Yale University

eReg Training Session for Multi-Site Access

YCCI — Yale Center for Clinical Investigation

Training Objective

Provide System Overview

Provide a comprehensive overview of how to electronically maintain regulatory and essential documents for clinical research studies using the Advarra eRegulatory (hereafter referred to as eReg) system.

Discuss System Updates

Discuss recent eReg system updates and new features.

Answer Questions

Answer questions related to electronic maintenance of regulatory and essential documents.

Agenda

- eReg System Overview
- Getting Started
- Maintaining eReg Trial Master File and Participating Site File(s)
- Setting Up eReg for Use by External Monitors and Auditors
- Closing Statements

eReg System Overview

eReg System Overview

- Advarra's eReg system is an electronic regulatory binder management system which is designed to increase regulatory compliance and efficiency

- eReg supports regulatory workflows across the School of Medicine and allows for management of a portfolio of protocols including multi-site protocols

eReg System Overview – Advantages to eReg Binder

Documents can be compliantly (21 CFR Part 11) routed for electronic signature, eliminating time-consuming administrative tasks and providing the ability for study staff to signoff on regulatory documents at anytime

Staff credentials and organization (laboratory and Institutional Review Board) documents are maintained in one place and flow to all necessary protocols, allowing for central management

Increased security, user roles and account permissions allow Yale to control and monitor who sees what and when

Increased accessibility, allows remote management of essential and regulatory documents and remote reviews by monitors, auditors, and/ or inspectors

eReg System Overview – Document Management

- Documents are maintained in three (3) locations
- Each location contains documents which are essential to maintaining a complete regulatory file
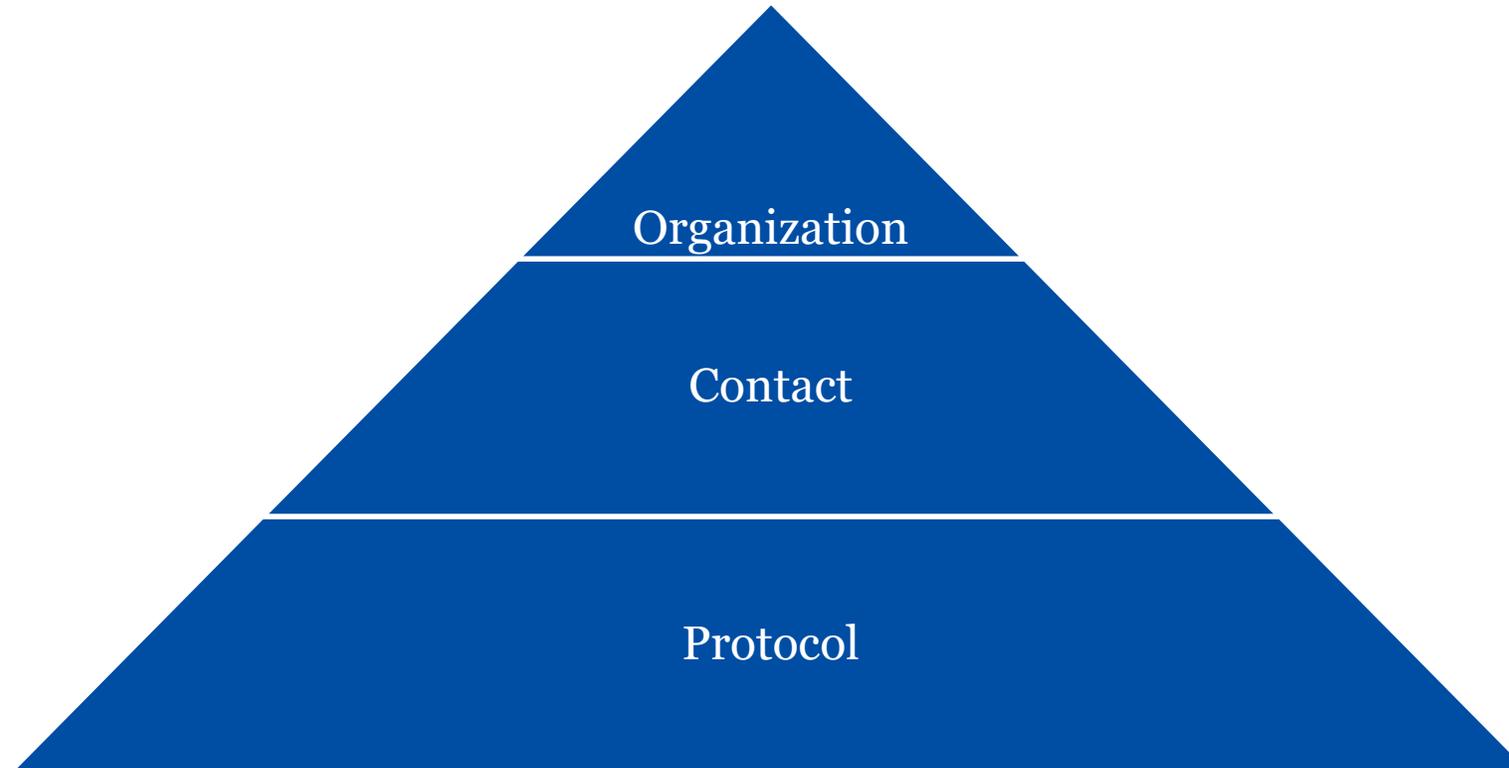
eReg System Overview – Document Management

Organization
- IRB - Federalwide Assurance Number, Roster, OHRP Registration, Compliance Statement
- Laboratory - Certifications and Accreditations (CAP, CLIA, COLA, State Certifications), Lab Director CV and ML, Normal Range Values

Contact
- CVs, MLs, GCP Training, Signature Sample, additional credentials determined by the department

Protocol
- Consent Templates, Assent Templates, Protocols, Investigator's Brochure, Instructions for Use, Sample Label for Investigational Product, Study Manuals, Training Records, Vendor Information, Master Enrollment Log, Study Correspondence, etc.

eReg System Overview – Document Management

YCCI Responsibility (Central Management)

Yale-affiliated Organization regulatory tracking items

Contact level staff credentials (GCP, Signature sample, CVs, MLs)

Study Team Responsibility

External Organization regulatory tracking items

Protocol level regulatory and essential documents

If you believe an Organization that is not affiliated with Yale is widely used and could be managed centrally, please submit a request to YCCI (eReg.Credentials@yale.edu).

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eReg System Overview – Multi-Site Document Management

- Multi-Site Protocols are maintained in three (3) sections:
  - Participating Sites
    - A side – where Yale staff maintain copies of participating site documents which are stored by the participating site in their investigator site file
    - B side (optional) – where external (non-Yale) staff maintain (copies of) the investigator site file
  - Document inbox – where copies of documents from participating sites and emails are received
  - Summary section – where Yale staff maintain the trial master file

eReg System Overview – Regulatory Templates

- YCCI has developed regulatory templates to guide study teams and ensure GCP and regulatory requirements are met.
  - As future needs arise, additional templates may be developed

	Yale Standard Templates		
Regulatory Templates	**Drug**	**Device**	**Behavioral**
Investigator Site File	✓	✓	✓
Participating Site File	✓	✓	✓
Trial Master File	✓	✓	✓
Trial Master File/Investigator Site File Combination	✓	✓	✓

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eReg System Overview – Investigator Site File

Facilitates Organization

Organizes regulatory and essential documents, provides easy access to documents by the trial monitor, auditor, Institutional Review Board (IRB), and/ or regulatory authorities for review/audit purposes, and allows research team members to reference information and documentation.

Contains Study Documents

Investigator Site Files (also known as regulatory binders, investigator binders, study binders, etc.) contain study-specific information and regulatory documentation. This term is applied to files maintained by the participating site staff.

Investigator Site Files

Demonstrates Compliance

Investigator Site Files serve to demonstrate compliance with Good Clinical Practice (GCP), all applicable regulatory requirements and the IRB approved protocol.

eReg System Overview – Trial Master File

Contains Sponsor Documents

The Trial Master File contains the essential and regulatory documents required to be maintained by the Sponsor or Sponsor-Investigator. It should be set up at the start of a study and continuously maintained throughout the conduct of the study.

Permits Trial Re-creation

It permits the study to be independently re-created from the filed study records. It is a quality process which includes documentation of the activity that has been performed during the study. This is critical in ensuring study participant rights are protected and that regulators have access to robust, reliable clinical trial documents.

