UH Clinical Research
Standard Operating Procedures

STANDARDIZED PROCESSES

The SOPs within this manual describe standardized processes and provide instruction for various procedures related to the conduct of clinical research at University Hopsitals and are meant to promote consistency for those involved.

The SOPs are reviewed every three years for possible revisions needed due to updates or changes in regulations, local policies or procedures, and to maintain compliance with applicable regulations, policies, or laws.

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GA-101 - Development and Maintenance of Standard Operating Procedures

1. PURPOSE:

This Standard Operating Procedure (SOP) describes the standard format and method the UH Clinical Research Center (CRC) Policy Oversight Committee will use in writing and maintaining the Research SOPs for University Hospitals. This SOP also describes how the research community may use these SOPs as guidelines and examples in developing their own SOPs.

2. SCOPE:

This SOP will provide instruction and promote consistency across University Hospitals Health System for those involved in the conduct of research and the development of research SOPs.

3. RESPONSIBLE INDIVIDUALS:

3.1 The UH CRC Policy Oversight Committee is responsible for:

    3.1.1 Preparing, revising and implementing the SOPs to serve as a reference or guidance for the research community on appropriate research practices; and

    3.1.2 Obtaining input and feedback from investigators.

3.2 The UH Clinical Research Center is responsible for:

    3.2.1 Monitoring compliance with Research SOPs at UH;

    3.2.2 Maintaining current SOPs on the UH website;

    3.2.3 Ensuring timely review of SOPs; and

    3.2.4 Providing training to research team members on implementing Research SOPs in their area.

3.3 The Investigator is responsible for:

    3.3.1 Developing specific SOPs, as necessary but not conflicting with institutional policies, local, state, and federal laws and regulations;

    3.3.2 Ensuring compliance with site specific SOPs; and

    3.3.3 Training research team members on implementing site-specific SOPs in their particular research area.

4. RELATED TERMS AND DEFINITIONS:

Standard Operating Procedure (SOP) - Detailed written instructions to maintain standardization of a specific function.

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:

This SOP must be used as a guide to write, format, implement, and maintain Research SOPs for University Hospitals. SOPs are not intended to supersede existing institutional

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policies, or local, state, and federal laws and regulations.

6. PROCEDURES:

    6.1 <u>Identifying the Need for SOPs</u>

        6.1.1 Institutional Level
The UH CRC Policy Oversight Committee will determine the priority of the SOPs to be completed, revised, and formally implemented at UH. The priorities will be based on the input from each of the Committee members who will be representing their department or investigators.

        6.1.2 Department/Investigator Level
Priorities should be based on the need of the Department or Investigator.

    6.2 <u>Writing the SOP</u>

        6.2.1 Institutional Level
The UH CRC Policy Oversight Committee determines the level of detail for the SOP. After the first draft of the SOP is completed, each SOP is reviewed by the members of the Committee for accuracy and clarity. Include tools designed to be used with the SOP such as forms, templates, checklists, etc. if applicable.

        6.2.2 Department/Investigator Level

            6.2.2.1 Depending on the nature of the SOP, the appropriate individuals should determine the level of detail for the SOP. After the first draft of the SOP is completed, each SOP must be reviewed for accuracy and clarity. Include tools designed to be used with the SOP such as forms, templates, checklists, if applicable.

            6.2.2.2 Each research area ensures that the site procedures and activities detailed in the SOP accurately reflect how the tasks are performed within their research area. If revisions are required to reflect how the tasks are performed within each research area, the Department Chair, Principal Investigator, or other designee must ensure these revisions are made to the SOP and implemented within the research area. These changes should be documented in a site-specific or protocol specific SOP, as needed.

    6.3 <u>Format</u>
SOP GA-101 may be used as a template in formatting new and revised SOPs with regards to spacing, margins, indentation, numbering structure, etc. Alternatively, a Microsoft Word template can also be provided by contacting ClinicalResearch@UHhospitals.org and include the following items and sections:

TITLE of SOP: Descriptive statement that represents the document's purpose. The wording should be descriptive, but concise.

1. **PURPOSE**: Qualifies and describes the intent of the SOP.

2. **SCOPE**: Statement that describes the personnel and situations to which the SOP applies.

3. **RESPONSIBLE INDIVIDUALS**: Documents the parties involved and specific performance standards or requirements for the procedure.

4. **RELATED TERMS AND DEFINITIONS**: A brief, precise statement of the meaning of key words or phrases within the SOP.

5. **POLICY STATEMENT**: The governing statement of standards for a specific activity.

6. **PROCEDURES**: A description of the tasks or step-by-step procedures necessary for completion of the activity. Include definitions as necessary.

7. **REFERENCES**: A list of regulations, policies and guidelines applicable to or referenced in the SOP. The citation in the SOP will also identify documents to review for additional information regarding a specific activity.

8. **FORMS OR ATTACHMENTS**: A list of reference materials such as appendices, forms, checklists, or other additional information that may be utilized in the implementation of the SOP.

6.4   Implementation
   6.4.1   Signature
      6.4.1.1   Institutional Level
         The Draft SOP will undergo formal review and approval by the Associate Chief Scientific Officer and other designee, as appropriate (Chief Scientific Officer; Legal Counsel; HRPP; Pre-Award Grants & Contracts; Research Integration & Education, etc.).

      6.4.1.2   Department/Investigator Level
         The Draft SOP will undergo formal review and approval by the Department Chair or other designee, as appropriate.

   6.4.2   Formal Notice and Training
      6.4.2.1   Institutional Level
         After the SOP is finalized, the SOP will be posted on the UH Clinical Research website and notification will be distributed throughout the research community through the clinical research distribution list. The SOP will be effective 60 days after the formal announcement.

         When a new SOP is approved or when there are significant revisions to an existing SOP, Research Integration & Education will

organize education within this 60-day period for the research community. This will help ensure an understanding of the requirements and activities necessary for adherence to the SOPs. Appropriate individuals should participate in the training pertaining to the announced SOP. This includes investigators, research staff, and any individuals whose scope of practice or research assignment is related to the SOP. The training will be made available in the UH GPS Learning Management System.

