

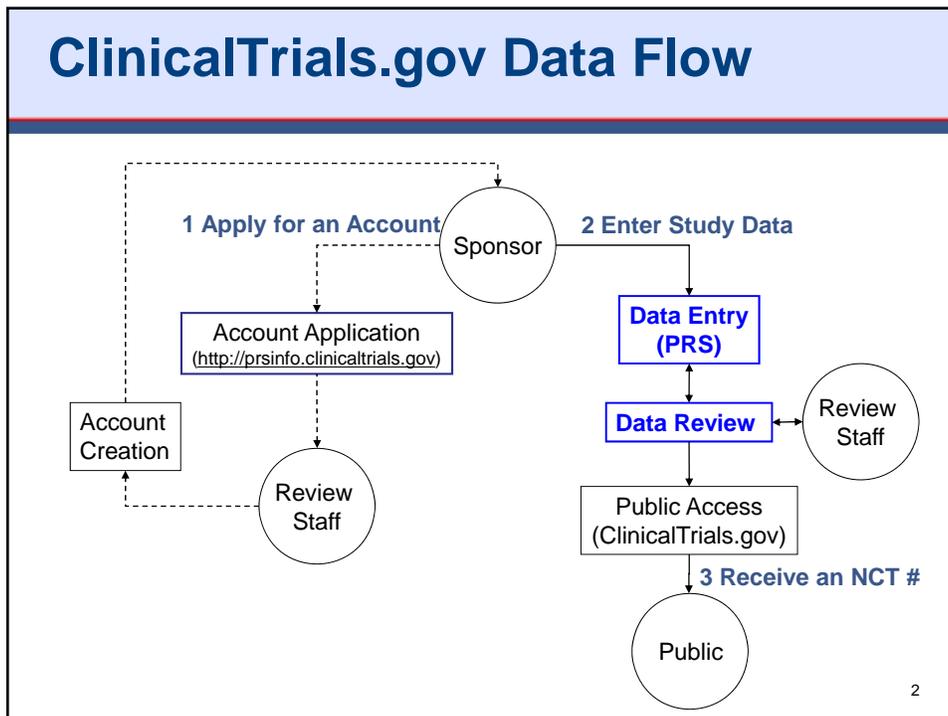
ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Protocol Registration System (PRS) Information and Data Review Process

Tony Tse, Ph.D.
Program Analyst, ClinicalTrials.gov
National Library of Medicine



<http://ClinicalTrials.gov>



The ClinicalTrials.gov Protocol Registration System (PRS)

PRS Basics

- Web-based data entry system for summary protocol and results information
 - Requires organizational account, user name, password
 - Contact organizational account “administrator” or email register@clinicaltrials.gov
- Required and optional structured data elements
 - Pull-down menus
 - Free text

PRS Basics (cont'd)

- Organizational Accounts
 - Established by the sponsor
 - Used to enter, review, submit, and update protocol and result information for studies (“records”) sponsored by the organization
- PRS Roles
 - Administrator: creates user accounts, edits and approves records, point of contact
 - User: creates, edits, and modifies records