Trial Master Files

Demonstrates Compliance

Trial Master Files serve to demonstrate compliance with Good Clinical Practice (GCP), all applicable regulatory requirements and the approved protocol.

eReg System Overview – Participating Site Files

Participating Site Files

Contains Site-Specific Documents
The Participating Site File contains the essential and regulatory documents required to be maintained by the Sponsor or Sponsor-Investigator for each site that participates in a multi-site trial. Within eReg, it's also a place where external participating sites can file regulatory and essential documents to share with the Sponsor or Sponsor-Investigator.
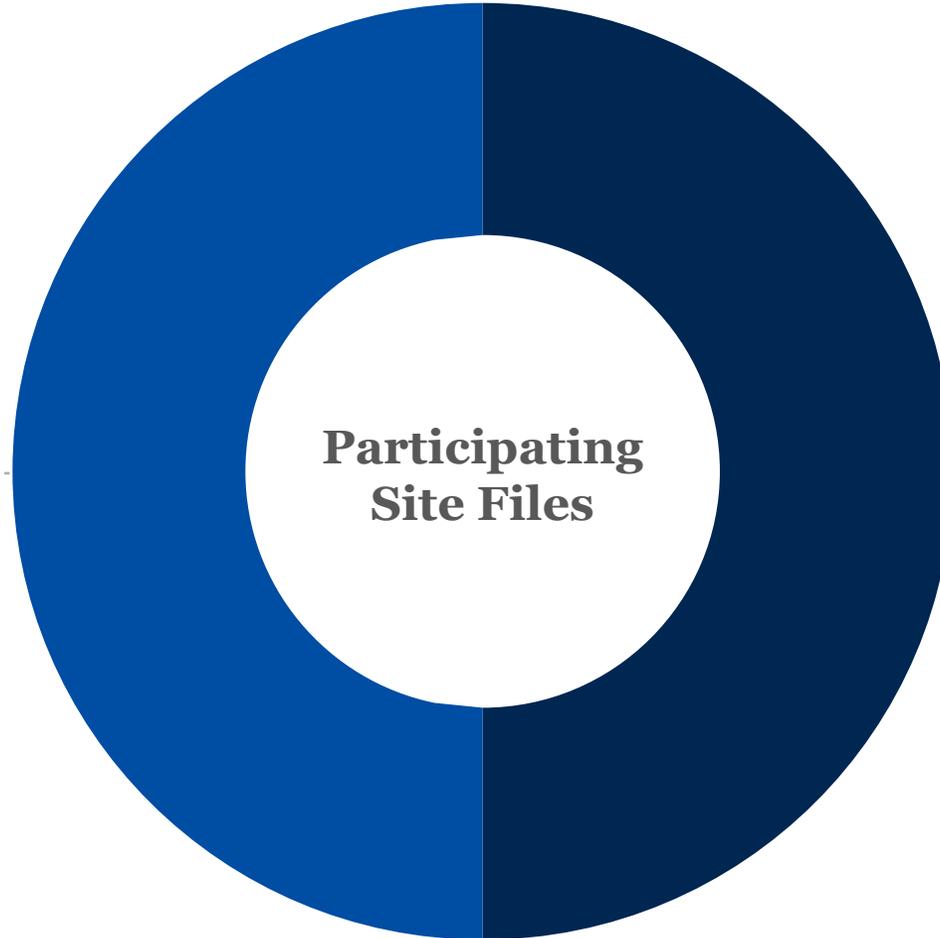
Demonstrates Compliance
Participating Site Files serve to demonstrate compliance with Good Clinical Practice (GCP), all applicable regulatory requirements and the approved protocol.

Getting Started

Building Multi-Site Protocols

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Building Protocols – Protocol Import

- Studies requiring ICH GCP compliance are expected to be maintained in eReg for those departments using eReg or if the PI intends to maintain regulatory files electronically.
- eReg Support will import the record from OnCore and select the appropriate regulatory template based on study attributes and management type. This will be done after YCCI has completed the risk assessment on the study or upon receipt of a request for import.
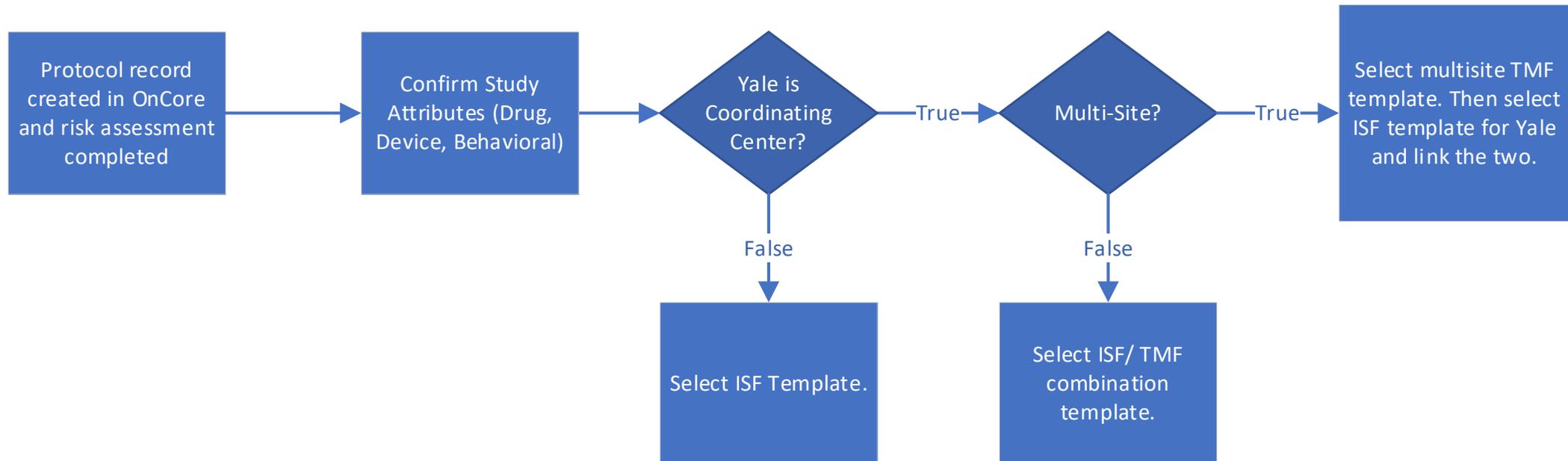
Building Protocols – Adding Protocol Details

- When a protocol is imported from OnCore, the following details captured in eReg will be imported along with it:
  - Protocol Number
  - Title
    - Sponsor protocol number may be included at the front of the title to ensure it is included within the delegation of authority log
  - Short Title
  - NCT Number
    - Note: The NCT Number must be entered to link a Trial Master File to an Investigator Site File in eReg.
  - IRB Protocol Number
- Sponsor, Study Site and Departments will be manually added after import by eReg Support and/ or the study team member responsible for maintaining the Trial Master File (or Investigator Site File if not a multi-site study). Identifiers can be optionally added.

Protocol Number

Title

Short Title

NCT Number

Sponsor

Departments

Study Site

IRB Protocol Number

Identifiers

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Building Protocols – Creating Multi-Site Protocols

- eReg Users with a role of Multi-Site Access – Department level and eReg Administrators can import multi-site protocols from OnCore. All other eReg Users will send an email to eReg.Support@yale.edu to request import of a multi-site protocol.

- Multi-site protocols permit Yale to manage their own sponsor-level documents related to the study in a Trial Master File, list participating sites and manage documents for participating sites (internal and external) as well as receive, review, and file documents sent from participating sites on the protocol in a Trial Master File and/ or Participating Site File. This is accomplished via Document Inbox.

- Participating sites can be added to multi-site protocols as:
  - Research Center Study Sites
  - Data Exchange Affiliates
    - Note: Data Exchange sites must be configured by eReg Support. Confirm with eReg Support before adding a Data Exchange site. eReg Support has a list of sites who can be set up through Data Exchange.
  - Non-Data Exchange Affiliates

Building Protocols – Participating Sites

Participating Site Types

Research Center

- Part of the coordinating center organization (Yale University).
- Can upload documents into their own protocol records and route documents for signature prior to sending copies to the coordinating center.

Data Exchange

- Outside of the coordinating center's organization.
- Have their own eReg instance.
- Can upload documents into their own protocol records and route them for signature prior to using Data Exchange to send copies to the coordinating center.

