Procedures

The IRB is committed to making the submission process as smooth as possible. In this section, you will find definitions, explanations and procedures for submitting an application and any other form that may be required during the course of a study.

If you have any questions, please contact us at irbora@unmc.edu

- Adverse Event Reporting
- ClinicalTrials.gov (CT.gov)
- Emergency Treatment
- Exempt Studies
- Incidents (Non-compliance/Problems)
- Protocol Deviations
- Submission Process

Adverse Event Reporting

Adverse Events (AEs)

An Adverse Event is defined by the NIH as: Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

The IRB requires submission of an AE report form when the event is unexpected and related/possibly related to the research. Adverse events occurring on a study which satisfy these criteria must be submitted to the IRB within the timeline specified in the policy. Any death, which occurs while the subject is being treated on protocol or occurs within 30 days of completing research related interventions, must be reported immediately if it meets the reporting criteria.

For more information, please refer to HRPP policy 8.1

AEs will be submitted through the RSS system.

External Adverse Events

External Adverse Events are defined as: adverse events that occur at a site under external IRB oversight. External AEs are not reported to the IRB unless they require a change in protocol or revision of the consent document. These are not reported on an Adverse Event report form. The external AE report (i.e., IND Safety Report) is used as justification for the required changes.

External Adverse Device Effects (UADEs)

Unanticipated Adverse Device Effects (UADEs) are defined as: Unanticipated adverse device effect means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

External AEs for device studies must be reported to the IRB (in no case no later than 5 business days following PI notification from the sponsor that the event occurred) in accordance the requirements of 21 CFR 812.150(b)(1).

The PI should submit the report received from the sponsor along with any required Request for Change.

Once the status of a study is changed to “completed,” the IRB will no longer accept external UADE reports except under circumstances where the report involves important new risk information.

For more information, please refer to HRPP policy 8.1

For any questions, please email irbora@unmc.edu

ClinicalTrials.gov (CT.gov)

Check back to this page for more updates regarding clinicaltrials.gov information.

Please contact oract.gov@unmc.edu for more information.

When requesting a new user account for ClinicalTrials.gov, please provide the following information:

- Preferred user name
- Institutional email address or, if none, other email address
- Office phone number

Once the account is created, ClinicalTrials.gov will send an email with login information.

> Note: For Student Principal Investigators, if your research study will be registered on ClinicalTrials.gov, please list your Faculty Advisor as the Responsible Party and yourself as Record Owner.

CITI TRAINING COURSE FOR CLINICALTRIALS.GOV

A new CITI training course is available to UNMC and UNO learners that provides video instructions for registering, uploading documents, and submitting results in ClinicalTrials.gov. Currently optional, the course is highly recommended as a guide to investigators new to ClinicalTrials.gov requirements and to experienced investigators needing a refresher.

- Login into your UNMC or UNO CITI account
- Scroll down to 'Add a Course'
- Click the box for Protocol Registration and Results Summary Disclosure in ClinicalTrials.gov
- Click 'Next'.

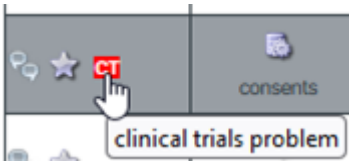
When you have successfully completed the course, please email a copy of the Completion Certificate to oract.gov@unmc.edu.

CLINICALTRIALS.GOV ICONS IN RSS

IRB protocols that are investigator-initiated and registered on ClinicalTrials.gov with an NCT# will now be denoted by an icon in RSS.

A green icon means no problems are currently identified by ClinicalTrials.gov on the record associated with the study.

A red icon means ClinicalTrials.gov has identified problems on the associated record.



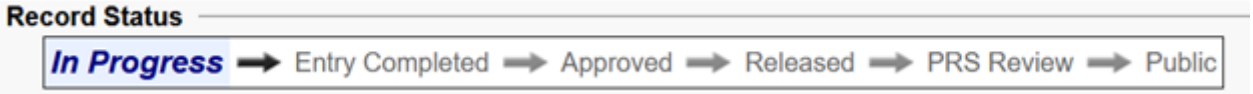
If your study has a red icon, please login at https://register.clinicaltrials.gov to correct the problem(s). Icons are updated daily, Monday-Friday, so once problems are resolved, the icon will be green after the next daily update. If you have difficulty correcting a problem in https://register.clinicaltrials.gov, please contact oract.gov@unmc.edu for assistance.

Outstanding problems with the ClinicalTrials.gov record may delay the review and approval of IRB submissions. Please ensure all problem records are addressed as soon as possible (UNMC HRPP Policy 1.29).