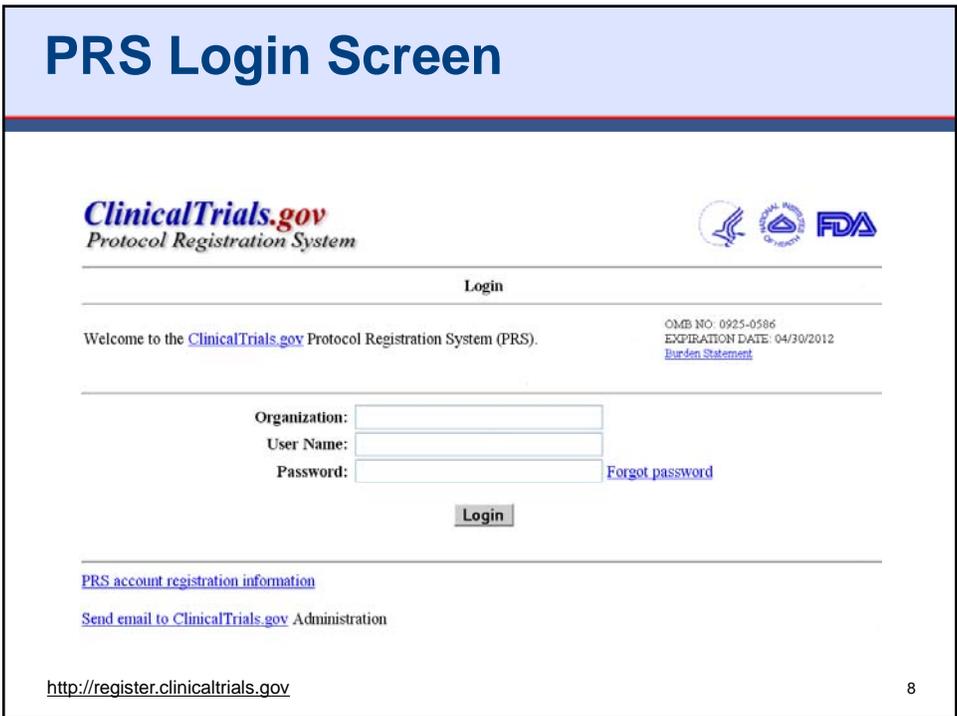
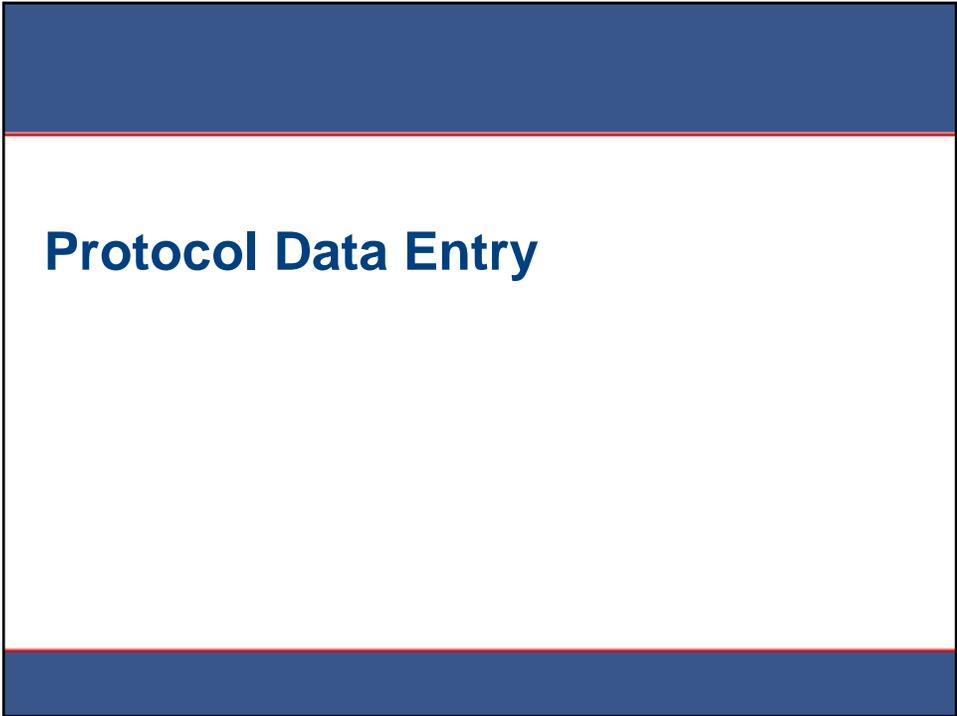
5

PRS Basics (cont'd)