Non-Data Exchange

- Outside of the coordinating center's organization.
- Granted access to Yale's eReg instance.
- Can log in, upload documents to a protocol record, and send copies of documents to the coordinating center.
- Limited capabilities in eReg. They can't, for example, route documents for signature.

Building Protocols – Adding Participating Sites (Demo)

- After the multi-site protocol is imported from OnCore, eReg Users with Multi-Site – Department level, Multi-Site – Assigned level and eReg Administrators can add participating sites to create Participating Site Files for each site.
  - Multi-Site – Assigned Users can only view sites they added or sites for studies on which they are assigned (listed as staff in eReg)
  - Multi-Site – Department Users can view all participating sites on all multi-site protocols
- To add participating sites:
  1. Open the Participating Sites section of the protocol record
  2. Click + Add Participating Site.

Building Protocols – Adding Participating Sites

- The Participating Site pop-up window will open where you can select the study site(s).
- Study Sites are based upon a list of organizations maintained within OnCore. If the Study Site is not available from the list, contact OnCore.Support@yale.edu and ask that the Study Site be added to OnCore.
- When you click Continue to add the site, a new pop-up window will allow you to select the Regulatory Template for the participating site file. Consider the study attributes when selecting the Regulatory Template.

Building Protocols – Connecting to Yale ISF

- eReg Users with Multi-Site – Department level, Multi-Site – Assigned level and eReg Administrators can invite the Yale site staff to link the Investigator Site File maintained in eReg to the Trial Master File.

- Follow the steps for adding participating sites in the previous slide. Ensure the NCT number and site name matches.

- Participating Site tiles will show the status of the link when viewing the Participating Sites section of the multi-site protocol.

Connection Pending
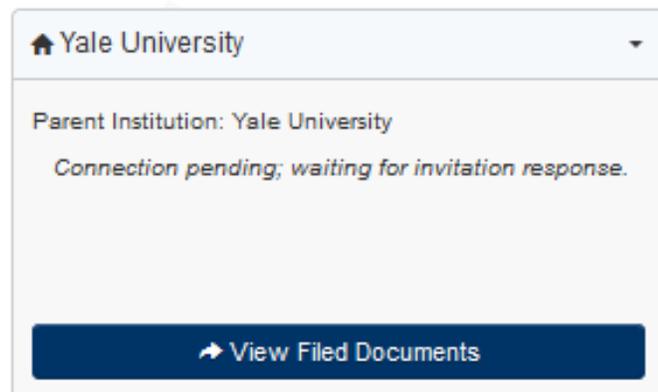
Invitation Accepted
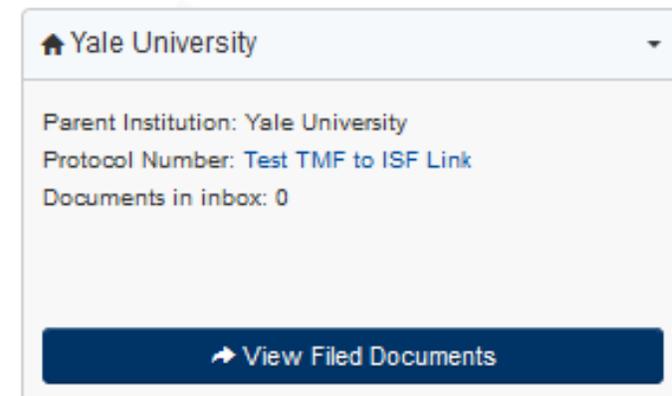
Building Protocols – Connecting to Yale ISF

- The following information can be given to Yale Site Staff to facilitate connecting the Yale ISF to the TMF.

- Regulatory Coordinators, Regulatory Managers and eReg Administrators can accept invitations to link the Yale ISF to the TMF.

- To accept the invitation:
    1. Click on the Overview Section of the ISF.
    2. Within the Multi-Site Protocol Connection tile, click the button to View Invitation.
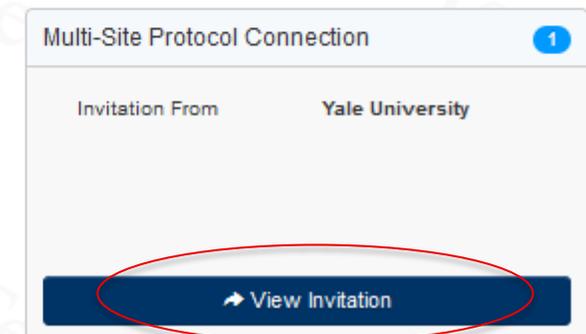
Building Protocols – Connecting to Yale ISF

- Click the Accept Invitation button on the Connections landing page.

- After the invitation is accepted, the Connections landing page will show who accepted the invitation and when it was accepted.

Building Protocols – Viewing Participating Site Files

- Participating Sites are displayed as tiles in the Participating Sites section of the record.
- Documents filed by the Yale team member responsible for maintaining the TMF including the participating sites files can be viewed by clicking View Filed Documents. YCCI eReg Support refers to this as the A side of the record.
- Documents filed by participating sites can be viewed by clicking the hyperlink following Protocol Number. Limited eReg user roles have permission to view these documents. YCCI eReg Support refers to this as the B side of the record.
  - Most users will require a Review Session to view documents filed by the Research Center (home site) and data exchange site(s). These documents are their Investigator Site Files.

Building Protocols – Document Inbox

- The Document Inbox is used to receive copies of documents from participating sites directly in eReg and, if configured, via email.

- Documents and URLs maintained within eReg, including contact credentials and organizational regulatory tracking items, can be sent directly within eReg.
  - If a member of the Yale Center for Clinical Investigation's (YCCI) monitoring team is designated as the monitor of the study, this individual can also send copies of documents.
  - Refer to *eReg Guidance Document for Sending Documents from Investigator Site File to Trial Master File* for more information related to the participating site team's processes for sending copies.

Building Protocols – Document Inbox

- Documents received in the inbox can be reviewed and filed or rejected by the Multi-Site User responsible for maintaining the TMF.
- An inbox is created for each participating site and for email, if configured.

Building Protocols – Document Inbox

- Click the download icon to review the file in the inbox.

- After reviewing the file, click Review and File or click Reject.
- When rejecting a document, a pop-up window will open to warn the user that rejecting the document will cause it to disappear from the inbox and to alert the user that the participating site will not be notified.
  - Contact the participating site staff outside of eReg to inform them that the document was rejected, provide a rationale for rejection and request an updated document, if necessary.

Building Protocols – Document Inbox

- When Review and File is clicked, a pop-up window will open.
- Indicate the file location (Section and Requirement) and update the document name, effective date and valid until date. Fields marked with an asterisk are required.
- Fields will auto-populate with information from the ISF, if applicable, and may be revised before filing in the TMF.
- Revisions are reflected in the document details within the TMF and will not impact the document details in the ISF.
- Confirm all details are correct, then click File.
- To exit out without filing the document or URL, click Cancel.
- Documents within a site-specific inbox can be filed within that site's participating site file only.
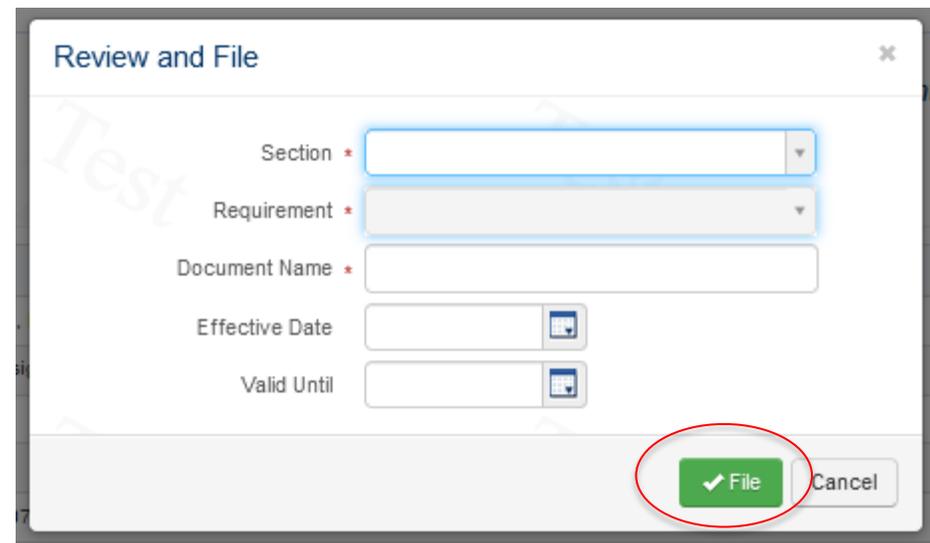
Building Protocols – Email Integration (Demo)

- The Trial Master File can be configured to allow eReg Users to email documents to it.
- Emailed documents are delivered to an inbox within the protocol record. Emailed documents are then reviewed and filed or rejected.
- All eReg Users are set up to send documents.
    - The User must send emails from the email address listed in their eReg contact card.

