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Protocol Registration System (PRS) Overview and Resource Orientation

Results Database Train-the-Trainer Workshop
October 2012

http://ClinicalTrials.gov

Using the Protocol Registration System (PRS)

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PRS Basics

- Web-based data entry system for summary protocol and results information
  - Requires organizational account, user name, password
- PRS Organizational Accounts
  - Established by an organization
  - Used to enter, review, submit, and update protocol and results information for studies ("records") sponsored by the organization or conducted by sponsor-investigators at the organization

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PRS Basics (cont.)

- PRS Roles
  - Administrator: organization point of contact
    - Maintains PRS Organizational Account
    - Creates User accounts
    - Has access to all study records
    - Monitors records in account for Problems
    - Approves and releases records when the Organization is the Sponsor and Responsible Party
  - User: creates and edits records
    - Only has access to records in which they are the Record Owner or on the Access List
    - Approves and releases records when a Sponsor-Investigator or Principal Investigator is the Responsible Party

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PRS Basics (cont.)

- PRS Roles
  - Record Owner (may be a User or Administrator)
    - Considered the primary contact for a study record
    - Initially assigned to person who created the study record; record ownership can be transferred

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PRS Basics (cont.)

- Required* and optional structured data elements
  - Pull-down menus and/or free text
- Business rules
  - ERROR - Study cannot be released; must be addressed
  - WARNING - FDAAA item; should be addressed
  - NOTE - Helpful hints; may or may not apply
- Review criteria applied by ClinicalTrials.gov Staff
  - Logic and internal consistency
  - Apparent validity
  - Meaningful entries
  - Formatting

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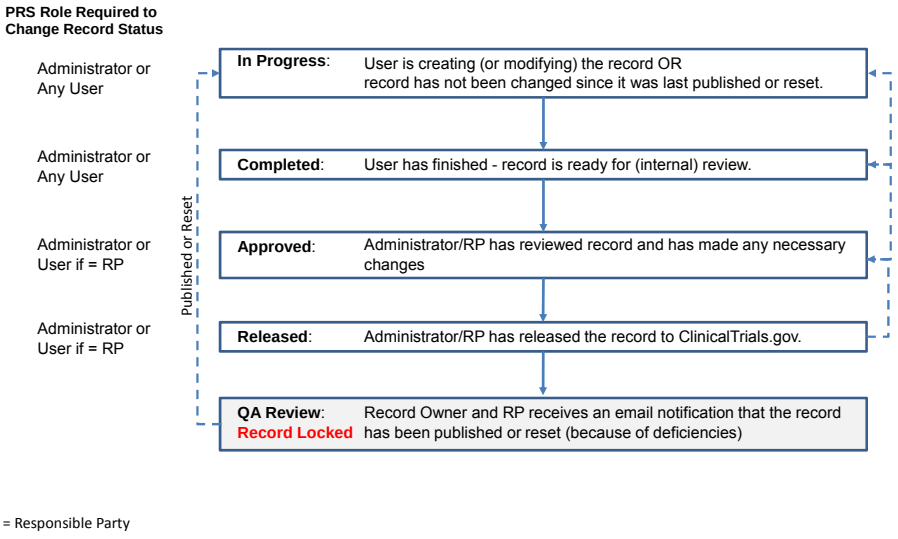
Record Flow
Record Status and Action Required



RP = Responsible Party

PRS Information Resources

- User's Guide [PRS Main Menu]
- Protocol Registration
  - Data Elements
  - Review Criteria
- Results
  - Data Elements
  - Review Criteria
  - Simple Results Templates
  - Helpful Hints and Common Errors

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

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Items To Consider Before Registering a Protocol

- Each protocol can only be registered once
  - Avoid duplicate registrations (i.e., multiple records for same study)
    - Agree on the Sponsor and the Responsible Party ahead of time
    - Multisite studies are NOT registered by each individual site
    - Multi-collaborator/funder studies need to designate a single entity to register the study
- Studies must be registered by the Responsible Party (study Sponsor or designated Principal Investigator [PI])

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

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PRS Responsible Party Format

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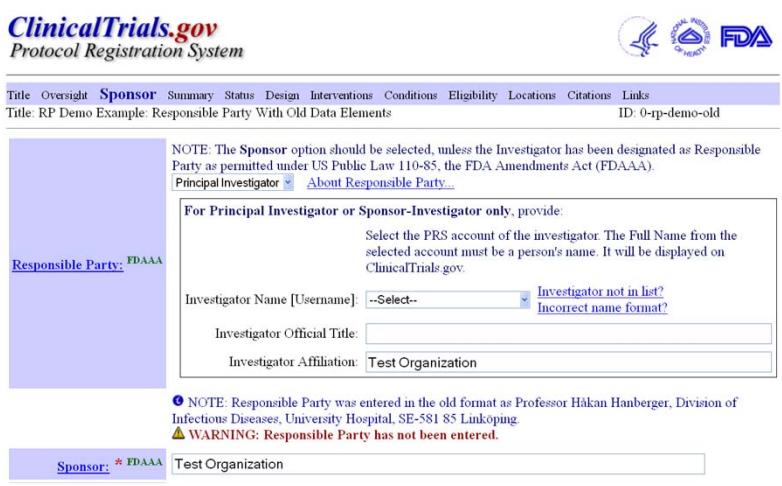
PRS Responsible Party Format



