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Participant Flow Module

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Outline

- Overview of Participant Flow module
- Required data elements
- ClinicalTrials.gov Review Criteria
- Examples

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Purpose

- The Participant Flow module is designed to provide information about the study design by documenting the "flow" of participants through different stages of the study
- The module should account for all enrolled participants, and should inform the interpretation of study outcomes by illustrating which participants were analyzed

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FDAAA* Provision

"A table...,including the number of patients who dropped out of the clinical trial and the number of patients excluded from the analysis, if any."

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

*Food and Drug Administration Amendments Act of 2007

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Description of the Participant Flow Module

- Tabular presentation of progress of research participants through each stage of trial
  - Arms are “copied” from Protocol Section, but may be modified
  - Table may consist of a single Period or multiple Periods, to represent different stages of the trial (e.g., “double-blind period,” “open-label period”)
  - Each Period must include two Milestones: Number STARTED and Number COMPLETED

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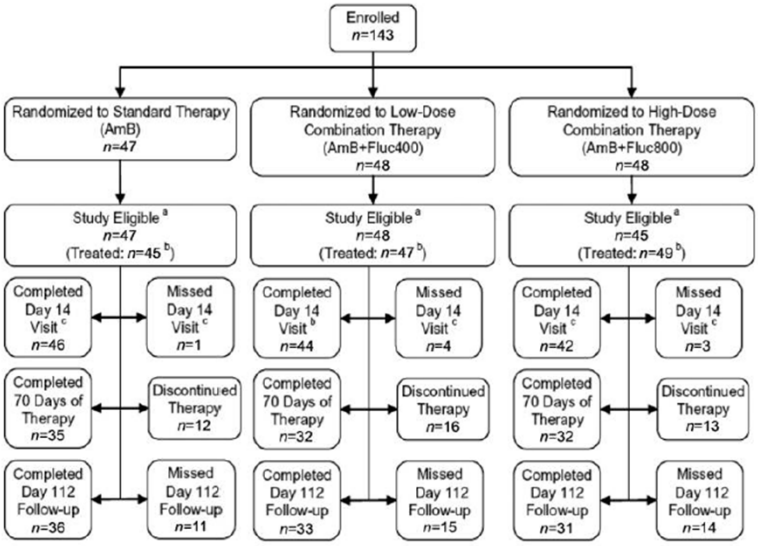
Flow Diagram (“Figure 1” Format)



Pappas PG, Chetchotisakd P, Larsen RA et al. Clin Infect Dis. 2009

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Recruitment Details

Key information relevant to the recruitment process for the overall study, such as date of recruitment period and locations
Subjects were screened and enrolled at 10 sites in the US and 5 sites in Thailand.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
AmphoB Standard	Amphotericin B 0.7 mg/kg for 14 day followed by fluconazole 400 mg daily for 8 weeks. For subjects in the standard therapy arm whose Amphotericin B dose is continued beyond 14 days, fluconazole initiation will be delayed.
AmphoB+Fluc400	Amphotericin B 0.7 mg/kg and the randomized dose of fluconazole at 400 mg/day for the first 14 days, then the randomized dose of fluconazole at 400 mg/day respectively for an additional 8 weeks.
AmphoB+Fluc800	Amphotericin B 0.7 mg/kg and the randomized dose of fluconazole at 800 mg/day for the first 14 days, then the randomized dose of fluconazole at 800 mg/day respectively for an additional 8 weeks.

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Participant Flow: Overall Study

	AmphoB Standard	AmphoB+Fluc400	AmphoB +Fluc800
STARTED	**47**[1]	**48**[2]	**48**[3]
COMPLETED	**36**	**33**	**31**
NOT COMPLETED	**11**	**15**	**17**

[1] 47 subjects randomized; 45 subjects treated
[2] 48 subjects randomized; 47 subjects treated – 2 subjects randomized to AmphoB rec'd AmphoB+Fluc400
[3] 47 subjects randomized; 49 treated – 3 subjects randomized to AmphoB+Fluc400 rec'd AmphoB+Fluc800

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Data Elements

- Recruitment Details
- Pre-assignment Details
- Arm/Group*
  - Title
  - Description
- Period Title(s)*
  - "Overall Study" (default) if single period
- Milestones
  - STARTED Data*
    - Comments
  - Milestone Title
    - Data
      - Comments
  - COMPLETED Data*
    - Comments
  - Reason Not Completed
    - Type (e.g., Death)
      - Data