Building Protocols – Email Integration

- The Trial Master File(s) must be configured to receive emails.

- Select the Document Inbox from the Summary Section of the Trial Master File home page. Before the inbox is configured, you will see a message indicating it is not configured.
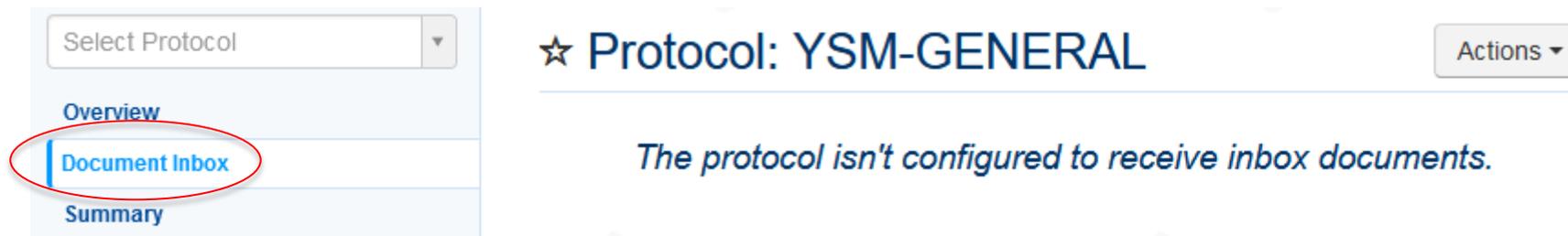
- Select Settings in the Action menu, then click Edit in the Email Settings section.
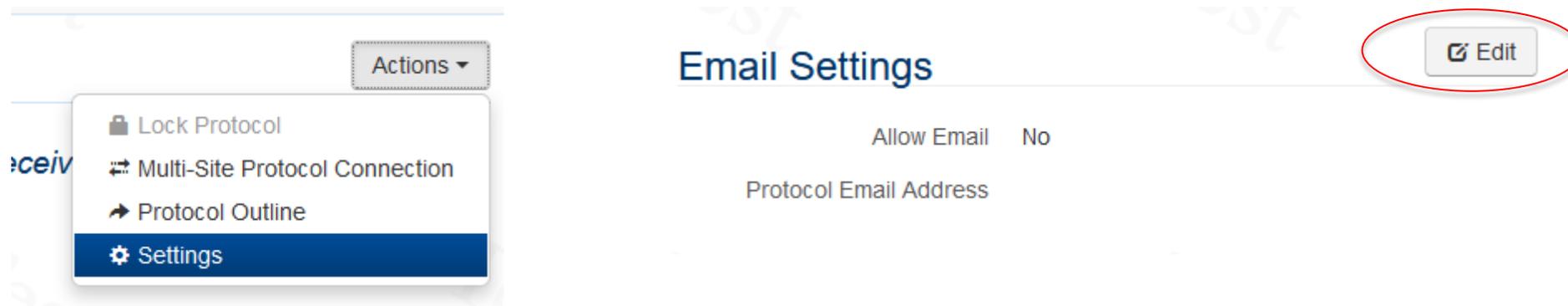
Building Protocols – Email Integration

- Toggle Allow Email setting from No to Yes, then click Save.
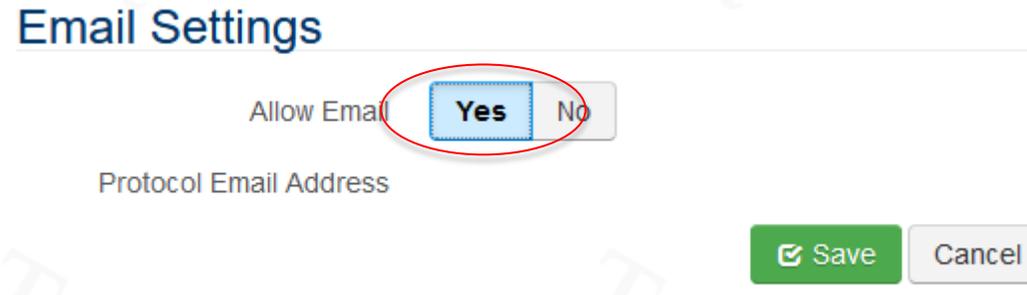
- An email address will be generated. Use the Copy button to copy the address and add it to your email contacts (or send it to a user who will be sending documents to the protocol). Only Users who are set up to Send Documents on their contact card can use this feature.

Building Protocols – Email Integration

- Once configured, documents in the email inbox can be reviewed and filed or rejected like all other documents within the inbox.

- An additional field is included when you review and file the document which allows you to select where the document or URL is filed. You may select to file within:
  - This multi-site protocol (TMF)
  - A participating site file (each site provided as an option)
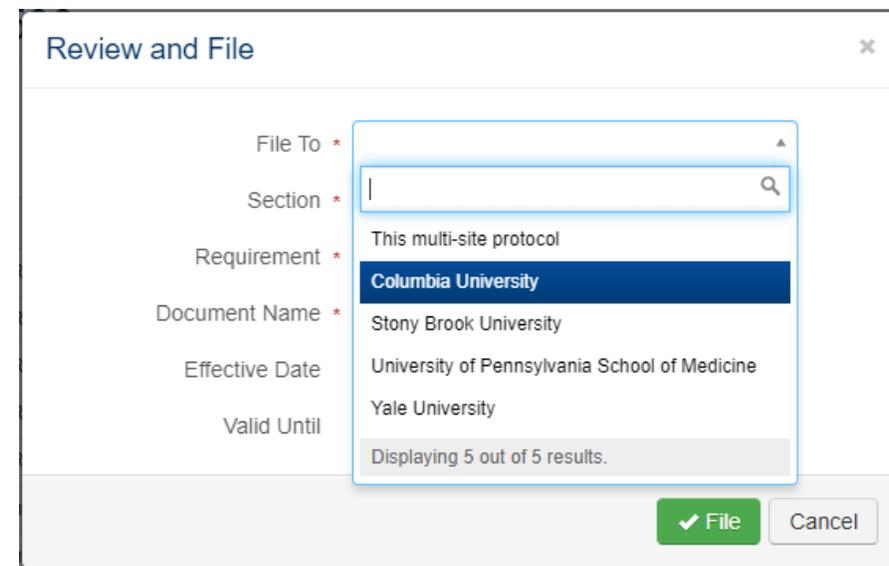
Building Protocols – Template Section and Requirements

- Regulatory templates are organized into Sections with Requirements found under each Section.
  - A section is similar to a file folder or tab within a physical paper binder
  - A requirement is similar to a document contained within that file folder or tab

Building Protocols – Protocol Outline (Demo)

- Remove sections and requirements that are not applicable to the study before the study begins when you are setting up your Trial Master File and Participating Site File(s).
  - This does not include sections/requirements in which there is nothing filed yet, however there is a possibility for future use. Consult departmental documentation requirements, if available.
- Changes to the sections and requirements are made by accessing the Protocol Outline. To do this, choose Protocol Outline from the Actions button menu.
  - You must access and change the protocol outline for the TMF and each PSF (A and B side) within the protocol record. If Affiliate Sites are logging into our instance of eReg to upload documents, the protocol outline for their ISFs must be accessed and changed by the Sponsor team as well.
  - The Yale Sponsor team cannot change the protocol outline for Data Exchange sites. Any filing requirements will need to be discussed directly with the Data Exchange site.

☆ Multi-Site Protocol: YSM-GENERAL

Actions ▾

🔒 Lock Protocol
➜ Protocol Outline
⚙ Settings

Summary

Details

📝 Edit

Building Protocols – Protocol Outline (Sections)

- To remove Sections:

  1. Navigate to "Choose Sections" within the protocol outline

  2. Use the check boxes to select and unselect Protocol Sections

  3. Select "Save" when complete

Building Protocols – Protocol Outline (Requirements)

- To remove Requirements:

  1. Select "Choose Requirements"

  2. Use the arrow functions to select and unselect requirements

  3. Select "Save" when complete

*Do not customize Requirements. If you believe you will need a Requirement that is not currently available, consult eReg Support (eReg.Support@yale.edu).