Training can be completed via UH GPS. Individuals should consult with their manager or Department Chair to determine the applicability of the SOP. Investigators or managers will be responsible for registering themselves and their direct reports for training.

Documentation of this training will be maintained in UH GPS

6.4.2.2 Department/Investigator Level
After the SOP is final, the Department Chair or other designee, as appropriate, should ensure that all appropriate individuals are trained. Documentation of this training should be maintained.

6.5 SOP Revisions and Retention
6.5.1 Institutional Level
SOPs are reviewed every three years for possible revisions needed due to updates or changes in regulations, local policies or procedures, and to maintain compliance with applicable regulations, policies, or laws. The revised SOP will be included in the SOP Manual posted on the website. The SOP will be effective 60 days after the formal announcement of the revision. Research Integration & Education will maintain all old versions of the institutional SOPs for monitoring or audit purposes.

6.5.1.1 Retraining will occur as described above in Formal Notice and Training

6.5.2 Department/Investigator Level
6.5.2.1 Each research area ensures that the site procedures, and activities detailed in the SOP accurately reflect how the tasks are performed within their research area. If revisions are required, the Department Chair, Principal Investigator, or other designee must ensure these revisions are made to the SOP and implemented within the research area. Documentation of retraining must be maintained. For monitoring or audit purposes, all versions of the SOP must be maintained and is the responsibility of the Department Chair, Principal Investigator, or other designee.

6.5.3 In the event of a regulatory audit, the regulatory agency may audit a study against the SOP that was in effect at the time of study conduct, and thus appropriate documentation must be maintained.

7. REFERENCES
- Food and Drug Administration (FDA) Federal Regulations (21 CFR 50, 54, 56, 312, 314, 600, 601, 812 and 814) http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm
- Department of Health and Human Services (DHHS) Regulations (45 CFR 46 Subparts A, B, C, and D) http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
- International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines https://www.fda.gov/media/93884/download
- University Hospitals Clinical Policies, UH Clinical Research Center Policies
  - https://uhcommunity.uhhospitals.org/SystemPolicies/Pages/Table_of_Contents.aspx (DWP)
  - https://www.uhhospitals.org/uh-research/for-researchers/research-and-clinical-trials/policies-and-procedures/research-standard-operating-procedures
  - https://www.uhhospitals.org/about-uh/mission-vision-values/code-of-conduct

8. FORMS OR ATTACHMENTS
Microsoft Word SOP Template – Contact ClinicalResearch@UHhospitals.org for a copy.

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – August 26, 2022

University Hospitals
Clinical Research Center

GA-102 - Use and Disclosure of Protected Health Information Preparatory to Research

1. **PURPOSE:**
   To define the procedures necessary to use or disclose University Hospitals (UH) patient Protected Health Information (PHI) preparatory to research.

2. **SCOPE:**
   This SOP applies to University Hospitals (UH) personnel who desire to use or disclose PHI preparatory to research (Investigator). Non-UH personnel are permitted to use PHI preparatory to research only if credentialed through the UH Research Credentialing process and under the direction of a UH sponsor who has met the requirements of this SOP.

   This SOP applies to UH patient PHI, whether in paper or electronic form.

3. **RESPONSIBLE INDIVIDUALS:**
   UH employees interested in using or disclosing PHI preparatory to research are responsible for completing the required steps set forth below. Prior to giving access to PHI, UH employees and workforce members must take reasonable steps to ensure that the procedures stated herein have been followed by the Investigator.

4. **RELATED TERMS DEFINITIONS:**
   Preparatory to Research - Activities that include:
   - Preparing a research protocol;
   - Developing a research hypothesis; and
   - Identifying prospective research participants. Prospective research participants can be identified but cannot be contacted as part of preparation for research.
   When the goal of the activity is solely to identify prospective research participants for recruitment purposes, this should be included in a full protocol submission to the IRB. The IRB will review and approve that activity under a waiver of HIPAA authorization.

   Disclose - The release, transfer, provision of, access to, or divulgence of PHI to a person or entity outside UH.

   Use - Sharing, employing, applying, utilizing, examining, or analyzing PHI within UH.

   Protected Health Information (PHI) – Information created or received by a UH entity related to (a) the past, present or future physical or mental health or condition of a patient; or (b) payment for the provision of healthcare to a patient that is transmitted or maintained in any form or medium. PHI contains identifiers, such as demographic or insurance information, medical record number, physician, admission date or photographic images, for which there is a reasonable basis to believe the information can be used to identity a patient. Any individually identifiable information of a person deceased more than 50 years is not PHI.

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Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. **POLICY STATEMENT:**

A UH employee who desires to use or disclose PHI preparatory to research must agree to the following:

5.1   The use or disclosure is sought solely to review PHI as necessary to prepare a research protocol, develop a research hypothesis, or identify prospective research participants.

5.2   No PHI will be removed from UH (the Covered Entity) during the review. (Remove means the act of providing, transferring, or storing paper or electronic PHI offsite of UH premises. Examples include: providing PHI on an external device for use offsite of UH premises, emailing PHI to a non-UH email account, and/or storing electronic PHI on Google.Docs).

5.3   The PHI that the Investigator seeks to use or disclose is necessary for the research purpose.

6. **PROCEDURES:**

6.1   The Investigator who desires to use or disclose PHI preparatory to research, must complete and submit the Use and Disclosure of Protected Health Information Preparatory to Research Investigator's Certification (Certification Form) to the UH Privacy Officer, Compliance@UHhospitals.org. By completing the Certification Form, the Investigator agrees to the following:

6.1.1   The Investigator is preparing and/or considering a research protocol.

6.1.2   In order to prepare or determine the feasibility of the research protocol, the Investigator requires access to certain PHI.

6.1.3   The requested PHI is necessary to prepare for the particular research.

6.1.4   The PHI requested is limited to only that which is essential to conduct the activity related to preparation of the proposed protocol.

6.1.5   The Investigator has provided a complete list of the names of the individual(s), who will be reviewing the information being sought.