*Required by ClinicalTrials.gov

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Basic Information Needed

	Arm Title* **Arm Description**	**Arm Title*** **Arm Description**
(Period Title, if more than 1 Period)		
STARTED*	# participants	# participants
(Milestone Title)	(# participants)	(# participants)
COMPLETED*	# participants	# participants
Not Completed [calculated]		
Reasons Not Completed		
Adverse Event	(# participants)	(# participants)
Death		
Lack of Efficacy		
Lost to Follow-up		
Physician Decision		
Pregnancy		
Protocol Violation		
Withdrawal by Subject		
Other (Specify)		

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Best Practices

- Specific Periods to reflect study design
- Use of Milestones to convey key events
  - e.g., number received intervention
- Reasons for non-completion

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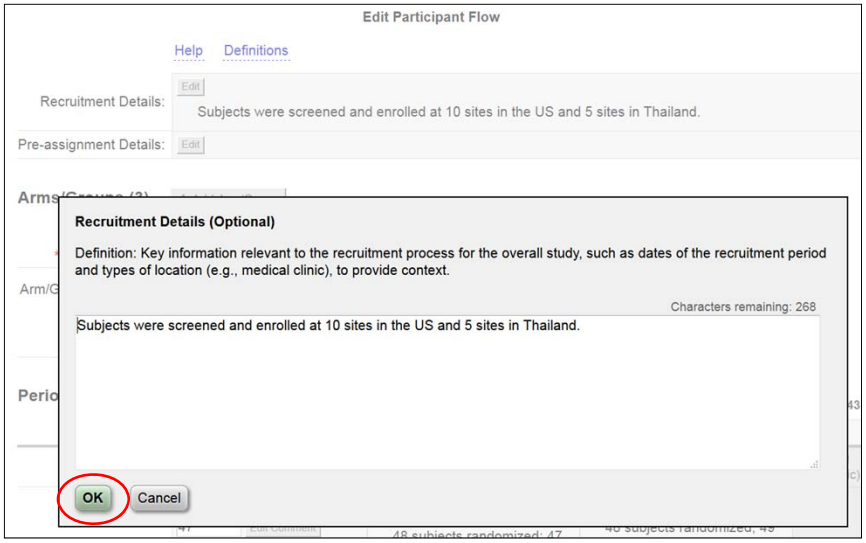
PRS: Edit Recruitment Details



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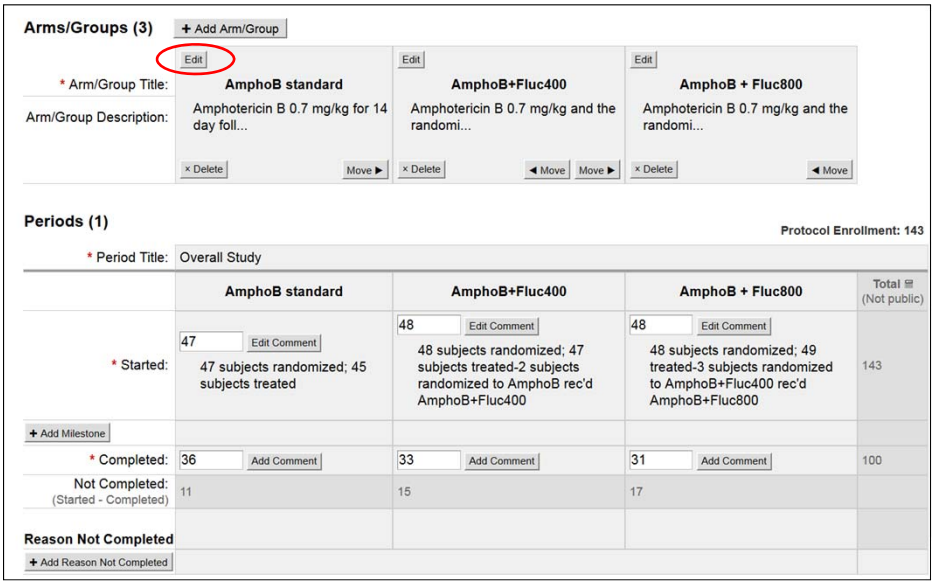
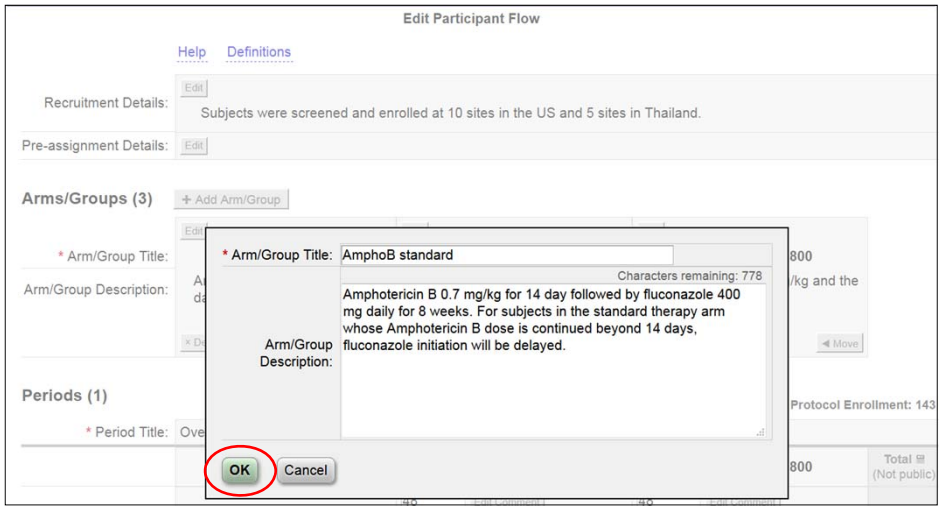
PRS: Arms/Groups