Building Protocols – Protocol Outline Changes

Some Sections and Requirements will not be applicable to every Trial Master File. Consult departmental documentation requirements, if applicable.

If the study…		
	Is an Open Label study	Remove the requirement "Unblinding Procedure" from the "Study Conduct Documents" section
	Contains safety information within an Investigator's Brochure	Remove the requirement "Package Insert(s)" from the "Investigational Product" section
	Contains safety information within a Package Insert	Remove the requirements "Investigator's Brochure" from the "Investigational Product" section

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Building Protocols – Protocol Outline Changes

Some Sections and Requirements will not be applicable to every Participating Site File. Consult departmental documentation requirements, if applicable.

If the study…		
	Is not a pediatric study	Remove the requirements "IRB-approved Assent Forms" and "IRB-approved Parental Consent Forms" from the "Consent Documents and HIPAA Authorization Forms" section
	Contains safety information within an Investigator's Brochure	Remove the requirement "Package Insert(s)" from the "Investigational Product" section
	Contains safety information within a Package Insert	Remove the requirements "Investigator's Brochure" and "Investigator's Brochure Receipt Page" from the "Investigational Product" section

Building Protocols – Required Credentials for Staff

- Required credentials for Staff are indicated within the Regulatory Template. If a credential is not available within eReg, contact eReg.Support@yale.edu to discuss.

- TMF templates do not include required credentials for staff.

- PSF templates include the following required credentials by staff role:
  - Principal Investigator and Sub-Investigator:
    - Curriculum Vitae
    - GCP Training
    - Medical License
    - Signature Sample
  - Pharmacist, Pharmacy Technician, Clinical Research Assistant, Clinical Research Coordinator, Protocol Coordinator, Regulatory Coordinator, Regulatory Manager, Research Laboratory:
    - GCP Training
    - Signature Sample
  - Research Nurse:
    - GCP Training
    - Medical License
    - Signature Sample

Building Protocols – Required Credentials for Staff

- Required credentials for Staff within the PSF templates can be modified in the Protocol Outline.
- To modify the required credentials, access the Protocol Outline and click Edit.

- Checkboxes will appear within the table for each role and credential. Uncheck or check boxes to remove or add required credentials such as International Air Transport Association (IATA) training, Human Subjects Protection Training (HSPT), etc.
- This Section can be used to communicate general training requirements to participating sites.
- Listing staff within eReg grants them access to that protocol. For this reason, most external site staff will not be listed within eReg for Affiliate Sites. Instead, credentials may be stored within the Regulatory Documents section of the participating site file.

Building Protocols – Adding Organizations (IRBs) to TMF

Adding the IRB of Record as an Organization

FDA-regulated IND Studies

- For FDA-regulated investigational new drug (IND) studies using a single IRB, add the single IRB
- If sites are choosing their IRB of record, leave blank.

FDA-regulated IDE Studies

- For FDA-regulated investigational device exemption (IDE) studies using a single IRB, add the single IRB
- If sites are choosing their IRB of record, leave blank.

Non-FDA-regulated Studies

- For non-FDA-regulated studies or for studies that are FDA-regulated but not conducted under an IND or IDE and are using a single IRB, add the single IRB
- If sites are choosing their IRB of record, leave blank.

Note: When Yale Human Research Protection Program (HRPP) authorizes your study to be reviewed by an external single IRB, list the external IRB as the IRB of record.

Building Protocols – Adding Organizations (Laboratories) to TMF

Adding Laboratories as an Organization

FDA-regulated IND Studies

- For FDA-regulated investigational new drug (IND) studies, add the sponsor-designated laboratory(-ies) noted in Box 4 of the Form FDA 1572 template provided to sites

FDA-regulated IDE Studies

- For FDA-regulated investigational device exemption (IDE) studies, add the sponsor-designated laboratory(-ies) noted in the Investigator Agreement templates(s) provided to the sites

Non-FDA-regulated Studies

- For non-FDA-regulated studies or for studies that are FDA-regulated but not conducted under an IND or IDE, add the sponsor-designated clinical laboratory(-ies), testing facilities, analytical labs, and/ or laboratories supplying efficacy data

Building Protocols – Adding Organizations to PSF

- Local site organizations will not be added as an Organization within eReg. YCCI does not maintain regulatory tracking items for most external Organizations.

- External organizations utilized exclusively by an Affiliate Site, such as local IRBs and local laboratories, are not maintained within Yale's eReg and cannot be selected by the Affiliate Site.
  - IRB Regulatory Tracking Items associated with external local IRBs will be filed in the Regulatory Documents section of the site's Participating Site File.
  - Laboratory Documents (regulatory tracking items) associated with external local laboratories will be filed in the Study Conduct Documents section of the site's Participating Site File.

- Yale-affiliated Organizations can be added to Affiliate Site's Investigator Site Files. Provide eReg Support (eReg.Support@yale.edu) with the list of Yale-affiliated Organizations to which the Affiliate Site staff will require access. Direct the Affiliate Site to add the specific organizations to their Investigator Site File during study start-up or at the time of Site Initiation.

Building Protocols – Adding Organizations

- To add organizations, from the protocol home page select:
  1. Organizations
  2. Add Organization

Building Protocols – Adding Organizations

- **Organization**: Select the IRB or Laboratory you would like to add
- **Start Date (required)**: For Single IRB: Use the date first submitted to IRB of record; For Laboratories: Use the date when the laboratory manual was finalized for Yale-affiliated laboratories; use the date that the contract with the third-party vendor was fully executed for external laboratories
- **Stop Date**: Use the date that the Organization stopped being used for the study
- **IRB?**: This will automatically populate when the Organization is selected
- **Laboratory?**: This will automatically populate when the Organization is selected

Building Protocols – Adding New Staff to eReg

- Staff members and external collaborators must have a contact record in eReg before they can be added to a protocol and an active user account before they can sign documents in eReg. External collaborators cannot sign documents in eReg.

- The User Access Request Form can be located on the YCCI eReg website

Requesting Access	Completing Training	Account Creation	Adding Staff to Protocols
• Staff member will complete a User Access Request Form with information about their name, role and study tasks	• Staff member will be assigned the appropriate training based on the information provided. This training must be completed and current credentials filed before moving on to the next step.	• eReg Support Staff will use the information provided to create an account with the correct User Role(s), Staff Role(s), and granting the staff member with the correct access and permissions.	• Staff member will now have an eReg account and can be added to any protocols with which they are associated.

Building Protocols – Adding Staff to Protocols

- Principal Investigators, Yale Regulatory Managers, Yale Regulatory Coordinators, those with Multi-site Access, and select Administrative roles can add staff members to protocols.

- To add staff, from the protocol home page select:

  1. Staff in the left-hand (Section) menu

  2. Add Staff

Building Protocols – Adding Staff to Protocols

- **Contact:** Select the study staff member you want to add.
- **Protocol Staff Role(s):** Select one of the Protocol Staff Role(s) designated to that individual in their contact record.
- **Start Date:** Enter the date you want this staff person to gain access to the protocol record.
- **Stop Date:** Enter the date you no longer want this staff person to have access to the protocol record.
- **Access Roles:** Leave blank.
  - When adding staff to the TMF, the access roles are not requested.

Maintaining eReg Binder

File Management

File Management – Adding Documents

- To file a protocol document, first navigate to the section and requirement where you would like to upload your document and select "New Document".
- Note the following:
  - Any document with a file name over 255 characters will become corrupt upon download. Please shorten file name before upload and consider characters within your file name from the file folder location.
  - Limit uploading zip files as they can cause issues during review session downloads due to the character limits outlined above. Zip files cannot be routed for electronic signature.