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PRS Business Rules: Responsible Party

- Responsible Party must Approve and Release record (but others may still assist with data entry)
  - If RP = Sponsor
    - Administrator “approves” and “releases” record
  - If RP ≠ Sponsor
    - Record is in the Sponsor’s organizational account
    - Investigator must be specified as a User in the PRS and name must be properly formatted (for display on ClinicalTrials.gov)
    - Investigator “approves” and “releases” record
      - Administrator receives notification after release
- See: “Responsible Party FAQ” on PRS Main Menu under Help for more information

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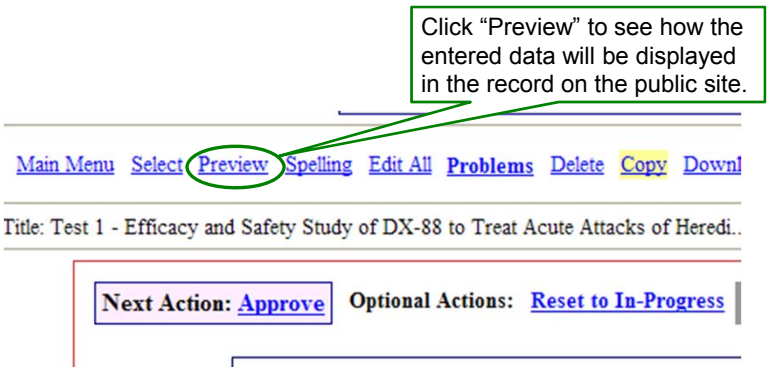
https://register.clinicaltrials.gov/

Previewing the Record: Viewing the Public Display



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ClinicalTrials.gov
Protocol Registration System

Protocol Registration Preview

Continue Select

Test 1 - Efficacy and Safety Study of DX-88 to Treat Acute Attacks of Hereditary Angioedema (HAE)

This study has been completed.

Sponsor:	PRS Training
Collaborators:	
Information provided by (Responsible Party):	Rebecca Williams, PRS Training
ClinicalTrials.gov Identifier:	

Purpose

The purpose of this study is to determine if a subcutaneous dose of DX-88 (ecallantide; an investigational product) is safe and relieves symptoms of HAE in patients suffering from moderate to severe acute attacks of HAE.

Condition	Intervention	Phase
Hereditary Angioedema (HAE)	Drug: ecallantide Drug: Phosphate Buffer Saline (PBS),	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor), Randomized, Efficacy Study

Official Title: A Double-blind, Placebo-controlled Study (72 Patients, Randomized 1:1) Followed by a Repeat-dosing Phase to Assess the Efficacy and Safety of DX-88 (Ecallantide; Recombinant Plasma Kallikrein Inhibitor) for the Treatment of Acute Attacks of Hereditary Angioedema

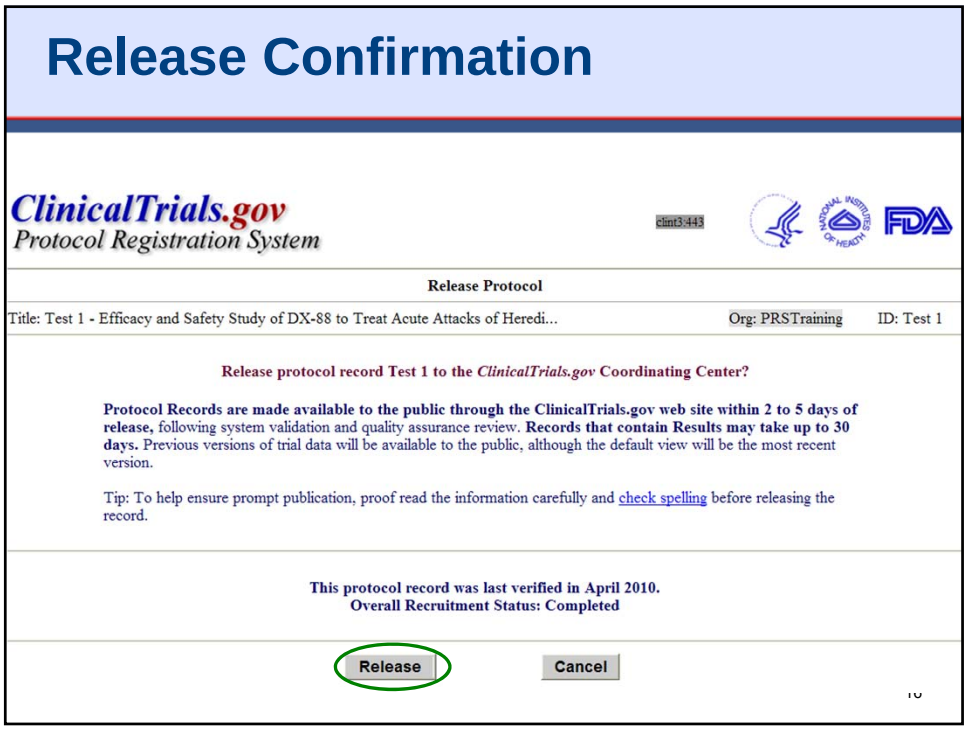
Further study details as provided by Rebecca Williams, PRS Training:

Enrollment: 91
Study Start Date: December 2005
Study Completion Date: February 2007
Primary Completion Date: December 2005

Arms	Assigned Interventions
Experimental: DX-88 (ecallantide) DX-88 (ecallantide) 30 mg given as three 10 mg/mL subcutaneous injections.	Drug: ecallantide dose of 30 mg (10 mg/ml) given as 3 subcutaneous injections.
Placebo Comparator: Placebo Phosphate Buffer Saline (PBS), pH 7.0 given as 3 subcutaneous injections.	Drug: Phosphate Buffer Saline (PBS), given as three 1mL subcutaneous injections.