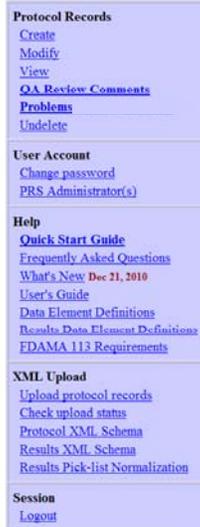
- Automated business rules for basic quality and completeness checks:
 -  **ERROR** - Study cannot be released; must be addressed
 -  **WARNING** - FDAAA* item; should be addressed
 -  **NOTE** - Helpful hints
- Additional review is conducted by ClinicalTrials.gov staff

*Food and Drug Administration Amendments Act of 2007

6



PRS Main Menu: Functions



- Create
 - Add new study
- Modify
 - Update existing study
 - Add results
- Review comments
 - Access comments from ClinicalTrials.gov staff review of study

9

Entering Protocol Data

ClinicalTrials.gov Protocol Data Element Definitions (DRAFT)

May 2010

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

<http://prinfo.clinicaltrials.gov/fdaaa.html>

10

Protocol Registration System (PRS) Information and Data Review Process

Title	FDA Oversight	Sponsor	Summary	Status	Design	Interventions	Conditions	Eligibility	Locations	Citations	Links	
Title: Amphotericin Alone or in Combination With Fluconazole for...											NCT00145249	ID: 03-154
Unique Protocol ID: * (FDAAA)		Enter sponsoring organization's unique identifier. 03-154										
Brief Title: * (Special characters) (FDAAA)		Use lay language. Example: Safety Study of Recombinant Vaccinia Virus Vaccine to Treat Prostate Cancer Amphotericin Alone or in Combination With Fluconazole for AIDS-Associated										
Acronym:		If there is an acronym or abbreviation used to identify this study, enter it here. <input type="text"/>										
Official Title:		Example: Phase 1 Study of Recombinant Vaccinia Virus That Expresses Prostate Specific Antigen in Metastatic Adenocarcinoma of the Prostate A Phase II Randomized Trial of Amphotericin B Alone or Combined With Fluconazole in the Treatment of AIDS-Associated Cryptococcal Meningitis										
Study Type: * (FDAAA)		<input checked="" type="radio"/> Interventional <input type="radio"/> Observational <input type="radio"/> Expanded Access About expanded access records										
FDA Regulated Intervention? (FDAAA)		Indicate whether this trial includes an intervention subject to US Food and Drug Administration regulations. Yes <input type="text"/>										
IND/IDE Protocol? * (FDAAA)		Indicate whether the protocol is subject to US Food and Drug Administration regulations, under an Investigational New Drug (IND) Application or Investigational Device Exemption (IDE). Yes <input type="text"/>										
 <p>NOTE: Secondary ID Type: data not entered.</p>												
<input type="button" value="OK"/> <input type="button" value="Cancel"/>		* Required by ClinicalTrials.gov										
11												

Title	FDA Oversight	Sponsor	Summary	Status	Design	Interventions	Conditions	Eligibility	Locations	Citations	Links	
Title: Amphotericin Alone or in Combination With Fluconazole for...											NCT00145249	ID: 03-154
Unique Protocol ID: *		Acronym Definition: Acronym or initials used to identify this study, if applicable. Enter only the acronym. If supplied, the acronym is automatically displayed 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 (WHI)										
Brief Title: * (Special characters) (FDAAA)												
Acronym:												
Official Title:		Example: Phase 1 Study of Recombinant Vaccinia Virus That Expresses Prostate Specific Antigen in Metastatic Adenocarcinoma of the Prostate A Phase II Randomized Trial of Amphotericin B Alone or Combined With Fluconazole in the Treatment of AIDS-Associated Cryptococcal Meningitis										
Study Type: * (FDAAA)		<input checked="" type="radio"/> Interventional <input type="radio"/> Observational <input type="radio"/> Expanded Access About expanded access records										
FDA Regulated Intervention? (FDAAA)		Indicate whether this trial includes an intervention subject to US Food and Drug Administration regulations. Yes <input type="text"/>										
IND/IDE Protocol? * (FDAAA)		Indicate whether the protocol is subject to US Food and Drug Administration regulations, under an Investigational New Drug (IND) Application or Investigational Device Exemption (IDE). Yes <input type="text"/>										
 <p>NOTE: Secondary ID Type: data not entered.</p>												
<input type="button" value="OK"/> <input type="button" value="Cancel"/>		* Required by ClinicalTrials.gov										
12												