6.1.6   At no time during the review will the Investigator or others remove the PHI from UH premises.

6.1.7   The Investigator will only disclose PHI to non-UH personnel who have been researched credentialed.

6.1.8   Neither the Investigator nor his/her staff will contact patients about the proposed study or conduct any research until the Investigator submits and receives IRB approval for the research protocol.

6.1.9   Review of PHI will commence only on or after the date of the approval of the Certification Form.

6.1.10 After the Certification Form expiration date, the Investigator will not use or disclose the PHI for research preparation, unless the Investigator has submitted a request for an extension and received approval from the UH Privacy Officer.

6.1.11 The Investigator will retain the PHI in accordance with the policies on human subject research, only if needed as part of an approved research protocol from UH. If no longer needed, the Investigator will destroy the PHI to ensure privacy and confidentiality of the PHI in accordance with UH policies and procedures.

6.1.12 The Investigator will abide by UH policies to ensure the privacy and security of

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UH PHI.

6.2   The Investigator maintains a copy of the Certification Form with the Investigator's study documentation.

6.3   The Investigator may not use PHI obtained pursuant to this SOP to contact potential study subjects, unless the Investigator receives IRB approval for the study protocol and that approval permits using patient information to contact about participation in the study.

6.4   After the Certification Form expiration date, the Investigator will not use or disclose the PHI for research preparation, unless the Investigator has submitted a request for an extension and received approval from the UH Privacy Officer. The Investigator will retain the PHI in accordance with the policies on human subject research, only if needed as part of an approved research protocol from UH. If no longer needed, the Investigator will destroy the PHI to ensure privacy and confidentiality of the PHI, in accordance with UH policies and procedures.

7. REFERENCES:

- UH System Policies in UH PolicyStat:
  - R-3 - Uses and Disclosure of Protected Health Information (PHI for Research)
  - PH-15 - De-Identifying Protected Health Information (PHI)
  - PH-16 - Limited Data Set: Permitted Purposes for Use/Disclosure
- UH Clinical Research SOP Manual
  - GA-103 - UH Research Credentialing
  - SS-309 – REDCap Project Access for UH Employees
  - SS-310 – REDCap Project Access for Research-credentialed Users
  - SS-311 – REDCap Project Access for External, Non-research-credentialed Users

8. FORMS OR ATTACHMENTS:

- Use of Protected Health Information Preparatory to Research Investigator's Certification
- Preparatory to Research Flowchart
- FAQs - Access & Use of Patient Records for Research Purposes

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – October 31, 2023

GA-103 UH Research Credentialing

Step-by-step instructions on how to complete the research credentialing process are contained in this document. **The link to access the credentialing application is on page 6.** PLEASE READ THESE INSTRUCTIONS

1. PURPOSE:

To define the procedures necessary for non-University Hospitals (UH) personnel to obtain access to UH Protected Health Information (UH PHI), UH patients, or UH property for purposes of conducting research.

The UH Research Credentialing Process:

1.1 Allows access to UH PHI, patients, or property for Institutional Review Board (IRB)-approved research protocols;

1.2 Permits the use and disclosure of UH PHI preparatory to research under the supervision of a UH employee who serves as the Responsible Investigator of the research protocol and who completes all of the required steps set forth in the Research SOP GA 102: Use and Disclosure of Protected Health Information Preparatory to Research;

1.3 Grants a UH-based title (Research Faculty or Research Associate);

1.4 Provides the non-employee with a UH e-mail address and access to UH IT systems required to complete the research project in accordance with the standard UH policies and procedures; and

1.5 Provides access to UH-sponsored training as well as research education programs.

2. SCOPE:

2.1 If the individual seeking credentialing is affiliated with one of the following institutions, they may proceed with the application:

   2.1.1 UH Affiliated Hospitals (including Southwest General and Firelands Regional Medical Center)

   2.1.2 Case Western Reserve University (CWRU)

   2.1.3 Kent State University Nursing Students

   2.1.4 Ursuline College

   2.1.5 Cleveland State Nursing Students

   2.1.6 Lake Erie College of Osteopathic Medicine (LECOM)

   2.1.7 Northeast Ohio Medical University (NEOMED)

   2.1.8 Sodexo

2.2 If the individual seeking credentialing is **NOT** affiliated with one of the listed institutions, please contact UHResearchCredentialing@UHhospitals.org for next steps **BEFORE** completing the application process. You will need to answer additional questions to obtain permission to be research credentialed.

2.3 Research Credentialing is not required for external study monitors (e.g., FDA Auditors,

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Sponsor Medical Monitors, etc.) to access UH PHI, UH patients, and UH property.

3. RESPONSIBLE INDIVIDUALS:
Applicant – All non-UH personnel interested in engaging in research at UH who need access to UH PHI, UH patients, or UH property.

UH Sponsor – A UH Employee with (1) knowledge of the Applicant's roles and responsibilities, (2) the ability to submit Sailpoint requests and provide the Applicant with appropriate access to UH IT systems, and (3) appropriate oversight of ongoing compliance with UH policies. The UH Sponsor is often the Department Administrator.

UH Principal Investigator – The UH Principal Investigator (PI) overseeing the studies where the Research Applicant is intended to engage. The UH PI can be the UH Sponsor, if the above criteria are met.

4. RELATED TERMS AND DEFINITIONS:
Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
All non-UH personnel who intend to participate in the conduct of research must complete the UH Research Credentialing Process in order to access UH patients, UH PHI, or UH property. Applicants must renew their UH Research Credentials annually in order to maintain access to research studies at UH with the exception of CWRU Medical Students who are granted approval until their expected graduation date which can be no more than 4 years (re-credentialing is required if graduation is delayed).

Compliance with this policy will be monitored. Failure to adhere to this policy may result in termination of research credentialing privileges.

UH Sponsor must:
1. Ensure any access provided to UH IT systems is properly granted and monitored (refer to *Institutional Policy, IS-14 Acceptable Use of Electronic Assets*). The access granted must be the minimum access necessary to complete the research project and be terminated as soon as the Applicant has completed their duties related to the research project.
2. Ensure the Applicant has been cleared by Employee Health (refer to *Institutional Policy, IC-7 Corporate Health Infection Control Program*) prior to their start date, if the Applicant will be present at a UH facility.
3. Notify the Research Credentialing Office (UHResearchCredentialing@UHhospitals.org) if an Applicant discontinues participation.