Sample PRS Edit Record Screen

Release Confirmation



Protocol Registration Receipt

ClinicalTrials.gov
Protocol Registration System

clint3:443

Protocol Registration Receipt
11/04/2011

Continue | Download PDF

Protocol Records are made available to the public through the ClinicalTrials.gov web site within 2 to 5 days of release, following system validation and quality assurance review. **Records that contain Results may take up to 30 days.** The ClinicalTrials.gov identifier (NCT number) will be assigned at that time, and will then be visible in the PRS.

Tip: Use the "Download PDF" link to get a printable record confirming the registration of this trial.

Test 1 - Efficacy and Safety Study of DX-88 to Treat Acute Attacks of Hereditary Angioedema (HAE)

This study has been completed.

Sponsor:	PRS Training
Collaborators:	
Information provided by (Responsible Party):	Rebecca Williams, PRS Training
ClinicalTrials.gov Identifier:	

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ClinicalTrials.gov
Protocol Registration System

Protocol Registration Receipt
11/04/2011

Grantor: CDER IND/IDE Number: 12345 Serial Number: 01

Test 1 - Efficacy and Safety Study of DX-88 to Treat Acute Attacks of Hereditary Angioedema (HAE)

This study has been completed.

Sponsor:	PRS Training
Collaborators:	
Information provided by (Responsible Party):	Rebecca Williams, PRS Training
ClinicalTrials.gov Identifier:	

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The purpose of this study is to determine if a subcutaneous dose of DX-88 (ecallantide; an investigational product) is safe and relieves symptoms of HAE in patients suffering from moderate to severe acute attacks of HAE.

Condition	Intervention	Phase
Hereditary Angioedema (HAE)	Drug: ecallantide Drug: Phosphate Buffer Saline (PBS),	Phase 3

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New Registrations: ClinicalTrials.gov Identifier (NCT Number)

- Records should be available on ClinicalTrials.gov within **2 to 5 business days** of release
- Where to find the ClinicalTrials.gov Identifier
  - **Email**: Sent to the RP and "record owner" (if different)
  - **PRS Account**: Appears in the "ClinicalTrials.gov ID" field
  - **ClinicalTrials.gov**: Search using Unique Protocol ID; the NCT number is listed at the top
- A study is not "registered" until it receives a ClinicalTrials.gov Identifier (NCT number)
  - Initial Release Date will be reported on public site
- Some studies will be "reset" without public posting
- Check the public site to ensure that a study is properly registered

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RP = Responsible Party

Review Comments

- When record "**reset"**, the Responsible Party and Record Owner (if different) will receive email
- Comments can be accessed from PRS Main Menu and within each record
- Specific comments are co-located in the section where the issue was identified
- May be pre-formatted "comment stamp" or customized comment for specific issue

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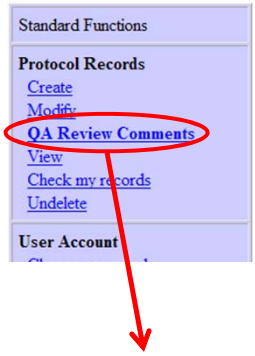
Accessing Review Comments
From the PRS Main Menu



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

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Review Comments
Data Provider Perspective

Collapse Section

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
[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.

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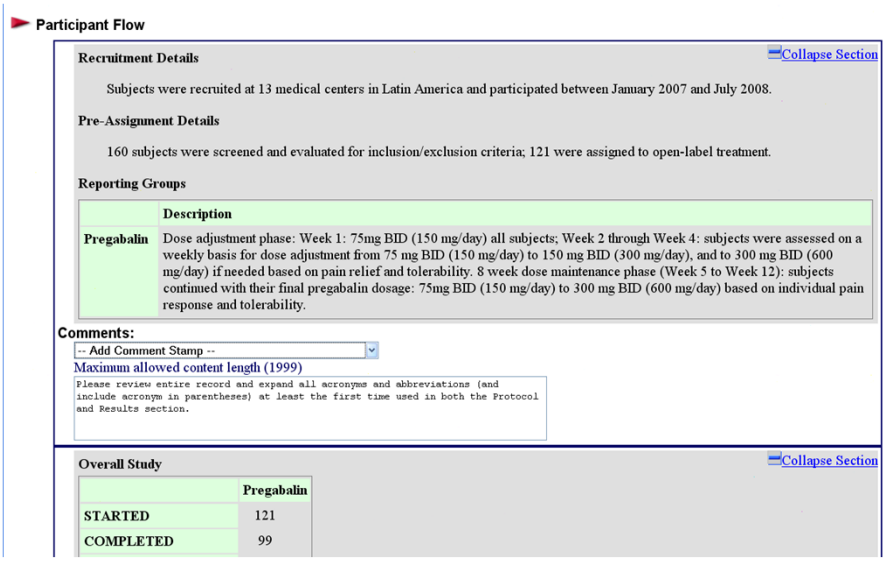
Review Comments
Reviewer Perspective