Results Data Entry

Entering Results Data

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

February 2010

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

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

14

Entering Results Data— Verify and Update Protocol First*

- Overall Recruitment Status
- Study Design
- Enrollment (number of subjects)
 - Verify number and ensure “actual”
- Primary and Study Completion Dates
 - Verify dates and ensure “actual”
- Arms and Interventions
- Outcome Measures

* Recommend rereleasing protocol prior to starting results data entry.

15

Protocol Data Copied to Results

The protocol information shown below will be copied into the results section of the record. Please review the information carefully. If the information is not correct, cancel and edit the protocol record. For each protocol arm an Arm/Group will be created in the results section.

Protocol Arm Label and Description	You may use the data entry system to modify the arms/groups. If modified, changes may need to be made in both protocol and results sections. Standard Therapy High-Dose Therapy
Protocol Primary Outcome Measures	For each protocol primary outcome measure, a primary outcome measure will be created in the results section. You may use the data entry system to modify the primary outcome measures. <ul style="list-style-type: none"> • Change in Viral Load at Week 4 Compared to Baseline [Baseline to Week 4]
Protocol Secondary Outcome Measure	For each protocol secondary outcome, a secondary outcome measure will be created in the results section. You may use the data entry system to modify the secondary outcome measures. Protocol has no secondary outcomes.

Create Results section of record 1234567?

OK Cancel

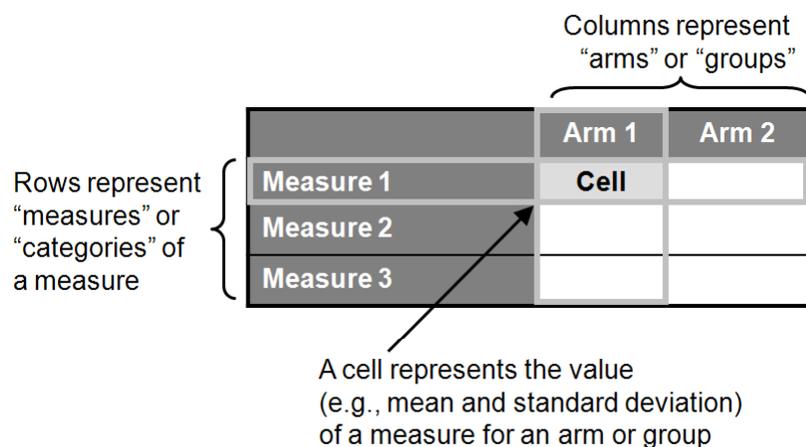
16

How Are Results Reported?

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

17

Results Data: Tabular Format



Tse T, Williams RJ, Zarin DA. Chest. 2009.

18

The ClinicalTrials.gov Review Process

Data Provider Record Flow

PRS – Data Provider Tasks

Enter Record Data

- Online data entry forms
- XML file upload

Review Record Data

- PRS automated messages
 - Review messages
 - Correct all errors
- Use detailed review items