File Management – Adding Documents to TMF

- **Requirement**: Automatically populates
- **File**: Select the file you wish to upload. File name should follow the suggested naming conventions.
- **Document Name**: Automatically populates with the file name. Document name does not need to be modified if file name follows the suggested naming conventions.
- **Effective Date**: Date the document went into effect
- **Valid Until**: Date after which the document is no longer valid
  - Date ranges in eReg are based on midnight.
- **Comments**: Any additional information
- **Signature requirement**:
  - "Electronic Signature" to route the document within eReg
  - "Wet Signature" if the document is wet ink signed or electronically signed outside of eReg
  - "None" if no signature is needed
  - Note: This field is not available for Participating Site Files
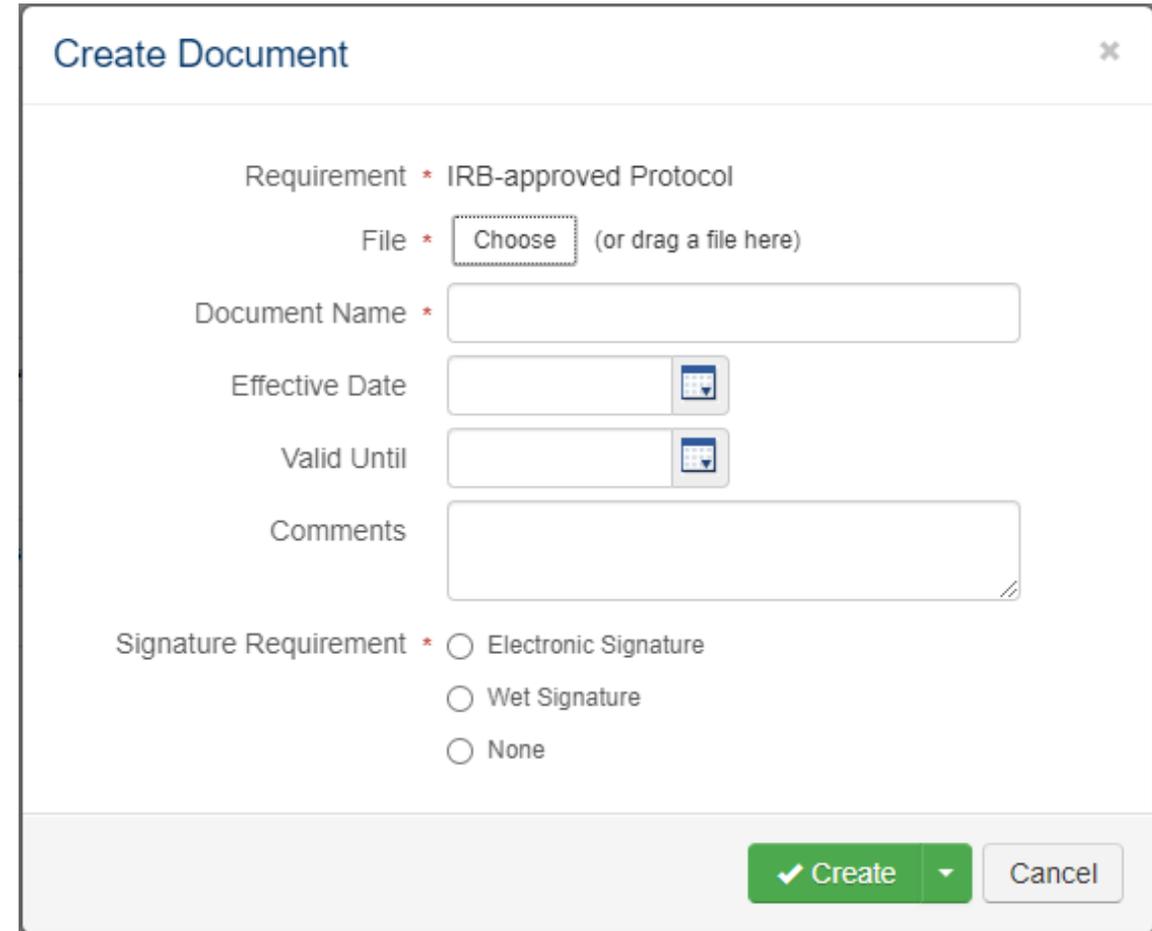
Create Document ✕

Requirement * IRB-approved Protocol

File * [Choose] (or drag a file here)

Document Name * [   ]

Effective Date [   ] 📅

Valid Until [   ] 📅

Comments [   ]

Signature Requirement * ○ Electronic Signature
○ Wet Signature
○ None

[✔ Create ▾] [Cancel]

File Management – Adding Documents to PSF

- **Requirement**: Automatically populates
- **File**: Select the file you wish to upload. File name should follow the suggested naming conventions.
- **Document Name**: Automatically populates with the file name. Document name does not need to be modified if file name follows the suggested naming conventions.
- **Effective Date**: Date that the document went into effect
- **Valid Until**: Date after which the document is no longer valid
  - Date ranges in eReg are based on midnight.
  - A document with a Valid Until date of 13 Nov 2023 would be valid until 11:59 PM on 12 Nov 2023.
  - When entering an expiration date, enter the expiration date + one day

File Management – Adding Documents (Dates)

- Not every document will have an Effective Date
  - If this is the case, use 01 Jan 1900 as the effective date
  - 01 Jan 1900 can be used as a placeholder date when the effective date will be the eReg signature date
- Some documents do not have a Valid Until date until the next version is available
  - If this is the case, leave Valid Until date blank until the new version of the document is available. Then change the Valid Until date for the prior version to equal the Effective Date of the new version.
  - Dates ranges in eReg are based upon midnight.

Effective Date   01 Jan 1900

Protocol_v1.0_2021.05.12.pdf

Details   Edit

File   Protocol_v1.0_2021.05.12.pdf
Effective Date   12 May 2021
Valid Until   12 Sep 2021
Comments
Signature Requirement   None

Related Documents (0) ›   Add Related Document

Protocol_v2.0_2021.09.12.pdf

Details   Edit

File   Protocol_v2.0_2021.09.12.pdf
Effective Date   12 Sep 2021
Valid Until
Comments
Signature Requirement   None

Related Documents (1) ›   Add Related Document

File Management – Version Control

- Version control typically includes a version number and version date.
- Update the version number when revising a document that was previously approved by the IRB or designated as a final version.
- Update the version date when a document is revised by any user until such time that the document is approved to proceed by the FDA, approved by the IRB (sponsor level, if applicable) or designated as a final version.
- Version dates are typically entered as effective dates.
- In certain instances, the version date of a document may not align with the effective date in eReg.

Document Type	Effective Date
Consent Documents and HIPAA Authorization Forms formatted for site use	IRB approval date
Sponsor Consent Templates	Version date of the document
Paper Delegation of Authority Log	Date the study was activated
Documents approved by the IRB such as protocols, Investigator's Brochures, Package Inserts, Instructions for Use, etc.	IRB approval date or IRB acknowledgement date
IRB and Other Committee Approval or Acknowledgement Letters	Date of the letter
Regulatory Documents such as Financial Disclosure Forms, Form FDA 1572s, Investigator Agreements, Protocol Signature Pages, Investigator's Brochure receipt pages, etc.	Date the document is signed
Staff Training	Date the training was conducted/ completed by the staff member
Study Conduct Documents	Version date of the document
Email or Telephone Correspondence	Date of first communication on the specific topic
Notes to File	Version date of the document
Study Correspondence	Date included on memo, letter, newsletter, etc.
Study Logs	Date the study was activated or date the log was put into effect for use

File Management – Version Control

- Not all documents will include a valid until (expiration) date.

- If a document does not include an effective date, version date, and valid until date, a date must still be entered in eReg for either effective date or valid until date.

- Use 01 Jan 1900 as an effective date for documents without any version control.

Document Type	Valid Until Date
Consent Documents and HIPAA Authorization Forms formatted for site use	IRB expiration date + one day, if applicable Reminder: Date ranges in eReg are based on midnight
Documents approved by the IRB such as protocols, Investigator's Brochures, Package Inserts, Instructions for Use, etc.	IRB expiration date + one day, if applicable Reminder: Date ranges in eReg are based on midnight
Other documents	Valid until or expiration date + one day noted within the document

File Management – Sending Copies

- When the ISF is also maintained in eReg, the Regulatory Coordinator, Regulatory Manager or a YCCI Reviewer (Monitor) will send copies of regulatory and essential documents from the ISF directly to the TMF within eReg.

- To do this, staff navigate to the document and click the hyperlink to view the details. Click Send Copy. Confirm details on the pop-up screen then click Send.

- Refer to the *eReg Guidance Document for Sending Document from ISF to TMF* for more information.

File Management – Adding Related Documents

- Related documents can be added to single documents and should be used to tie documents together like a paper clip.

- This functionality is not available in the Participating Site File maintained by the sponsor team (A side).

