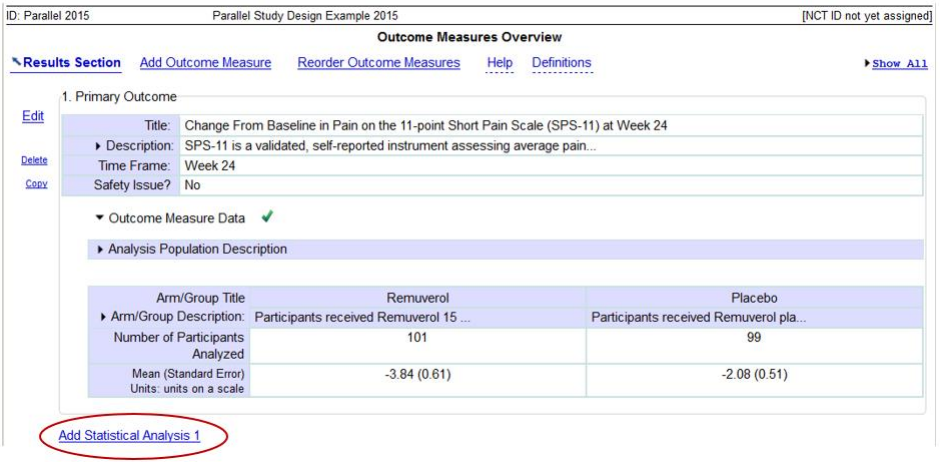
Outcome Measures Overview



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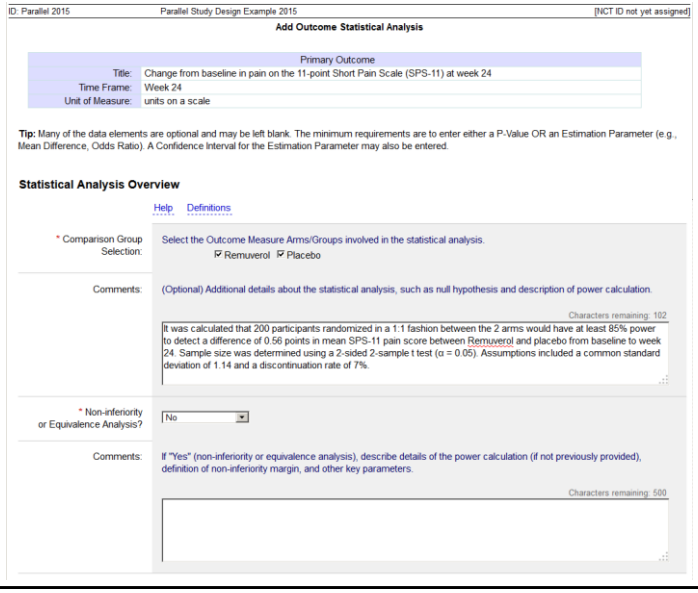
Add Outcome Statistical Analysis



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Add Outcome Statistical Analysis (cont.)

Statistical Test of Hypothesis

Help Definitions

P-Value: (If applicable)

0.002 (e.g. <0.01)

Comments: (Optional) Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the *a priori* threshold for statistical significance.

Characters remaining: 250

Method: (Required if a P-Value is entered)

Mixed Models Analysis If other, please specify:

Comments: (Optional) Any other relevant information, such as adjustments or degrees of freedom.

Characters remaining: 150

Save Validate Cancel

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Outcome Measures Overview

ID: Parallel 2015 Parallel Study Design Example 2015 [NCT ID not yet assigned]

Outcome Measures Overview

Results Section Add Outcome Measure Reorder Outcome Measures Help Definitions Show All

1. Primary Outcome

Edit Delete Copy

Title:	Change From Baseline in Pain on the 11-point Short Pain Scale (SPS-11) at Week 24
Description:	SPS-11 is a validated, self-reported instrument assessing average pain...
Time Frame:	Week 24
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

Arm/Group Title	Remuverol	Placebo
Arm/Group Description:	Participants received Remuverol 15 ...	Participants received Remuverol pla...
Number of Participants Analyzed	101	99
Mean (Standard Error) Units: units on a scale	-3.84 (0.61)	-2.08 (0.51)

Edit Statistical Analysis 1

Delete

Statistical Analysis Overview	Comparison Groups	Remuverol, Placebo
	Comments	It was calculated that 200 participants randomized in a 1:1 fashion between the 2 arms would have at least 85% power to detect a difference of 0.56 points in mean SPS-11 pain score between Remuverol and placebo from baseline to week 24. Sample size was determined using a 2-sided 2-sample t test ($\alpha = 0.05$). Assumptions included a common standard deviation of 1.14 and a discontinuation rate of 7%.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.002
	Comments	[Not specified]
	Method	Mixed Models Analysis
	Comments	[Not specified]

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Enter Outcome Measures

- Example Study Designs
  - Factorial
  - Crossover
  - Cluster Randomized
  - Dose Escalation
  - Multiple Period

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