PROCESS FOR UPDATING A RECORD

Whenever a ClinicalTrials.gov record is updated, the process must be completed by approving and releasing the update.

Steps for completing an update of any type are displayed in the “Record Status” at the top of the record.

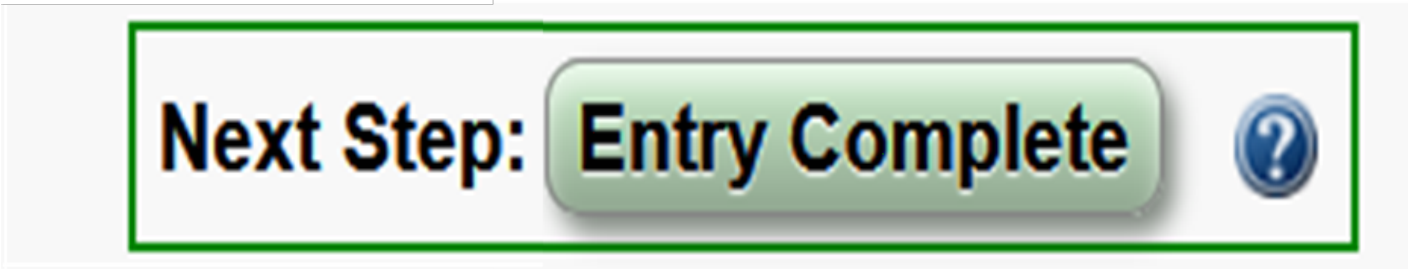


The “Next Step” box is displayed immediately below which describes the next action needed.

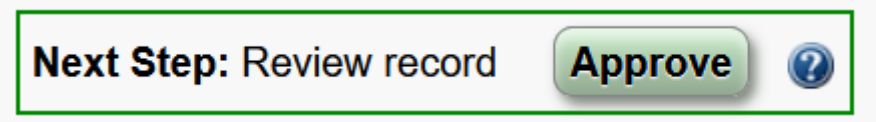
Any problems with the update are listed in the “Next Step” box and may include:

- Correct Error(s)
- Enter Results
- Finish Protocol/Documents/Results section
- Address Review Comments

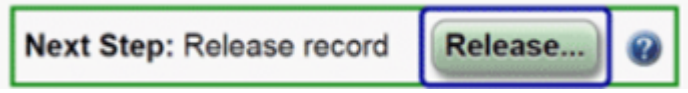
Once the update problems are resolved, the next step is to click the “Entry Complete” button:



The following step is to review the update, then click the “Approve” button:

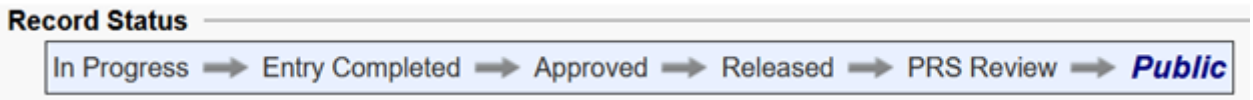


The last step is to click the “Release” button if you are the Responsible Party for the record:



If you are the Record Owner, this “Next Step” box will be displayed, and the Responsible Party will need to login and release the update.

When any problems with the update are resolved and the update has passed PRS review, the update is released to the public ClinicalTrials.gov site.



All the steps on the “Record Status” will be highlighted in blue.

POSTING CONSENT FORMS

For any clinical trial conducted or supported by a federal agency or department or agency, Federal Regulations require the awardee of a grant to post one IRB approved informed consent form used to enroll subjects on a publicly available Federal Web site.

“Clinical trial” means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

The PI must post:

- Only if the organization (UNMC, Nebraska Medicine, UNO or CHMC) is the lead site or grantee organization.
- Only clinical trials (defined above). As a general rule, if you reported to clinicaltrials.gov then you will also have to post the consent form.
- Only if conducted or supported by a Federal department or agency.

The PI only needs to post **ONE** consent form used to enroll subjects anytime during the course of the study.

The consent form must be posted no later than 30 days after the last subject is enrolled.

If your study is utilizes the Clinical Trials Monitoring System (CTMS) you will receive notification when your last subject is enrolled. The notification includes instructions about the requirement, and how to post to clinicaltrials.gov.

If your study does not utilize CTMS it is your responsibility to track subject enrollment, and post no later than 30 days after the last subject is enrolled.

Specific instructions on how to register with ClinicalTrials.gov and upload documents can be found here.

Emergency Treatment

The contact list for Emergency Treatment authorization can be found here in RSS.