PRS: Edit Arm/Group



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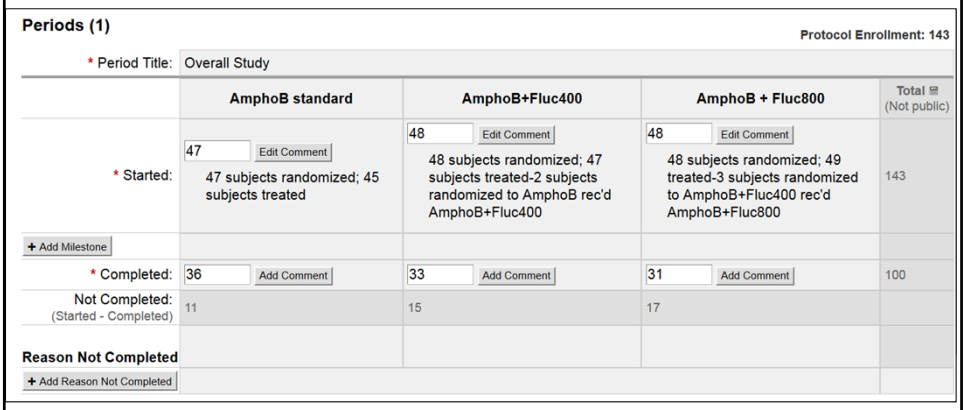
PRS: Edit Milestone Data



Periods (1)

Protocol Enrollment: 143

* Period Title:	Overall Study			
	AmphoB standard	**AmphoB+Fluc400**	**AmphoB + Fluc800**	**Total** (Not public)
* Started:	47 Edit Comment 47 subjects randomized; 45 subjects treated	48 Edit Comment 48 subjects randomized; 47 subjects treated-2 subjects randomized to AmphoB rec'd AmphoB+Fluc400	48 Edit Comment 48 subjects randomized; 49 treated-3 subjects randomized to AmphoB+Fluc400 rec'd AmphoB+Fluc800	143
+ Add Milestone				
* Completed:	36 Add Comment	33 Add Comment	31 Add Comment	100
Not Completed: (Started - Completed)	11	15	17	
Reason Not Completed				
+ Add Reason Not Completed				

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General Review Criteria

- Abbreviations are expanded first time used
- No spelling errors exist
- Informative Titles (Arm/Group, Period, Milestone)
- Arm/Group Descriptions are descriptive; contain information about the interventions administered (e.g., dosage, dosage form, frequency of administration) or groups evaluated
- Information is consistent with other sections of record (or discrepancies explained)
- No written results or conclusions

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Specific Review Criteria

- Overall structure of Arms and Periods makes sense
  - Can follow “flow” of participants in study
- Consistent with Protocol Section
  - Arm and Intervention information
  - Actual Enrollment is same as Total STARTED (or discrepancy explained)
- Pre-assignment and Recruitment Details
  - Content is relevant to data element

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PRS: Participant Flow Overview

Recruitment Details	Subjects were screened and enrolled at 10 sites in the US and 5 sites in Thailand.
Pre-Assignment Details	

Arm/Group Title	AmphoB Standard	AmphoB+Fluc400	AmphoB + Fluc800	Total (Not public)
▸ Arm/Group Description	Amphotericin B 0.7 mg/kg for 14 day...	Amphotericin B 0.7 mg/kg and the ra...	Amphotericin B 0.7 mg/kg and the ra...	
Period Title: **Overall Study**				
Started	47 [1]	48 [2]	48 [3]	143
Completed	36	33	31	100
Not Completed	11	15	17	43

[1] 47 subjects randomized; 45 subjects treated
[2] 48 subjects randomized; 47 subjects treated-2 subjects randomized to AmphoB rec'd AmphoB+Fluc400
[3] 48 subjects randomized; 49 treated-3 subjects randomized to AmphoB+Fluc400 rec'd AmphoB+Fluc800