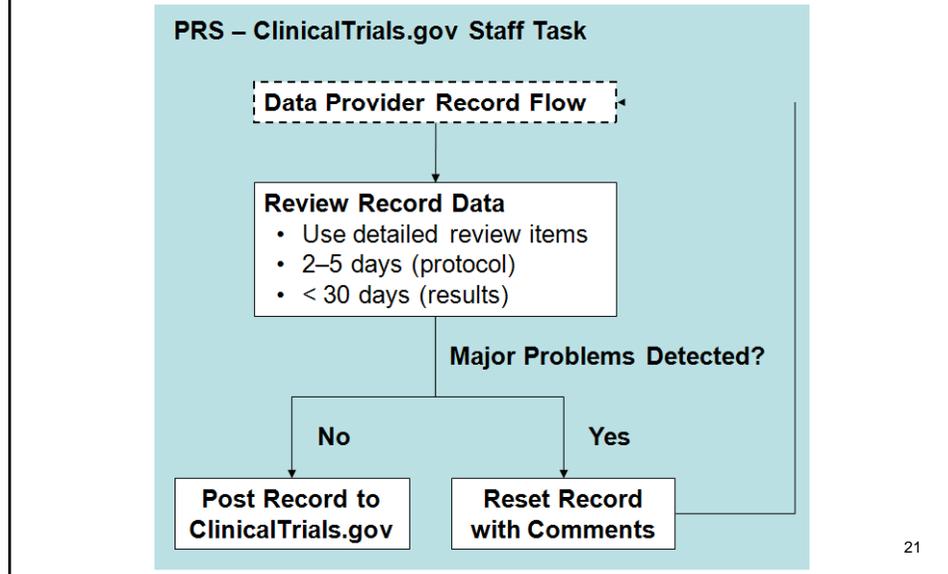
Release Record

- “Locked”- cannot be edited

ClinicalTrials.gov
Record Flow

20

ClinicalTrials.gov Record Flow



Protocol/Results Review Criteria

- Protocol and results must be clear and informative
- Review focuses on:
 - Logic and internal consistency
 - Apparent validity
 - Meaningful entries
 - Formatting

PRS Information Resources

- Protocol Registration
 - Data Elements
 - Detailed Review Items
- Results
 - Data Elements
 - Detailed Review Items
 - Pre-submission Checklist
 - Helpful Hints and Common Errors
- User's Guide [PRS Main Menu]

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

23

Protocol Detailed Review Items

- Formatting, spelling
- Internal Consistency
 - Recruiting Status
 - Study Start Date
 - Primary and Study Completion Dates
- Study Type accurate
- Outcome Measure & Time Frame specific
 - E.g., “efficacy” and “safety” not sufficient
- Arms and Interventions
 - Consistent use of drug name in record
 - Arm Type accurate
 - Structure is logical
- Eligibility Criteria
 - Formatting
- No narrative results or compensation information

24

Results Review Focus

- Concept: Tables should convey the design, conduct and analysis of the data
- Logical table structure
- Measure Title/Description and Units of Measure consistent
- Complete scale information
 - Construct and domain
 - Best/worst values
 - “Units on a scale” if no other units

25

Results Review Focus (cont'd)

- Data appear valid
- All results in tabular format (i.e., no results or conclusions in free text)
- Consistency between modules, including the protocol section

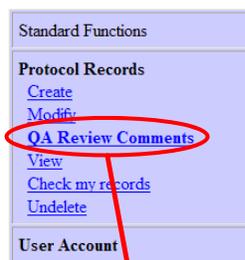
26

Review Comments

- When record posted or reset, data providers will receive email
- Comments can be accessed from PRS Main Menu and directly in each record
- Specific comments are collocated in the section where the issue was identified
- May be preformatted “comment stamp” or customized for specific issue

27

Accessing Review Comments From the PRS Main Menu



Protocol ID	ClinicalTrials.gov ID	Brief Title	has Results	Comment Date	Release Date
03-154	NCT00145249	Amphotericin Alone or in Combination with Fluconazole for AIDS-Associated Meningitis	Results	06/22/2010	09/16/2010

28

Review Comments Data Provider Perspective

Overall Study [Collapse Section](#)

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

Comments:

The Enrollment number in the protocol section conflicts with the number of participants Started 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 more than the number of participants randomized.