The UH PI must:
1. Monitor the performance of all activities completed by the Applicant and ensure

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compliance with UH policies and procedures.

2. Ensure any PHI provided to Applicant is in accordance with UH Policies.
3. Ensure the Applicant is only given access to the minimum necessary information to perform research duties.
4. Notify the Research Credentialing Office (UHResearchCredentialing@UHhospitals.org) of any changes in status.

6. PROCEDURES:

If you have any questions, reach out to UHResearchCredentialing@UHhosptials.org.

The following steps must be completed in order to be granted access to UH Patients, UH PHI (including UH IT Systems that contain PHI for the purpose of conducting research); or UH property:

6.1 Work with the Principal Investigator overseeing the research protocol(s), the UH Sponsor, or Department Administrator(s) for assistance in completing the required documentation and application process outlined below.

6.2 Complete and sign the "**UH Sponsor Certification Form**" with their help. Save as an electronic copy.

6.3 Review and sign "**UH Electronic Systems Agreement**" document. Save as an electronic copy.

6.4 Complete a **UH Criminal Background Check** by following the process below:
   If you are a CWRU Medical Student or Minor High School Student, skip this step

   6.4.1 Go to www.CorporateScreening.com/vendor and click on Vendors/Contractors button.
   6.4.2 Enter the special promotional code: **uhresearcher** and then hit the "GO!" button. Complete the online application in its entirety.
   6.4.3 Have a credit card (Visa/Mastercard/American Express/Discover) ready – complete with pertinent IRB study information ready in order to process payment. The cost is approximately $25.00.
   6.4.4 Click "Submit" button at the end of the process. You will be provided with an electronic receipt and confirmation code at the time of completion.
   6.4.5 A unique login that can be used to view your results will be e-mailed to your e-mail address. Reports can be retrieved at www.CorporateScreening.com/vendor by clicking on the "Retrieve Background" button.
   6.4.6 Attach a copy of your background check to the Research Credentialing application in REDCap.
   6.4.7 An updated background check is required every 5 years. It is the Applicant's responsibility to ensure this is kept up-to-date.

6.5 CREC/CITI training is required for all individuals listed as study personnel. CREC certification can be obtained initially by completing CITI training or by obtaining CREC

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credits. For more information regarding how to obtain CREC certification, please visit the CREC Website or email CREC@Case.edu.

6.5.1 Applicants that completed CITI training at another institution within the last 2 years, are eligible to affiliate their CITI training account to CWRU CREC Program to see if credits are transferrable.

6.5.2 CREC/CITI training expires after 3(three) years. It is the responsibility of the Applicant to ensure CREC/CITI certification is current by acquiring 12 (twelve) CREC credits prior to expiration in order to renew the certification for an additional 3 (three) years.

6.6 **Documentation / Important Items Necessary to Complete the Application:**
Blank forms can be found on the Research Credentialing Website or by accessing the application listed in section 6.7.

6.6.1 If the Applicant is not a U.S. citizen, a copy of their Permanent Resident or VISA status, if applicable.

6.6.2 Institutional identification (ID) card or Driver's License.

6.6.3 Expected graduation date from the CWRU School of Medicine, if applicable.

6.6.4 A copy of the Applicant's completed Corporate Screening Background Check (less than 5 years old).

6.6.5 Date of completed CITI/CREC certification.

6.6.6 Completed electronic copy of the **UH Sponsor Certification Form**.

6.6.7 Completed electronic copy of the **UH Electronic Systems Agreement**.

6.6.8 A copy of MD, DO, or RN license in the State of Ohio or corresponding training certificate in the State of Ohio.

6.6.8.1 If the applicant does not have a license in the State of Ohio, the applicant must complete the form entitled "Rules for Non-Licensed Researchers in a Clinical Setting" in the credentialing application.

6.6.9 Educational Experience Affiliation Agreement, High School Student Waiver and Confidentiality Agreement, and Minot Student Confidentiality Agreement, if applicable.

6.6.10 Proof of payment ($150 for initial application, $100 for renewal applications) *OR* Department Payment Form, if applicable

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6.6.11 Document and information requirements by application type.

Requirements by Application Type	Initial Application	Annual Renewal Application	CWRU Medical Student Application	< 18 High School Student Application	18+ High School Student Application
VISA or Permanent Resident Verification	*	*	*		
Institutional ID or Driver's License	✓	✓	✓		
UH Electronic Systems Agreement	✓		✓	✓	✓
UH Sponsor Form	✓	✓	✓	✓	✓
Background Check	✓	†			✓
Expected CWRU SOM Graduation Date			✓		
CWRU SOM background check verification			✓		
CREC/CITI Certification	✓	✓	✓		✓
UH GPS HIPAA Training	✓		✓	✓	✓
Authorization & Release from Liability Form	✓	✓	✓		
Ohio License or Rules for Non-Licensed Researchers in a Clinical Setting Form	✓	✓	✓		✓
Educational Experience Affiliation Agreement				✓	✓
High School Student Waiver and Confidentiality Agreement				✓	✓
Minor Student Confidentiality Acknowledgement				✓	
Department Payment Form	✓	✓			

* Applicable if the applicant is not a U.S. citizen.

† If background check is >5 years old, the Applicant will need to obtain a new background check.

6.7 **Completing the REDCap Application**

Click here to begin an online application

6.7.1 Select the appropriate application type:
- **Initial Application:** For new applicants including individuals who were approved through the "Out of Policy" procedure. Does not include new applicants enrolled in the CWRU School of Medicine
- **Annual Review Application:** To be completed annually by all applicants with the exception of CWRU Medical Students
- **CWRU Medical Student Application:** For Medical Students enrolled in the CWRU School of Medicine
- **High School Student Enrolled in the Educational Experience Program Application:** For high school students who have enrolled in the UH Clinical Research Center's Educational Experience Program. Requires prior approval.