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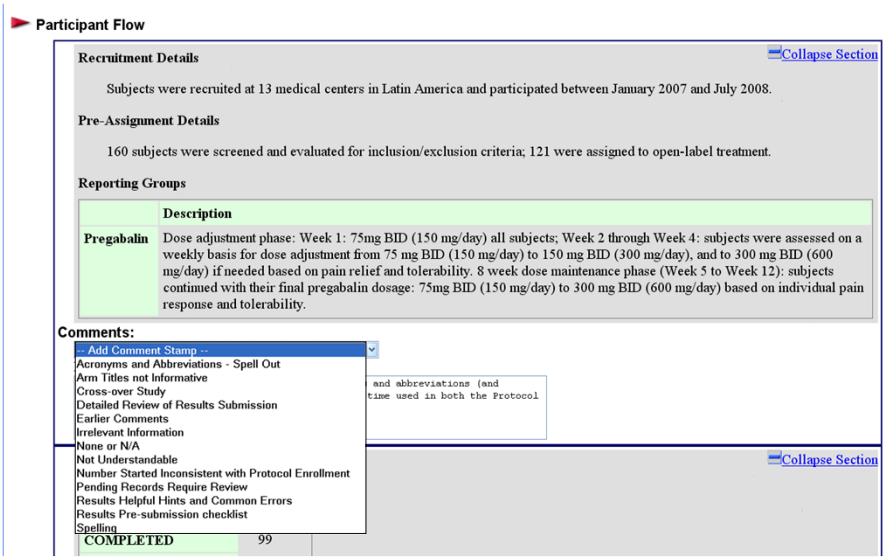
Review Comments
Reviewer Perspective



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Review Comments (cont.)

- If record reset without public posting, then major review findings must be addressed
  - Modify record to address comments and re-release record
- Email register@clinicaltrials.gov if questions on content of comments
  - Include NCT Number (or Unique Protocol ID prior to posting), date of comments, and description of question w/ any supporting info
  - May also request teleconference

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Review Comments - Protocol

- Insufficient Outcome Measures are the primary reason protocol records are reset
  - Be familiar with the Protocol Review Criteria for Outcome Measure Title, Description, and Time Frame

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http://prsinfo.clinicaltrials.gov/ProtocolDetailedReviewItems.pdf

Caveats Regarding Posting at ClinicalTrials.gov

- **Responsible Party must ensure that records meet review criteria**
  - Responsible parties 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

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PRS Tools for Administrators

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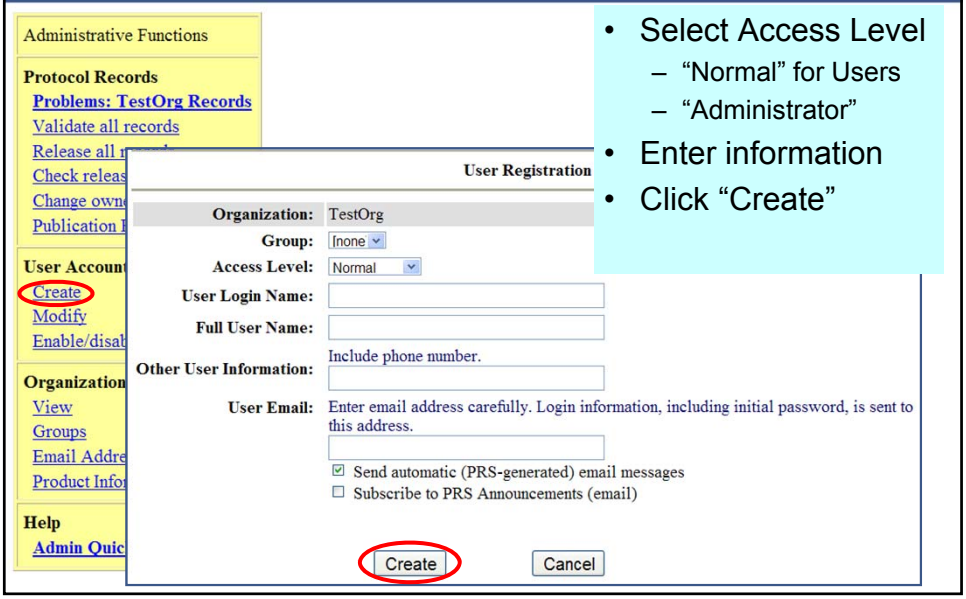
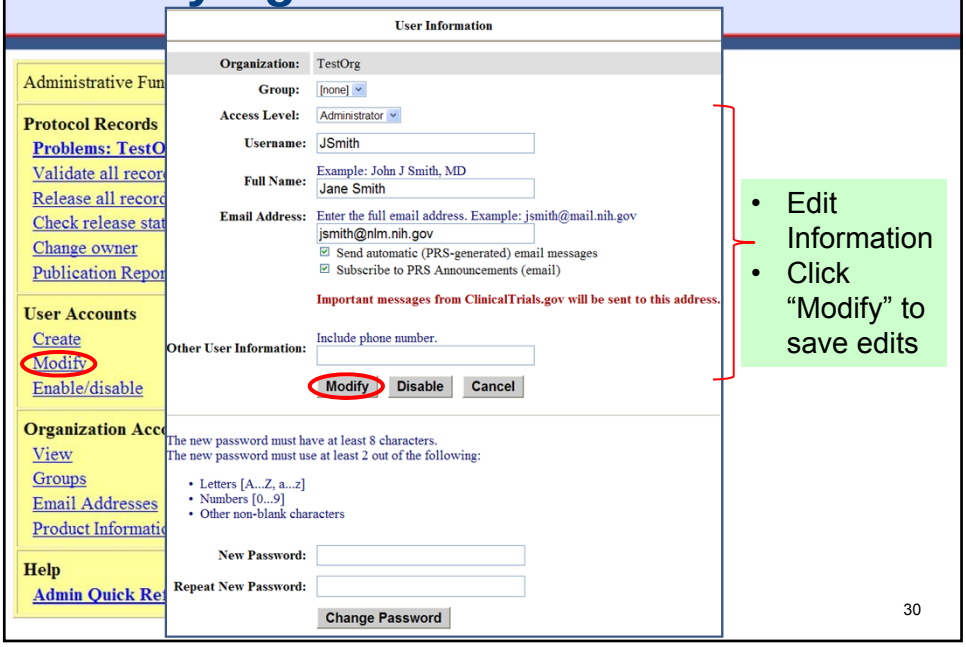
Creating User Accounts