- Example: For IRB and other committee approvals:
  - Main file = Approval Letter
  - Related documents = Submission documents, Acknowledgements of Receipt, Correspondence, Approval documents not filed elsewhere, etc.
    - Note: Related documents cannot be routed for electronic signature. Copies of related documents cannot be sent to a Multi-Site protocol maintained in eReg.

File Management – Adding Related Documents in TMF

- Utilize the related documents filing feature for the following document types within the TMF:
  - IRB approvals letters for sponsor-level submissions
  - IRB acknowledgement letters for sponsor-level submissions
  - FDA submissions
  - Training Records
  - Data and Safety Monitoring Board/ Committee decision letters
  - External Safety Reports
  - Sponsor Correspondence (all types)
  - Summary of Changes and Protocol Clarification Letters
- Refer to the *eReg Guidance Document for Trial Master File Regulatory Templates* for more information.

File Management – Adding New Versions in TMF

- If there is more than one version of the same document, they will be stacked (added as a new version on top of the existing version, not as a new document). This functionality is not available in the Participating Site File maintained by the sponsor team (A side).

Examples of Documents to Stack

- Protocols
- Investigator's Brochures/ Instructions for Use
- Sponsor Templates for Consents and Patient Facing Materials
- Staff Credentials
- Study Manuals and Conduct Documents

Examples of Documents to File Separately

- IRB approval letters
- Correspondence
- DSMB Decision Letters
- FDA Serial Submissions

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File Management – Adding New Versions in TMF

- To stack a document or URL, select "New Version"
- Choose the format for the new version: Document or URL

File Management – Adding New Versions in TMF

- When viewing a Section, click the link for a Requirement (document) within the Section to see all versions of that Requirement.

- On the Versions page, you can view the details, related documents, and signature status for each stacked version.

- Signature Status details are not available in the Participating Site File.

File Management – Naming Conventions

- Follow naming convention guidelines set forth by YCCI eReg Support or your department for the File and Document Name. YCCI eReg Support naming conventions are available in the *eReg Guidance Document for Trial Master File Regulatory Templates* found on the [YCCI eReg website](#).

- It is best practice to utilize naming conventions which include a brief description of the document, who or what it associates to, and version control to include version number and version date.
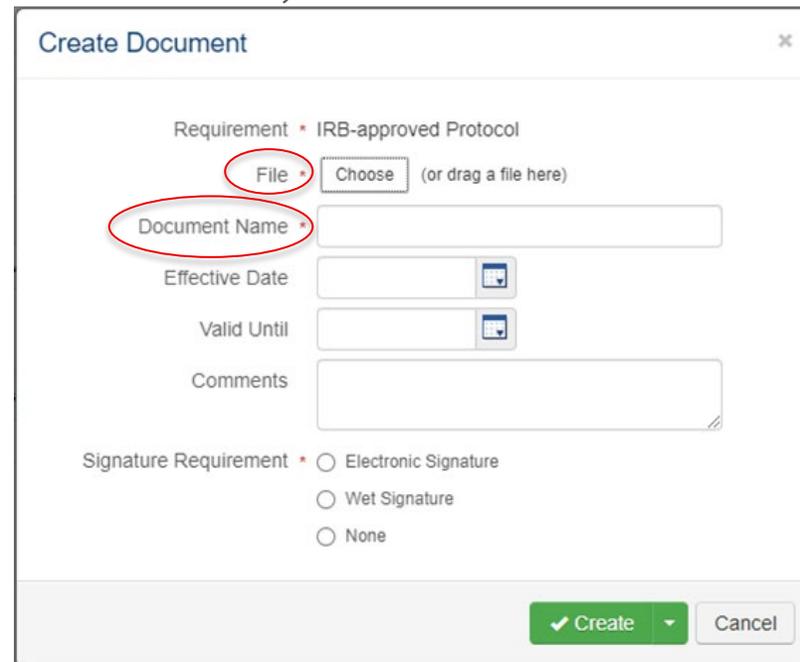
File Management – Naming Conventions

- Sample YCCI eReg Support naming conventions from eReg Guidance Document:

Document Type	Naming Convention
Clinical Study Report	Clinical Study Report_yyyy.mm.dd
Instructions for Use	[Device Short Name] Instructions for Use_v[#]_yyyy.mm.dd
Investigator's Brochure	IB for [Drug Short Name]_v[#]_yyyy.mm.dd
Data Safety Monitoring Board Charter	DSMB Charter_v[#]_yyyy.mm.dd
Sponsor Consent Template	ICF Sponsor Template_v[#]_yyyy.mm.dd
Certificate of Analysis for Investigational Product	IP Certificate of Analysis_yyyy.mm.dd
Copy of Label submitted to FDA in initial IND application	IP Label_yyyy.mm.dd
Lab Director CV	Last Name, First Name_CV_exp yyyy.mm.dd
Laboratory Normal Ranges	[Name of Lab]_Normal Ranges_yyyy.mm.dd
Serial Submission to FDA	IND Submission_SN[XXXX]_yyyy.mm.dd
FDA OK to Proceed Letter	FDA OK to Proceed_yyyy.mm.dd
Transfer of Regulatory Obligations	Transfer of Regulatory Obligations_yyyy.mm.dd
Sponsor Staff Protocol Training	Last Name, First Initial_Training Attestation_v[#]_yyyy.mm.dd
External Safety Reports	INDSR_[Tracking Number]_yyyy.mm.dd
UADE Safety Reports	UADE Safety Report_yyyy.mm.dd
eCRF Guidelines	eCRF Guideline_v[#]_yyyy.mm.dd
Third Party Vendor Contracts/ Agreements	[Vendor Name] Contract_yyyy.mm.dd
Statistical Analysis Plan	SAP_v[#]_yyyy.mm.dd
Specimen Requisition Form	[Biospecimen Type] Requisition Form_v[#]_yyyy.mm.dd
Notes To File (NTF)	NTF_[Brief Description]_yyyy.mm.dd
Trial Master File Plan	TMF Plan_v[#]_yyyy.mm.dd

File Management – Signature Requirements in TMF

- Signature requirements apply to contact credential documents and protocol documents.
- URLs and regulatory tracking items cannot be signed.
- Electronic signatures cannot be obtained in Participating Site Files maintained by the sponsor team (A side) or Affiliate Sites (B side) for any document type.
- eReg includes three signature requirement options:
  - Electronic Signature with three signature meanings:
    - Approved
    - Read and Understood
    - Reviewed
  - Wet Signature
  - None
- Refer to the *eReg Guidance Document for Electronic Signatures* found on the YCCI eReg website for more information.

File Management – Signature Requirements

Signature Requirement	Use	Signature Placement
Electronic Signature	Select for documents to be routed for electronic signature within eReg.	Default Location or Custom Location*
Wet Signature	Select for documents signed in wet ink and/ or electronically signed outside of the eReg system. This requirement may be selected for documents including but not limited to: • Investigational Product/ Device Documents • Other documents that have been digitally signed outside of eReg (using 21 CFR Part 11 compliant software, if necessary) • Transfer of Regulatory Obligations (TORO)	N/A
None	Select for documents that are not signed and will not be routed for electronic signature within eReg.	N/A

* Default Location (appended to the last page of the document) must be used for Staff Training requirements and for documents requiring multiple signers. At this time, Custom Location can only be used for FDA documents (ex. Forms FDA 1571 and 1572). All information must be entered into the FDA forms before being uploaded to eReg and routed for placed signature.

File Management – Electronic Signature Meaning and Suggested Use

Signature Meaning	Documents	Signature Placement	Due Date
Approved	Curriculum Vitae (CV)	Default location	
	Data Management Plan	Default location	
	Investigator's Brochure	Default location	
	Instructions for Use	Default location	
	Notes To File (NTF)	Default location	
	Sponsor Specific Standard Operating Procedures (SOPs)	Default location	
Read and Understood	Protocol	Default location	Ensure protocol training is obtained before the study staff person participates in the conduct of the study.
	Sponsor Team Training Documentation	Default location	Ensure training is documented before the sponsor team member begins work on the study.
	Other Protocol Specific or System Training	Default location	Ensure training is documented before the sponsor team member uses the system.
Reviewed	Investigator's Brochure Receipt Page	Default location	Contemporaneous to receipt of the Investigator's Brochure.
	Protocol Signature Page	Default location	Contemporaneous to the receipt of the protocol.
	Safety Reports	Default location	Contemporaneous to notification of the safety event.
	SAE Reports	Default location	Contemporaneous to notification of the safety event.