6.7.2 Complete all applicable application questions.
Incomplete applications will not be accepted. Please ensure each section of every form is complete prior to uploading to the application.

    6.7.2.1 In the Application Type, General Information, Academic Affiliation, and Employment Section, include the Applicant's email address from their affiliated institution.

    6.7.2.2 The documents listed in section 6.6 will need to be uploaded to specific questions within the Training, Agreements, and Forms section of the application.

        6.7.2.2.1 Apply an electronic signature within the applicable to acknowledge the terms of the **Authorization and Release from Liability** form.

        6.7.2.2.2 If the Applicant does not have a valid clinical license, the **"Rules for Non-Licensed Researchers in a Clinical Setting"** document must be completed and uploaded to the application.

    6.7.2.3 Read the Payment Options and Instructions section carefully. CWRU Medical Students are exempt from the Research Credentialing fee.

        6.7.2.3.1 **Do NOT submit payment until you have confirmed you are eligible for Research Credentialing. Fees may not be refundable based on payment method.**

        6.7.2.3.2 Provide proof of payment of the Research Credentialing fee by attaching a copy of your receipt to the online application or by providing the date of your email confirmation of payment. See **Appendix A** for payment options.

6.7.3 After completion of the application in its entirety, click "**Submit**" at the bottom of the application.

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6.8 **UH Research Credentialing Notification Process**

6.8.1 Once all documentation and the completed application are received by the UHCRC, allow up to seven (7) business days for processing.

6.8.2 The UHCRC will notify the applicant if any document is incomplete or if the request for access is satisfactory via email.

6.8.3 The UHCRC will notify the applicant and appropriate parties via email that all the required steps of the UH Research Credentialing Process have been completed and the date of expiration.

6.8.4 The Applicant is not research credentialed until they have received an approval email with an attached Research Credentialing certificate.

6.8.5 After completing the research credentialing process, all research credentialed personnel are required to complete clinical research education. Contact ClinicalResearch@UHhospitals.org for more information.

6.9 **CWRU Medical Student Application**

6.9.1 Follow procedures in section 6.7

6.9.2 A background verification is required with the School of Medicine rather than a Corporate Screening background check.

    6.9.2.1 Visit http://casemed.case.edu/registrar/forms/

    6.9.2.2 Click the "Student Letter Request Form."

    6.9.2.3 Select "Background Check Verification Letter" option.

    6.9.2.4 Login with your CWRU ID and passphrase.

    6.9.2.5 Complete the form and select "Email" as the Delivery Method and have the letter emailed to UHResearchCredentialing@UHhospitals.org.

6.10 **High School Student Enrolled in the Educational Experience Program Application**

6.10.1 Follow procedures in section 6.7.

6.10.2 If the Applicant is 16 or 17 years old, they will need to have a parent or guardian help complete the necessary paperwork.

6.10.3 High School applicants must reach out to CRC Research Integration & Education (ClinicalResearch@UHhospitals.org) to enroll in the CRC's Educational Experience Program prior to completing the Research Credentialing application and accompanying documentation.

6.10.4 In order to participate in research at UH, high school applicants must have an **Educational Experience Affiliation Agreement** on file with UH Legal.

6.10.5 High School Applicants must additionally complete a **High School Student Waiver and Confidentiality Agreement** which must be then uploaded to the Research Credentialing application.

NOTE: There are additional requirements of the individual subsequent to Research Credentialing approval that grant the individual access to UH systems, UH property, and UH patients. Please carefully review the Research Credentialing approval email and work with your UH Sponsor.

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7 REFERENCES:

- [UH Research Credentialing Website](#)
- [UH Investigator Manual for IRB Submissions](#)
- [Requesting UH System Access for Non-Employees with Sailpoint Identity](#)
- [Corporate Screening](#)
- [UH System Policies](#)
  - IS-14 Acceptable Use of Electronic Assets
  - R-3 Uses and Disclosures of Protected Health Information (PHI) for Research
  - IC-7 Corporate Health Infection Control Program
  - PH-30 E-Mail Communication of Protected Health Information (PHI) Between Patients and Healthcare Providers and Internal Communications Containing PHI
  - EH-1 Mumps
  - EH-2 Rubella (German Measles)
  - EH-3 Rubeola (Measles)
  - EH-4 Varicella (Chicken Pox) and Varicella Zoster Virus (VZV, Shingles)
  - EH-5 Tdap (Tetanus, Diphtheria, Pertussis Vaccine) and Td (Tetanus and Diphtheria Vaccine)
  - EH-6 Fit Testing N-95 Respirator
  - EH-8 Hepatitis B
  - EH-9 TB Skin Testing/TB Surveillance
- UH Clinical Research SOPs
  - GA-102 - Use and Disclosure of Protected Health Information Preparatory to Research
- [CREC Website](#)
  - [Affiliate your CITI Training Account](#)

8 FORMS OR ATTACHMENTS:

- [Link to begin an online application](#)
  - UH Sponsor Certification (within online application)
  - Certification Authorization and Release for Liability (within online application)
  - UH Electronic Systems Agreement (within online application)
  - Rules for Non-Licensed Researchers in a Clinical Setting (within online application)
  - Authorization & Release from Liability (within online application)
  - Educational Experience Affiliation Agreement (within online application)
  - High School Student Waiver and Confidentiality Agreement (within online application)
  - Minor Student Confidentiality Acknowledgement (within online application)
  - Payment Reference Form / Department Payment Form (within online application)
- Appendix A - Payment Reference Form

APPROVALS

Signed by Grace A McComsey, MD, FIDSA, Director of the UH Clinical Research Center, University Hospitals Health System –
December 13, 2023

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APPENDIX A – Payment Options