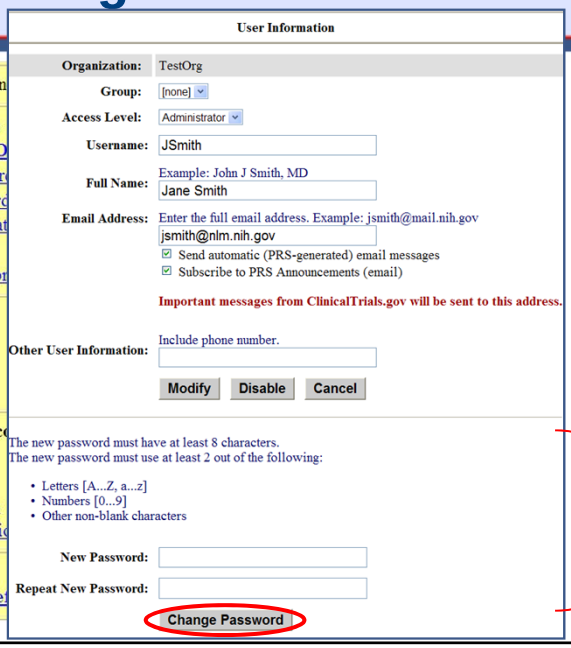
- Select Access Level
  - "Normal" for Users
  - "Administrator"
- Enter information
- Click "Create"

Modifying User Information



- Edit Information
- Click "Modify" to save edits

Resetting Passwords



- Enter new password
- Click "Change Password"

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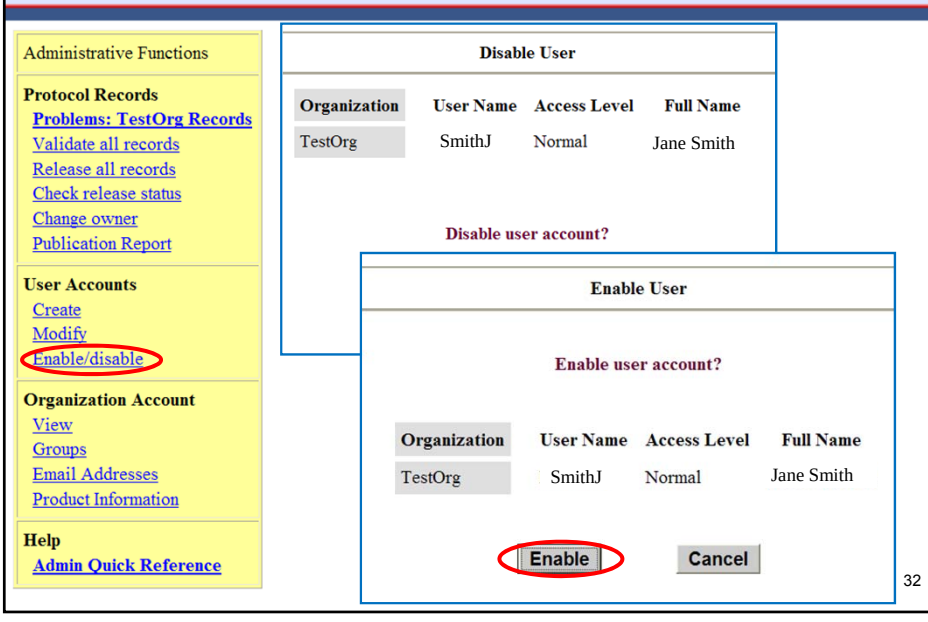
Enabling/Disabling User Accounts