29

Participant Flow [Collapse Section](#)

Recruitment Details
Subjects were recruited at 13 medical centers in Latin America and participated between January 2007 and July 2008.

Pre-Assignment Details
160 subjects were screened and evaluated for inclusion/exclusion criteria; 121 were assigned to open-label treatment.

Reporting Groups

Reporting Group	Description
Pregabalin	Dose adjustment phase: Week 1: 75mg BID (150 mg/day) all subjects; Week 2 through Week 4: subjects were assessed on a weekly basis for dose adjustment from 75 mg BID (150 mg/day) to 150 mg BID (300 mg/day), and to 300 mg BID (600 mg/day) if needed based on pain relief and tolerability. 8 week dose maintenance phase (Week 5 to Week 12): subjects continued with their final pregabalin dosage: 75mg BID (150 mg/day) to 300 mg BID (600 mg/day) based on individual pain response and tolerability.

Comments:

-- Add Comment Stamp --
 Maximum allowed content length (1999)
 Please review entire record and expand all acronyms and abbreviations (and include acronym in parentheses) at least the first time used in both the Protocol and Results section.

Overall Study [Collapse Section](#)

	Pregabalin
STARTED	121
COMPLETED	99
Not Completed	22
Adverse Event	9
Lost to Follow-up	4
Other: unknown	5
Withdrawal by Subject	4

Comments:
[Add Comment](#)

30

Participant Flow

Recruitment Details
Subjects were recruited at 13 medical centers in Latin America and participated between January 2007 and July 2008.

Pre-Assignment Details
160 subjects were screened and evaluated for inclusion/exclusion criteria; 121 were assigned to open-label treatment.

Reporting Groups

Pregabalin	Description
	Dose adjustment phase: Week 1: 75mg BID (150 mg/day) all subjects; Week 2 through Week 4: subjects were assessed on a weekly basis for dose adjustment from 75 mg BID (150 mg/day) to 150 mg BID (300 mg/day), and to 300 mg BID (600 mg/day) if needed based on pain relief and tolerability. 8 week dose maintenance phase (Week 5 to Week 12): subjects continued with their final pregabalin dosage: 75mg BID (150 mg/day) to 300 mg BID (600 mg/day) based on individual pain response and tolerability.

Comments:

Acronyms and Abbreviations - Spell Out
 Arm Titles not Informative
 Cross-over Study
 Detailed Review of Results Submission
 Earlier Comments
 Irrelevant Information
 None or N/A
 Not Understandable
 Number Started Inconsistent with Protocol Enrollment
 Pending Records Require Review
 Results Helpful Hints and Common Errors
 Results Pre-submission checklist
 Spelling

COMPLETED 99
 Not Completed 22
 Adverse Event 9
 Lost to Follow-up 4
 Other: unknown 5
 Withdrawal by Subject 4

31

Review Comments (cont'd)

- If record reset without public posting, then review findings must be addressed
 - Modify record to address comments and rerelease record
- Email register@clinicaltrials.gov if questions on content of comments
 - Include NCT number, date of comments, and description of question w/ any supporting info
 - May also request teleconference

Posting on ClinicalTrials.gov

- Indicates that no major problems were detected, such as:
 - Information internally consistent
 - Logical table structure
 - Measure title and units of measure consistent
 - Complete scale information
 - All results in tabular format (no written results)
 - Data appearing valid

33

Caveats Regarding Posting at ClinicalTrials.gov

- **Data provider is responsible for ensuring that records meet review criteria**
 - Data providers should assess their records using available review criteria prior to releasing the records
- Posting does not ensure that all review criteria were met
- Comments may still be provided “suggesting” improvements
- ClinicalTrials.gov may note issues and request revisions after record posted publicly

34

Additional Information

General ClinicalTrials.gov information:

<http://prsinfo.clinicaltrials.gov>

FDAAA related information:

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

Office of Extramural Research:

http://grants.nih.gov/Clinicaltrials_fdaaa/

Questions?

register@clinicaltrials.gov