A. Payment Option 1 – Credit Card, Google Pay, or Apple Pay
    1. Navigate to
       https://pay.instamed.com/Form/PaymentPortal/Default?id=research.credentialing
    2. If you are the Applicant submitting payment for UH Research Credentialing, your may leave the "Guarantor" sections blank.
    3. If you are someone paying on behalf of the Applicant, you are considered the Guarantor. Please complete the Guarantor information.
    4. If this is your first time going through the UH Research Credentialing process, select "INITIAL APPLICATION 150 DOLLARS" as the application type.
    5. If you submitting a renewal, select "RENEWAL 100 DOLLARS" as the application type.
    6. Click "PAY NOW".
    7. InstaMed may request you to create an account. If you'd rather not create an account, click "Continue as Guest" at the bottom of the page to proceed.
    8. Click on the "Payment Amount" box and type in the required fee amount (Initial = $150, Renewal = $100).
    9. If using a credit/debit card, key in the required information in the designated fields.
    10. Click "Next".
    11. You will be routed to a "Review & Confirm" screen. Please review all information to assure accuracy and click "CONFIRM".
    12. On the "Payment Summary" page, click "SHARE RECEIPT".
    13. In the pop-up window, email the receipt to UHResearchCredentialing@UHhospitals.org and click "Send".
    14. Please enter the date of the transaction in your REDCap application when prompted.

B. Payment Option 2- General Ledger Account, PTAEO or CWRU Speedtype
    1. Print the "Department Payment Form" attachment provided in the payment section of the online application.
    2. The form will need to be completed and emailed to UHCRCGrantsAccounting@UHhospitals.org.
    3. After payment has been processed, you will receive an email confirmation, with UH Research Credentialing copied. This email will serve as your receipt of payment, please enter the date of the email in your REDCap application when prompted.

Payments are non-refundable, so ensure you are eligible for credentialing (i.e. you are affiliated with one of the listed institutions, or you have explicit permission from the research credentialing office) BEFORE you pay the fee.

GA-104 – Scope of Practice

1. PURPOSE:
This Standard Operating Procedure (SOP) defines the roles and responsibilities associated with conducting research at University Hospitals Health System (UH), and to ensure that individuals to whom study tasks are delegated are appropriately licensed, qualified, delegated and trained on the specific task to which they are assigned.

2. SCOPE:
This SOP applies to all investigators and study personnel who interact with research participants within UH or under the purview of the UH IRB. Research personnel must work within their general scope of practice at the institution. Conducting research does not exempt personnel from complying with state requirements for the performance of clinical tasks. If personnel are not qualified to complete a clinical task in general clinical practice, they are not qualified to complete the task for research purposes. Some clinical tasks may require separate licensure or certification.

3. RESPONSIBLE INDIVIDUALS:
Appendix A serves as a reference to help indicate who is qualified to perform tasks related to conducting clinical research within UH. Appendix A is not an exhaustive list and if a question arises about whether it is appropriate to assign a task to a member of the study team, contact the UHCRC for guidance at ClinicalResearch@UHhospitals.org.

4. RELATED TERMS AND DEFINITIONS:
Medically Qualified - Competent to practice medicine or perform medical procedures determined by education, training, experience, certification, license, or study of medicine.

Healthcare License - An agency - or government-granted permission issued to a health care professional to engage in a given occupation on finding that the applicant has attained the degree of competency and met educational requirements necessary to ensure that the public health, safety and welfare are reasonably well-protected.

Adequate Training - Familiarity with the purpose of the study and the details of the protocol. Adequate understanding of the attributes of the investigational product needed to perform assigned tasks. Aware of the regulatory requirements and acceptable standards for the conduct of clinical trials and the protection of human subjects. Trained and competent as defined by licensure and the Principal Investigator (PI), department manager or UHCRC, to perform the tasks they are delegated. Informed of pertinent changes during the conduct of the trial and receive additional training as appropriate.

> **Other DEFINITIONS: per State of Ohio Board of Pharmacy**
> **Dispense:** The final association of a drug with a particular research participant pursuant to the prescription, drug order, or other lawful order of a prescriber and the professional judgment of and the responsibility for: interpreting, preparing, compounding, labeling, and packaging a specific drug.

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Administer: the direct application of a drug, whether by injection, inhalation, ingestion, or any other means to a person.

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms found in this SOP.

5. POLICY STATEMENT:

Completion of clinical research tasks should be approached as a concerted, cooperative and collaborative effort. Many clinical research tasks have responsibility designated under more than one job function. This allows the sharing of this task between the clinical and research staff and principal investigator, if allowable.

The PI and employee's supervisor must ensure that individuals to whom study tasks are delegated are appropriately licensed, qualified, and trained to perform the specific task of which they are assigned, and that these study tasks are documented and assigned to the employee on the Delegation of Authority Log/ Staff Signature Log for each protocol.

1.1   Competency
Some tasks may only be performed by licensed individuals. Licensed research personnel may not perform or be trained to perform procedures outside of those allowed under their respective license and credentialing per [UH Medical Staff Services and Credentialing.](#)

Unlicensed UH research personnel may be trained by a licensed medical professional to perform protocol specific procedures, as long as the tasks are within the background and education of the employee and the training is clearly documented.

1.2   Records
Refer to the Delegation of Authority Log/ Staff Signature Log with Instructions for documentation of study related tasks.

6. PROCEDURES:

Appendix A contains an example listing of some procedures as well as the employee(s) responsible for that action.

7. REFERENCES

- [UH Medical Staff Services and Credentialing](#)
- UH Institutional Policies:
    - [MM-4 Investigational Products](#)
    - [NP-3 Delegation](#)
- [Nursing Manuals by Entity](#)
- [The State Medical Board of Ohio](#)
- [State of Ohio Board of Pharmacy](#)
- [Ohio Administrative Code](#) » [4731 State Medical Board](#) - Chapter 4731-23 Delegation of

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Medical Tasks
- FDA guidance – [Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects](#) -10/2009
- For Nurses
  - [Ohio Board of Nursing - Nursing Practice](#)
- [Epic Workflow - Investigational Medication Ordering and Documentation](#)

8. FORMS OR ATTACHMENTS
- [Research Toolbox - Delegation of Authority and Staff Signature Log (Direct Download)](#)
- Appendix A: Scope of Principal Investigators and Key Study Personnel

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – October 31, 2023

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Appendix A: Scope of Principal Investigators and Key Study Personnel