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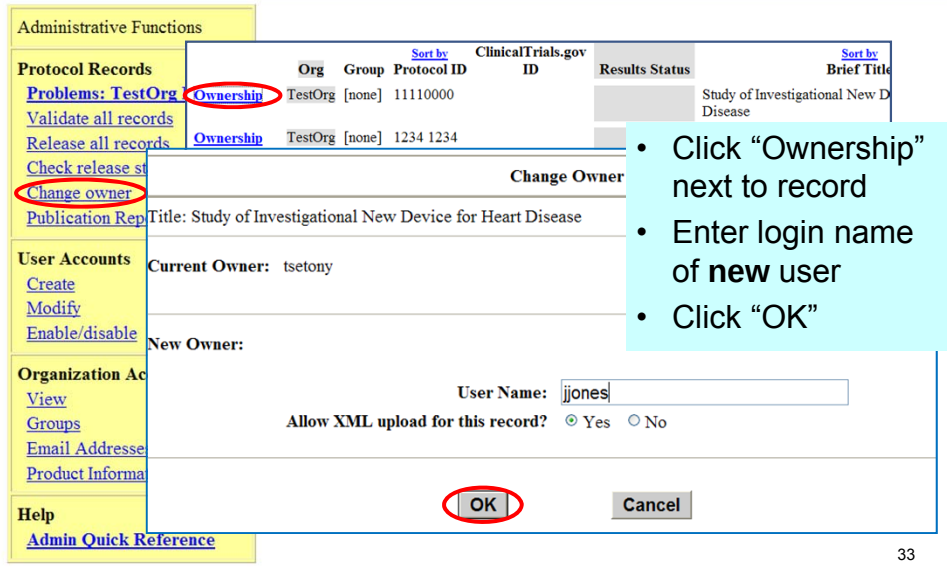
Changing Record Ownership



- Click “Ownership” next to record
- Enter login name of **new** user
- Click “OK”

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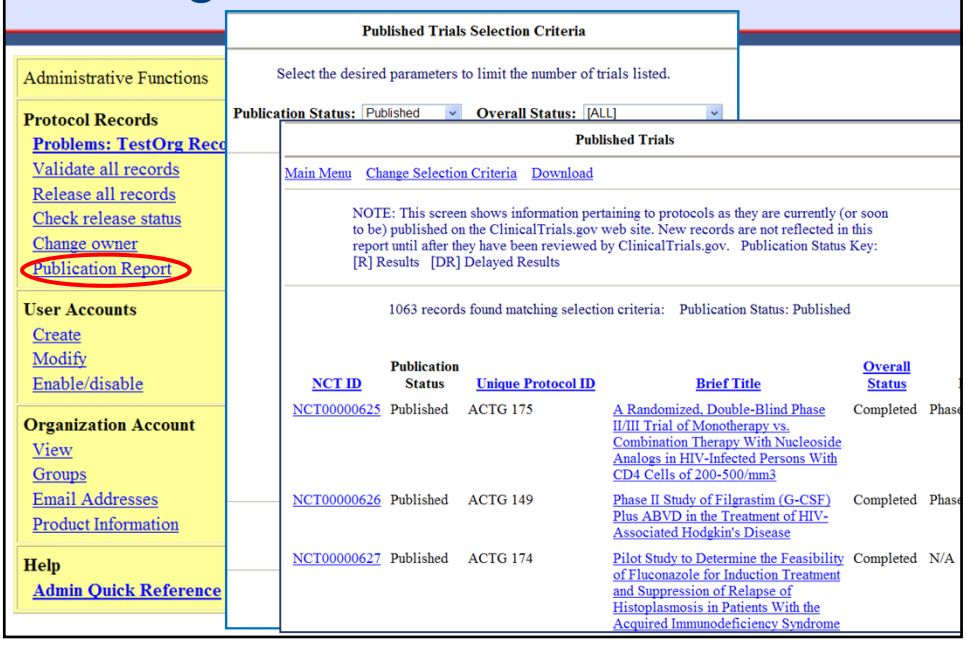
Listing of All Published Records



Listing of All Email Addresses

Convenient way to **copy and paste** email addresses for all Administrators and/or Users in the PRS Account into mass email messages

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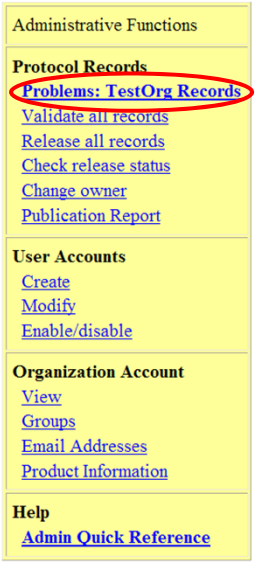
Identifying Problem Records



- Record Owner Issues: e.g.,
  - # record(s) have Review Comments that need to be addressed.
  - # record(s) for recruiting studies have not been updated or verified within the past six months.
- US Public Law 110-85 (FDAAA) issues: e.g.,
  - # record(s) are missing one or more data elements required by FDAAA…
  - # record(s) appear to be overdue for results submission per FDAAA.

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Problems Report – FDAAA Issues

- For Informational Purposes Only
- Determination of whether a trial is subject to FDAAA must be made by the Responsible Party
- How do I get my trial off the report?
  - Provide all FDAAA required data elements
  - Verify accuracy of data for the following data elements:
    - Study Type, Intervention Type, Study Phase, IND/IDE Protocol?, Facility Location(s), Completion Dates – Primary and Study
  - If applicable, submit results, certification or extension request
    - Note: The PRS cannot detect if the trial includes an unapproved product.