Under certain circumstances, a physician may treat a patient with an investigational (non-FDA approved) drug, biologic or device, or treat a patient utilizing a non-IRB approved protocol; Pursuant to FDA regulations, the patient must be suffering from a serious, life-threatening or debilitating illness for which there is no satisfactory treatment alternative(s) and there must not be sufficient time to obtain full IRB review and approval. Emergency treatment as defined here is not research. The FDA regulations do not provide for expedited IRB approval in emergency situations.

UNMC/Nebraska Medicine policy requires the IRB be notified prior to such use, by contacting the IRB office. This notification is not IRB approval. The IRB will only state it is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.102(d), 21 CFR 56.104(c), and the criteria in HRPP 6.4 Emergency Use of a Test Article, section 5.0 of the full policy.

The investigator is still required to obtain informed consent of the patient or the patient's legally authorized representative. The consent form must contain appropriate elements structured to reflect that consent is for treatment purposes as opposed to research. View a sample Consent Form for Emergency Treatment

A useful guide can be found here: Emergency Use vs Expanded Access

The UNMC Emergency Use of a Test Article Report form can be found in RSS and a signed copy of the consent form must be submitted to the IRB within 5 business days following the treatment.

Exempt Studies

It is understood this project will be conducted in full accordance with all applicable HRPP Policies. It is also understood that the ORA will be immediately notified of any proposed changes for your research project that:

1. Affect the risk-benefit relationship of the research
2. Pose new risks which are greater than minimal
3. Constitute a new risk to privacy or confidentiality
4. Involve sensitive topics (including but not limited to personal aspects of the subjects behavior, life experiences or attitudes)
5. Involve deception
6. Target a vulnerable population
7. Include prisoners or children
8. Otherwise suggest loss of the exempt status of the research.

No changes to exempt studies are required to be submitted for review, which is outlined in your approval letter. If you feel a change is warranted, please contact our office utilizing the message portal of the application in question.

You are encouraged to contact the ORA to discuss whether changes to exempt research requires review by the IRB or please view HRPP policy 2.6 (Exempt Research).

Incidents (Non-compliance/Problems)

Per HRPP policy 8.4 non-compliance (NC) involving the PI and/or study personnel must be promptly reported to the IRB. This non-compliance could involve failure to comply with the Federal Regulations related to the protection of human subjects of research, HRPP policies, or the requirements/determinations of the IRB.

Research related problems are incidents that do not involve NC on the part of the PI and/or study personnel. These occur during the course of the study and may include things such as: subject incorrectly adhering to instructions (taking a wrong dosage of study drug), research records being stolen/lost, etc. Research related problems must also be promptly reported to the IRB.

NC and problems are reported to the IRB by submission of an Incident Report Form. The Incident Report form is located in the Forms section of RSS. The PI is responsible for ensuring that the required reports are submitted promptly following discovery of the incident in accordance with HRPP policy 8.4.

If you have any questions regarding this submission process, please contact the IRB Office at irbora@unmc.edu

Protocol Deviations

A Single Subject Protocol deviation is a change in an IRB-approved protocol which is permitted for an individual subject when it is in the best interest of that subject and/or is necessary for research purposes (e.g., data completion). Protocol deviations are classified as either “minor” or “more than minor.” Once the form is received, the deviation will be reviewed and processed by the IRB. Deviations may be approved in one of two ways:

1. Deviations that are ***minor*** are eligible for expedited review under the provisions of HHS regulations at 45 CFR 46.110(b)(2) and FDA regulations at 21 CFR 56.110(b)(2), as applicable.
2. Deviations that are ***more than minor*** do not qualify for expedited review and therefore must be reviewed by the full IRB.

Once the deviation is approved, an approval letter for the Single Subject Protocol Deviation will be attached to the electronic IRB application. The PI and Lead Coordinator will be notified via email when this occurs.

To obtain Single Subject Protocol Deviation approval, a Single Subject Protocol Deviation Request must be submitted PRIOR to the implementation of the deviation. The instructions for submission are below:

RSS Studies & Existing Paper Format Studies

The Single Subject Deviation form can be created by pulling up the protocol in RSS. The 'Forms' section will be found in the left-side menu. When clicking on 'Forms' a list will appear allowing you to choose the 'single subject protocol deviation request'. Please follow the instructions provided to complete the form and once competed the PI will electronically sign and click 'SUBMIT'.

If you have any questions regarding this submission process, please contact the IRB Office at irbora@unmc.edu.

Submission Process

Full Board Review (initial submission)

Investigators will be notified of the assigned IRB# by email. Applications for Full Board Review will be reviewed at the next possible IRB meeting. Submission Deadlines can be found here.