	Medically Licensed			Unlicensed***
	Principal Investigator	**MD, DO, PA, CNP per state requirements**	**RN, LPN PharmD per state requirements**	**Research Coordinator or Assistant, Clinical Research Specialist, Clinical Research Regulatory Specialist, Clinical Research Data Specialist, Medical Assistant, Phlebotomist or Lab Tech**
Regulatory				
Prepare, submit, and maintain regulatory documents for submission, continuing review and protocol changes	X	X	X	X
Sign off on regulatory documents for submission, continuing review and protocol changes	X			
Maintain required and essential study documents throughout life of study	X	X	X	X
Budget/Financial				
Submit budget and protocol to Contracts Office, contact Research Finance team to complete a coverage analysis and provide required materials to grants accounting teams	X	X	X	X
Complete request forms as necessary - Invoiceable Fees Checklist, PI Compensation / Qualifying Status Form, DCRU Request Form, IDS Request Form. (UNDER MD'S DIRECTION)	X	X	X	X
Associate patients with their respective study during their screening visit in the appropriate CTMS (Velos or OnCore), update and maintain research billing patient calendar in (e.g. Velos eResearch, Complete Encounter Linking in Epic, Research Billing Notification Form [RBNF], etc.) *If Applicable*	X	X	X	X
Study Participant Management				
Conduct the Informed Consent Process and document appropriately	X	X	X	X **
Discuss risks, benefits, and alternatives to participation for therapeutic studies	X	X	X	
Review participant eligibility (e.g. inclusion and/or exclusion) and document appropriately	X	X	X	X
Final confirmation and sign-off of participant eligibility	X	X		
Assign tasks to staff, ensure adequate training and competency of staff for tasks that have been delegated, and oversee all aspects of study conduct	X			
Document adverse events and concomitant medications	X	X	X	X
Report adverse events and concomitant medications	X	X	X	X
Assign causality to adverse events or medically significant events	X	X		
Document Serious Adverse Events (SAEs)	X	X	X	X
Report Serious Adverse Events (SAEs)	X	X	X	X
Collect and process blood, tissue or specimen samples and document appropriately	X	X	X	X*
Perform protocol-specific physical exams	X	X		
Perform protocol assessments (e.g. EKG, scans, etc.*) and document appropriately	X	X	X	X
Orders- Labs, Radiology, Medications				
Prescribe treatment per protocol and document appropriately	X	X		
Dispense treatment per protocol and document appropriately	X	X	X	
Administer treatment per protocol AND per physician's order and document appropriately	X	X	X	
Order all tests and procedures per clinical practice guidelines, e.g., medications/study treatments/interventions, radiology scans, and laboratory tests	X	X		
Review and sign off on laboratory results e.g. high and low or abnormal values	X	X		
Conduct questionnaires and other surveys and document appropriately*	X	X	X	X
Call pharmacy with prescriptions fills or refills per physician's order and document appropriately	X	X	X	

* Some types of assessments may require additional training or certification by the sponsor

**Risks, benefits, and alternatives to participation must be discussed by an appropriately qualified and licensed physician or medical provider for treatment, therapy or drug studies.

***These individuals may have certifications, specific training, areas of expertise or knowledge, but are still considered unlicensed as defined as one who gives medical advice, one who diagnoses, treats and/or prescribes. They are required to have appropriate delegation and supervision prior to the execution of any aforementioned research or standard of care tasks listed in this table or in general.

Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

GA-105 - Investigator Responsibility for Study Team Training and Documentation

1. PURPOSE:
To describe the Good Clinical Practice Guidelines for training and documentation of training of the study team involved with the conduct of clinical research at University Hospitals (UH).

2. SCOPE:
This SOP applies to all individuals participating in the conduct of clinical research at UH. All staff to whom an investigator assigns a study task, whether or not they are a UH employee, are required to follow this SOP.

3. RESPONSIBLE INDIVIDUALS:
The Principal Investigator (PI) is responsible for ensuring that all persons assisting with the trial are adequately informed about:
3.1   the protocol;
3.2   the investigational product(s); and
3.3   their trial-related duties and functions and that they have been properly trained for their role on the study.

The PI is also responsible for ensuring that study staff are only delegated tasks to which they are qualified by education, training, experience or licensure to complete.

NOTE: It is necessary to complete a delegation log for each study in order to document the study staff to whom the PI has delegated protocol specific tasks.

Study team personnel are responsible for following the procedures described in this policy.

4. RELATED TERMS AND DEFINITIONS:
CITI - Collaborative Institutional Training Initiative provides web-based research education content *"To promote the public's trust in the research enterprise by providing high quality, peer reviewed, web based, research education materials to enhance the integrity and professionalism of investigators and staff conducting research."* - CITI Program Mission Statement**.**

CREC - The CWRU Continuing Research Education Credit (CREC) Program is the mechanism used at University Hospitals to provide documented training, education, and certification in human subjects protections.

Initial entry and certification in the CREC Program is earned by successful completion of the initial core training in the protection of human subjects through the Collaborative Institutional Training Initiative CITI Program (https://www.citiprogram.org). For more information, please visit the UH Clinical Research Education & Training Website

Please reference the Standard Operating Procedures Glossary of Terms for complete

definitions of terms found in this SOP.

5. POLICY STATEMENT:
The UH IRB requires CREC certification of the PI and all individuals listed on the study personnel table on any research protocol regardless of funding.

6. PROCEDURES:
6.1   Initial Training for non-UH research staff
    6.1.1   Complete UH Research Credentialing (see UH Research SOP GA-103 - University Hospitals Research Credentialing)

6.2   Initial Training for all (UH research employees and non-UH research staff)
    6.2.1   UH-specific training as arranged by UH employee's Manager, or for non-UH study personnel, the appropriate UH Department Administrator. The required training will vary depending upon the role, department and staff responsibilities. For questions please contact Manager, Research Integration & Education.

    6.2.2   CITI Basic training and CREC Program entry and certification.

    6.2.3   Good Clinical Practice (GCP) Training for staff of NIH funded studies. Documented GCP Training may be completed via the CITI website.