File Management – Adding Electronic Signatures

- **Default Location:** Signature manifestation is appended to the end of the document.
- **Choose Location for Signature Placement**: If you want to apply the electronic signature to a designated location on a form, you can choose to place the signature when you set it up for routing.
  - You can choose a signature placement location instead of using the default placement location only when:
    - the document is a protocol document that is a PDF,
    - it is being signed electronically,
    - one signer is specified, and
    - a signature meaning has been selected for the document.
  - When these criteria are met, the Choose Location button that was view-only changes to active in the Create Document window.

- To specify the Signature Placement location for a New Document:
  1. Locate the area of the document where you want to place the signature.
  2. Adjust the text box until it appears how you want it. You can move it around in the area and change its height and width.

     If you want to remove the box from where you placed it, click the X to delete it.
  3. When the box is where you want it to appear on the signed document, click Save Location to return to the Create Document window.

File Management – Editing Custom Location Electronic Signatures

- How to edit the Location for a Placed Signature on an existing document
  - You can change the location of a placed signature on a document <u>before</u> it is signed. You cannot change the location after the document is signed.
  - View the Versions page for the document. If you've already specified a signature location, you'll see "(placed signature)" in the Electronic Signature Routing section.

  - Click on the link "[Name] needs to electronically sign (placed signature)" to see Electronic Signature Details. Click Choose Location to specify a different location by following the workflow outlined in the Adding Electronic Signatures to Custom Location (previous slide).
  - After you've chosen a new location, click Save.

Maintaining eReg Binder

Locking Completed Studies

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Locking Completed Studies – Process for TMF

- To lock a TMF, Multi-Site Access Users, Regulatory Managers, Regulatory Coordinators, and Administrators can navigate to the protocol and select "Lock Protocol" from the Actions dropdown.
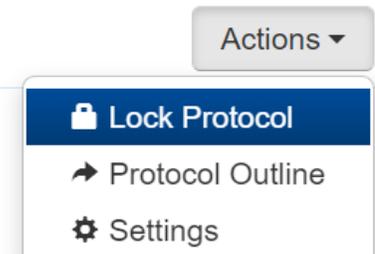
- After a study has been locked, a lock symbol will appear in the header, indicating that the study cannot be edited. If a study must be unlocked, reach out to the YCCI eReg Support Team with a valid reason (eReg.Support@yale.edu).
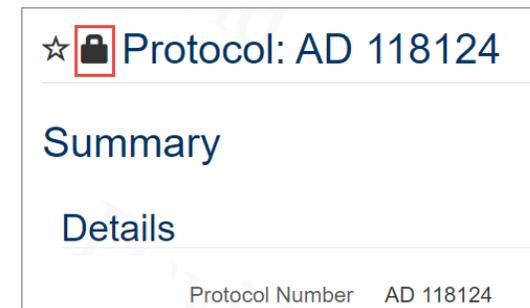
Locking Completed Studies – Process for PSF

- To lock a PSF maintained by the sponsor team (A side), Multi-Site Access Users and Administrators can navigate to the participating site file tile and select "Lock Participating Site" from the dropdown button.

- After a PSF has been locked, text will appear in the tile indicating that the site file is locked and cannot be edited. If a PSF must be unlocked, reach out to the YCCI eReg Support Team with a valid reason (eReg.Support@yale.edu).

Setting Up eReg for Use by External Monitors and Auditors

Review Sessions

YCCI Yale Center for Clinical Investigation

Review Sessions – Access Request (Demo)

Submit eReg Sponsor Account Request Form

- Monitors, Auditors and Inspectors will be required to take eReg training in Advarra University prior to account activation.
- Ensure YCCI eReg Support staff have sufficient time to coordinate training and access for external reviewers

Set up Review Session

- Create one review session per person.
- If you have multiple reviewers, you'll need to set up a review session for each reviewer.
- Date ranges in eReg are based on midnight. If a reviewer is granted access September 30 – October 1, the access will terminate at midnight on October 1. To ensure access through October 1, select an end date of October 2.

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Review Sessions – Create a Review Session

- Review Sessions can be configured for Trial Master Files.
- On the Review Sessions landing page, click New Review Session to open the Create Review Session window.

If both a Start Date and Stop Date are entered for the review session, the values must be unique. A review session can't be set up to start and stop on the same day.

Review Sessions – Customize Review Session

- If the reviewer should only review select documents, you can customize the sections and requirements available for review. If the reviewer needs to review the complete eReg binder, you do not need to customize the review session.

- To customize sections available for review, click the Choose Sections button and clear the checkboxes in front of the sections you do not want the reviewer to see in this review session.

- SOPs can be added to the review session by clicking Choose Sections.
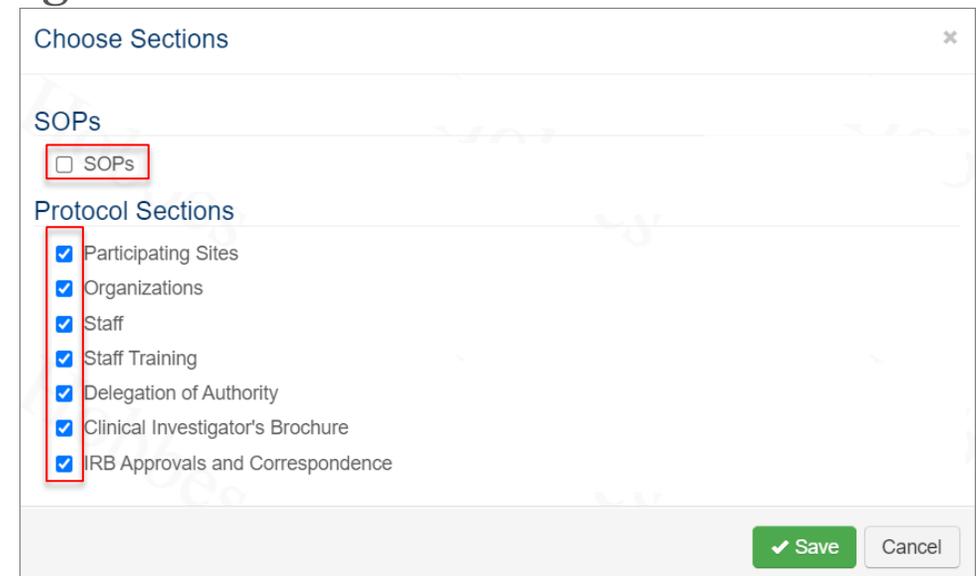
Review Sessions – Customize Review Session

- If the reviewer should only review select Participating Site File documents, you can choose the participating sites available for review. To do this, click the Choose Participating Sites button.

- Clear the checkboxes in front of the sites you do not want the reviewer to see in this review session. Click Save.

Review Sessions – Customize Review Session

- Click the Choose Requirements button in each section to configure which requirements you want to be visible to the reviewer during the review session.

- All requirements within a section are selected by default to allow the reviewer to see all the regulatory and essential documents housed in the eReg Binder. In most cases, you would grant access to the entire eReg Binder for review sessions.

- To limit the requirements (and therefore the documents) the reviewer has access to, clear the checkboxes next to any requirements that you don't want to appear in the review session. Then, click Save.

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Review Sessions – Customize Review Session

- Continue to configure the information and documents available to the reviewer in each section as needed.
- When finished:
  - Choose Back to Review Session Configuration from the Actions button menu.

Review Sessions – Review Session Features

- Through a review session, the reviewer can download all documents in the binder. This option is available in the Action Menu of a review session.

- Copies of documents cannot be sent within a Review Session. External Reviewers do not have the ability to send copies of documents from an ISF to a connected TMF in eReg.

Closing Statements

Closing Statements – Advarra University/Learning Resources

eReg Learning Resources

Advarra University http://university.advarra.com

Learning Portal in eReg
    -From the main page, click on the Rocket Icon or the Help option under your name to find the "Learning Portal"
    -Use the Table of Contents or the Search Bar to find topics

Link to YCCI website from eReg
    -From the main page, click on the Rocket Icon or the Help option under your name to find the YCCI eReg
    website link

Guidance documents are available on the YCCI eReg website.

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Closing Statements – YCCI eReg Support Staff

- If you have any further questions about the eReg system, please reach out to:
  - eReg Support (eReg.Support@yale.edu)

- If you have any further questions about maintaining documents, please reach out to:
  - Erica Rocco, Regulatory Project Manager (erica.rocco@yale.edu)