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Protocol Section (selected content)

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study

Official Title: A Phase II Randomized Trial of Amphotericin B Alone or Combined With Fluconazole in the Treatment of AIDS-Associated Cryptococcal Meningitis

Enrollment: 146
Study Start Date: May 2005
Study Completion Date: April 2008
Primary Completion Date: April 2008

Results Section - Participant Flow

Recruitment Details	Subjects were screened and enrolled at 10 sites in the US and 5 sites in Thailand.
Pre-Assignment Details	

Arm/Group Title	AmphoB Standard	AmphoB+Fluc400	AmphoB + Fluc800	Total (Not public)
▸ Arm/Group Description	Amphotericin B 0.7 mg/kg for 14 day...	Amphotericin B 0.7 mg/kg and the ra...	Amphotericin B 0.7 mg/kg and the ra...	
Period Title: **Overall Study**				
Started	47 [1]	48 [2]	48 [3]	143
Completed	36	33	31	100
Not Completed	11	15	17	43

[1] 47 subjects randomized; 45 subjects treated
[2] 48 subjects randomized; 47 subjects treated
[3] 48 subjects randomized; 45 were study eligible and 49 were treated

PRS Review Comments

Period Title: **Overall Study**				
Started	47 [1]	48 [2]	48 [3]	143
Completed	36	33	31	100
Not Completed	11	15	17	43

[1] 47 subjects randomized; 45 subjects treated
[2] 48 subjects randomized; 47 subjects treated
[3] 48 subjects randomized; 45 were study eligible and 49 were treated

Comments:

The Enrollment number in the Protocol Section (146) conflicts with the number of participants Started (143) in the Participant Flow module. Please verify and correct either or both of these data elements, as necessary.

Please provide an explanation for the last footnote. Specifically, it is not clear how the number of participants treated was greater than the number of participants randomized (Started).

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Specific Review Criteria

- Milestone
  - Number achieving Milestone is greater than or equal to Number COMPLETED the Period
  - Number STARTED is greater than or equal to Number COMPLETED
  - If multiple Milestones, generally Number for subsequent Milestone is not greater than the Number for the previous Milestone

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Example

Participant Flow: Overall Study

	5-FU/FA	Irinotecan + 5-FU/FA
STARTED	**160**	**161**
Treated	153	153
COMPLETED	**125**[1]	**115**[1]
NOT COMPLETED	**35**	**46**
Adverse Event	3	8
Death	1	0
Withdrawal by Subject	3	12
Relapse	15	7
Protocol Violation	2	2
Specified by site	4	9
Randomized Not Treated	7	8

[1] Received maximum number of cycles.

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Specific Review Criteria

- Period Titles are informative
- Number STARTED in a subsequent Period is the same as the Number COMPLETED in the previous Period
  - If not the same, discrepancy is explained in Comment data element

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Example – Potential Error

Period 1: Weeks 0 - 16

	Placebo	Drug X
STARTED	301	299
COMPLETED	291	290
NOT COMPLETED	10	9

Period 2: Weeks 17 – 32

	Placebo	Drug X
STARTED	291	285
COMPLETED	288	278
NOT COMPLETED	3	7

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Example – Corrected

Period 1: Weeks 0 - 16

	Placebo	Drug X
STARTED	301	299
COMPLETED	291	290
NOT COMPLETED	10	9

Period 2: Weeks 17 – 32

	Placebo	Drug X
STARTED	291	285
COMPLETED	288	278
NOT COMPLETED	3	7

[1] 5 participants did not enter Period 2 (4 ineffective treatment; 1 positive pregnancy test).

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Example – Cross-over Design

	Description
Placebo First, then Drug A	Placebo twice daily in first intervention period and Drug A 25 mg twice daily in second intervention period (after washout period).
Drug A First, then Placebo	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, then Drug A	Drug A First, then Placebo
STARTED	**65**	**63**
Received at Least 1 Dose of Drug	65	64
COMPLETED	**65**	**63**
NOT COMPLETED	**0**	**2**
Neutropenia	0	1
Withdrawal by Subject	0	1

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Example – Cross-over Design (cont'd)

Period: Washout Period of 2 Weeks

	Placebo First, then Drug A	Drug A First, then Placebo
STARTED	**65**	**63**
COMPLETED	**63**	**62**
NOT COMPLETED	**0**	**2**
Disease Relapse	2	1

Period: Second Intervention

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

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Additional Information

General ClinicalTrials.gov information:
http://clinicaltrials.gov

FDAAA-related information (see Submit Studies):
http://clinicaltrials.gov/manage-recs/fdaaa

Office of Extramural Research:
http://grants.nih.gov/Clinicaltrials_fdaaa/

Questions?
register@clinicaltrials.gov