These documents must also be attached in the "ADD DOCUMENTS" section of the online application at the time of electronic submission:

New Submissions (Initial)

1. Subject Recruitment Material (as applicable)
2. External study site approval letters (as applicable)
3. Full protocol (as applicable)
4. Investigator's Brochure (as applicable)
5. Grant application (as applicable)
6. Clinical Trial Master Matrix (as applicable)
7. Other relevant material (e.g. surveys) (as applicable)

Tabled — Re-Submissions

1. Investigator's response letter
2. Other revised materials (as applicable)

Expedited Review (initial submission)

Certain studies involving no more than minimal risk may qualify for expedited review status under 45 CFR 46.110 or 21 CFR 56.110. View a list of categories which may qualify for expedited review.

Expedited review of **new** protocols are handled through the electronic submission only. New submissions eligible for expedited review will be reviewed by the IRB Analyst with appropriate confirmation by the Executive Chair/designee and the investigator will be informed of the IRB's decision by email.

Exempt Protocols (initial submission)

Research activities in which the only involvement of human subjects will be in one or more of the categories specified by 45 CFR 46.101(b) are exempt from the requirements of 45 CFR 46. The exempt categories do not, however, apply to research involving deception of subjects, sensitive behavioral research, or to research involving pregnant women, prisoners, individuals who are decisionally impaired and other subject populations determined to be vulnerable.

Reviews of new Exempt protocols are handled through the electronic submission only. New Exempt submissions will be reviewed by a member of the Office of Regulatory Affairs (ORA) staff and the investigator will be informed of the ORA's decision by email.

Request for Change

Any proposed change in a research activity must be reviewed and approved by the IRB prior to implementation **except** when: 1) a change is necessary to eliminate an apparent immediate hazard to the subject(s), or 2) a subject needs to be advised immediately of significant new information. Administrative changes do not require IRB review and can, accordingly, be approved by ORA.

For studies submitted in electronic system, follow these steps:

- Reset the application to Edit
- Make changes to the IRB application and click SAVE
- Revise consent documents (if applicable) and click COMPLETE
- Upload any applicable documents using the Add Document function
- Click CHANGE REQUEST on the left-side menu and complete
- Sign the application (PI)
- Click SUBMIT

For Studies NOT Submitted in Electronic System, follow these steps:

- Complete, sign (PI), and upload the request for change form found here.
- Revise the current approved application using track changes
- Sign Section I of the application (PI)
- Revise current approved Consent document as applicable using tracked changes
- Complete and sign the appropriate Request for Change
- Upload all documents associated with this change (e.g., application, consents, Request for Change, etc) using the Add Document function

If you have any questions regarding this submission process, please contact the IRB Office.

Continuing Review Overview

Federal regulations require certain types of research undergo continuing review at least annually. Review and approval of continuing review must occur before the expiration date listed on the initial approval letter and, subsequent continuing review approval letters as the “valid until” date. Courtesy email reminder notifications are sent approximately two months before expiration and again two weeks later.

Federal regulations prohibit the IRB from granting extensions or temporary approval beyond the expiration date. Should expiration of IRB approval occur, all study related activities must cease as of the date of expiration.

A “Request to Continue Treatment for Enrolled Subjects on Approval Expired Studies” form must be submitted and approved to allow currently enrolled subjects to continue to receive study treatment. This form is available through the “Forms” link on study pages in RSS.

CR Electronic Submission

- Complete, sign (PI), and submit the continuing review form within RSS (located on the left side menu under “Forms”)
- Upload the following documents, as applicable, using the “Add Document” function:
  - Last signed consent form (only if a subject was consented or reconsented since the last continuing review). **These are no longer to be redacted** (i.e. subject identifiers do not need to be blacked out).
  - Scientific Review Committee (SRC) CR approval letters
  - DSMB or other safety review reports
  - Progress reports
  - Publications

CR Existing Paper Protocol Submissions

- Complete, sign (PI), and upload the continuing review form found here.
- Upload the following documents, as applicable, using the “Add Document” function:
  - Consent documents (Word format and clean to be date stamped)
  - Last signed consent form (only if a subject was consented or reconsented since the last continuing review). **These are no longer to be redacted** (i.e. subject identifiers do not need to be blacked out).
  - Scientific Review Committee (SRC) CR approval letters
  - DSMB or other safety review reports
  - Progress reports
  - Publications

Submission Deadlines

Studies requiring Full Board (convened IRB meeting) review, continuing review applications should be submitted 4-6 weeks before expiration.

Studies requiring expedited review, continuing review applications should be submitted four weeks prior to expiration, to allow time to address any required modifications.

Studies that do not require continuing review, are required to submit an annual update, which includes a report of subject demographics. Emails requesting the annual update are sent out the month the study will expire.

If you have any questions regarding this submission process, please contact the IRB Office at irbora@unmc.edu.