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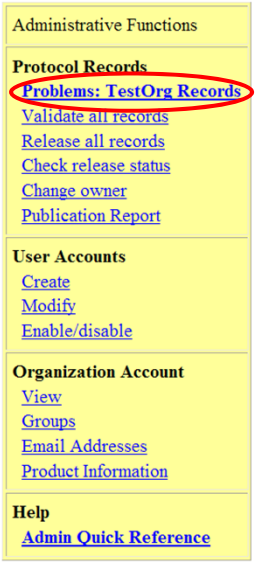
Identifying Problem Records (cont.)



- Administrator Issues: e.g.,
  - # record(s) are ready for review and approval.
  - # record(s) have never been released to ClinicalTrials.gov.

NOTE: A single record may be listed in multiple categories. Once a problem is resolved, the record will no longer be listed under that problem category.

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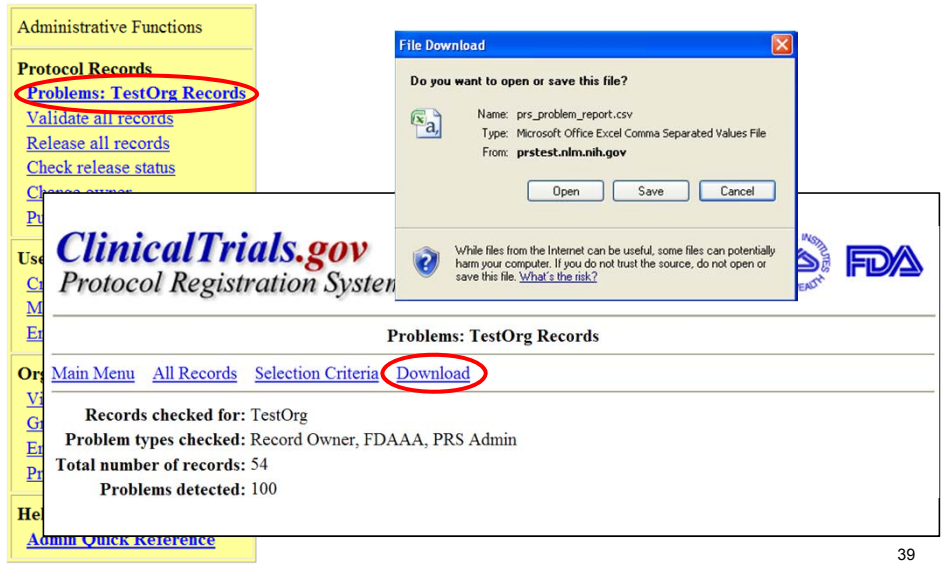
Downloading the Problem Report



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Problem Report File

	A	B	C	D	E	F	G	H	I	J
1	Problem Type	Protocol ID	ClinicalTrials.gov ID	Brief Title	Overall Status	Last Verified	Record Status	Owner	Updater	Last Update
2	Not Completed	0-rp-demo-old	N/A	RP Demo Example: Res	Active, not recruiting	2009-03	In Progress	jg	jg	8/1/2011 8:37
3	Never Released	0-rp-demo-old	N/A	RP Demo Example: Res	Active, not recruiting	2009-03	In Progress	jg	jg	8/1/2011 8:37
4	Ready for Review and Approval	0-rp-demo-pi	N/A	RP Demo Example: Res	Not yet recruiting	2009-07	Completed	jg	QAab	9/29/2011 12:25
5	Never Released	0-rp-demo-pi	N/A	RP Demo Example: Res	Not yet recruiting	2009-07	Completed	jg	QAab	9/29/2011 12:25
6	Ready for Review and Approval	0-rp-demo-s	N/A	RP Demo Example: Res	Active, not recruiting		Completed	jg	jg	7/23/2011 11:14
7	Never Released	0-rp-demo-s	N/A	RP Demo Example: Res	Active, not recruiting		Completed	jg	jg	7/23/2011 11:14
8	Ready for Review and Approval	0-rp-demo-si	N/A	RP Demo Example: Res	Active, not recruiting		Completed	jg	jg	7/23/2011 11:13
9	Never Released	0-rp-demo-si	N/A	RP Demo Example: Res	Active, not recruiting		Completed	jg	jg	7/23/2011 11:13
10	Never Released	1	N/A	Donepezil and Vitamir	Completed	2010-10	Approved	DBlacker	DBlacker	10/14/2010 22:22
11	Ready for Review and Approval	11110000	N/A	PARTICIPANT FLOW -2	Not yet recruiting	2007-01	Completed	CampionD	CampionD	11/7/2011 12:30
12	Never Released	11110000	N/A	PARTICIPANT FLOW -2	Not yet recruiting	2007-01	Completed	CampionD	CampionD	11/7/2011 12:30
13	Ready for Review and Approval	111999asdfasdfasd	N/A	PARTICIPANT FLOW - t	Not yet recruiting	2011-06	Completed	CampionD	Tony	11/7/2011 13:56
14	Ready for Review and Approval	1234 1234	N/A	BASELINE MEASURE an	Active, not recruiting		Completed	QAab	Tony	11/8/2011 12:40
15	Never Released	1234 1234	N/A	BASELINE MEASURE an	Active, not recruiting		Completed	QAab	Tony	11/8/2011 12:40
16	Not Completed	123456	N/A	Test	None		In Progress	QAab	QAab	4/1/2009 12:46
17	Never Released	123456	N/A	Test	None		In Progress	QAab	QAab	4/1/2009 12:46
18	Not Completed	1234567	N/A	Test Interventional Stu	Enrolling by invitation		In Progress	Tony	root	1/18/2011 9:42
19	Never Released	1234567	N/A	Test Interventional Stu	Enrolling by invitation		In Progress	Tony	root	1/18/2011 9:42
20	Not Completed	124345	N/A	This is a Test for Verification Date			In Progress	QAab	QAab	6/1/2009 9:05
21	Never Released	124345	N/A	This is a Test for Verification Date			In Progress	QAab	QAab	6/1/2009 9:05
22	Never Released	124356	N/A	Jgfsghs	Recruiting	2005-08	Approved	QAab	QAab	5/13/2009 7:15
23	Ready for Review and Approval	2007-1234	N/A	Study of Hypothetica l	Recruiting	2007-11	Completed	QAab	QAab	11/7/2011 14:20

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PRS Email Communication

Event	To: and cc:	Description
Record status changed by User ["completed" or reset to "completed" or "in-progress" status]	To: Responsible Party	Record may be waiting for "next action"
Record "released"	To: Responsible Party	Confirmation - record released to ClinicalTrials.gov for processing
Record "reset"	To: Record Owner cc: Responsible Party Last updater	Changes must be made - record (or updates) not published on ClinicalTrials.gov
Record "published"	To: Record Owner cc: Responsible Party Last updater	Notification - record will be published on ClinicalTrials.gov

Responsible Party = **Administrator(s)** if Sponsor; **User** if Sponsor-Investigator or Designated Principal Investigator

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PRS Email Communication (cont.)

Event	To: and cc:	Description
Problem Notification – Record Owners	To: Record Owner Administrator(s) Responsible Party	• QA Comments • Record was updated but not marked "Completed" • Recruiting (or not yet recruiting) studies have not been updated or verified within the past six months • Ongoing, non-recruiting studies have not been updated or verified within the past year.

Responsible Party = **Administrator(s)** if Sponsor; **User** if Sponsor-Investigator or Designated Principal Investigator

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PRS Email Communication (cont.)

Event	To: and cc:	Description
Problem Notification – Administrators and Responsible Party	To: Administrator(s) Responsible Party	• Records ready for review and approval (and release) • Records that have never been released to ClinicalTrials.gov • Records that have been updated and need to be re-released to ClinicalTrials.gov

Responsible Party = **Administrator(s)** if Sponsor; **User** if Sponsor-Investigator or Designated Principal Investigator

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PRS Email Communication (cont.)

Event	To: and cc:	Description
Problem Notification – All (FDAAA Issues)	To: Record Owner Administrator(s) Responsible Party	• Missing one or more data elements required by FDAAA, such as: Responsible Party, Study Start Date, Primary Completion Date and Primary Outcome Measure • Appear to be overdue for registration of results per FDAAA

Responsible Party = **Administrator(s)** if Sponsor; **User** if Sponsor-Investigator or Designated Principal Investigator

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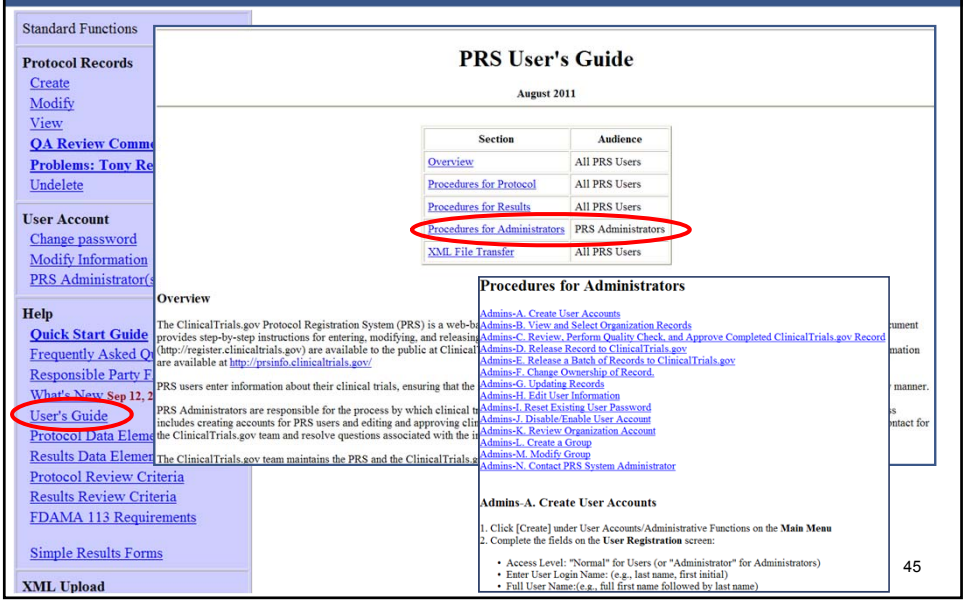
Seeking Help on PRS Functions



Login to PRSTest

- https://prstest.nlm.nih.gov
- Organization: PRSTraining [same for all]
- Username: User## [on folder]
- Password: User!password [same for all]

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Thank you!

Questions?

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