    6.2.4   Protocol-specific training and documentation for all studies to which the individual is assigned.

    6.2.5   UH CRC-mandated training to educate on the practice of clinical research at UH. Contact UH CRC Research Integration & Education to:
        6.2.5.1   Complete Investigator Training- Required for all PIs
        6.2.5.2   Register for the mandatory UH Clinical Research Orientation course:
            6.2.5.2.1   For Principal Investigators and Physicians
            6.2.5.2.2   For UH research staff & appropriate credentialed non-employees involved in research
        6.2.5.3   Sign up for the clinical research distribution list.
        6.2.5.4   Instructions on how to access the UH Clinical Research education curriculum, UH Clinical Research SOPs, and UH IRB Policies within the Investigator Manual for IRB Submissions.

6.3   Ongoing Training for all (UH research employees and non-UH research staff)
    6.3.1   Training as arranged by the UH employee's Manager, or for non-UH study personnel, the appropriate UH Department Administrator.

    6.3.2   CREC recertification every three years requires that 12 CREC credits be obtained. CREC credits can be obtained in the following manners
        6.3.2.1   Live education sessions offered through UH CRC Research Integration & Education curriculum
        6.3.2.2   Online education available in the UH GPS learning management

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system.

      6.3.2.3 Recorded presentation available on CWRU CREC website (https://case.edu/research/faculty-staff/education-and-training/continuing-research-education-credit-crec).

      6.3.2.4 Education and training activities involving the ethics of human subjects protections in research are eligible for CREC.

      6.3.2.5 CITI Courses [Examples: CITI Good Clinical Practice (GCP), Health Information Privacy and Security (HIPS)]

      6.3.2.6 Conferences hosted by national research organizations (Examples: Society of Clinical Research Associates - SOCRA, Association of Clinical Research Professionals - ACRP)

6.3.3 Training and documentation for all delegated, study-related tasks to which the individual is assigned and when:

      6.3.3.1 IRB-approved protocols are amended;

      6.3.3.2 IRB-approved consent forms change;

      6.3.3.3 Protocol deviations occur and if applicable, corrective and preventative action plans (CAPA) are implemented; or

      6.3.3.4 New information about a study or study product becomes available (e.g., Investigator Brochure, action letter, etc.).

6.3.4 UH CRC-mandated training and education on the practice of or compliance in clinical research at UH.

6.3.5 UH Clinical Research SOP Training

      6.3.5.1 UH Clinical Research SOP training is required:

            6.3.5.1.1 With significant changes to existing SOPs; and

            6.3.5.1.2 When new SOPs are approved.

6.4 <u>Documentation of training</u>

6.4.1 Document training in a training log, training signature sheet, or other format and to include (at minimum):

      6.4.1.1 Trainee name (clearly written)

      6.4.1.2 Date of training

      6.4.1.3 Title and brief description of training (if training syllabus is available, attach to training log)

      6.4.1.4 Trainer name

      6.4.1.5 Trainee(s) signature and date

6.4.2 Training records will be retained as per department and study guidelines and are subject to inspection by authorized regulatory agencies.

6.5 <u>Suggestions for the contents of individual training record</u>

6.5.1 Up-to-date signed and dated Curriculum vitae (CV) or resume

6.5.2 Current job description

6.5.3 Completed individual training log

6.5.4 UH Research SOP Training

6.6 Suggestions for the contents of the of protocol-specific training record
    6.6.1 Training logs to document that all personnel on the protocol have been appropriately trained on:
        6.6.1.1 protocol-specific tasks to which they have been assigned and when protocol revisions are IRB approved;
        6.6.1.2 IRB-approved consent form changes;
        6.6.1.3 identifying and reporting protocol deviations
        6.6.1.4 new information about a study or study product as it becomes available
        6.6.1.5 additional instructions or information as determined by the PI.

7. REFERENCES
- Guidance for Industry, E6(R2) Good Clinical Practice: Consolidated Guidance
- Guidance for Industry - Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects

- UH Clinical Research SOPs
  - GA-101 - Development and Maintenance of Standard Operating Procedures
  - GA-103 - UH Research Credentialing
  - GA-104 - Scope of Practice
  - SS-301 - Maintenance of Research Regulatory Documents

- Investigator Manual for IRB Submissions:
  - Chapter 4 - Required Training Necessary to Conduct Human Subject Research
  - Chapter 5 - Research Staff Responsibilities

- CWRU CREC Website

8. ATTACHMENTS
- Delegation of Authority and Staff Signature Log and Instructions
- Training Log
- Training Signature Sheet
- New Researcher Checklist

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center –September 19, 2022

Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

GA-106 - Transfer of Sponsor-Investigator Initiated FDA Regulated Studies

1. PURPOSE:

To outline the process for when Sponsors leave University Hospitals (UH) and how to properly close or transfer the sponsorship of investigator initiated investigations and related applications (IRAs) regulated by the U.S. Food and Drug Administration (FDA): Investigational New Drug Applications (INDs), Investigational Device Exemptions (IDEs), Master Files (MFs), Emergency Use Authorizations (EUAs) and corresponding clinical investigations.

2. SCOPE:

The policy applies to Sponsors who are:
2.1 transferring institutions and maintaining sponsorship of the IRAs
2.2 transferring the sponsorship to another individual within their institution
2.3 transferring the sponsorship to another individual outside of the originally approved research site
2.4 discontinuing or closing the IRAs

3. RESPONSIBLE INDIVIDUALS:

The Sponsor is responsible for ensuring that this SOP is followed.

4. RELATED TERMS AND DEFINITIONS:

Emergency Use Authorization (EUA)
Investigational Device Exemption (IDE)
Investigational New Drug (IND)
Institutional Review Board (IRB)

Master File (MF) – A collection of documents that must be produced in accordance with applicable international and local regulations containing essential documents that may be subject to regulatory agency oversight.

Sponsor – For purposes of this document includes IND or IDE Sponsor-Investigators.

Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:

A Sponsor who leaves UH must properly discontinue or transfer the sponsorship of investigator initiated research regulated by the U.S. Food and Drug Administration. Discontinue for the purposes of this document means that the IND, IDE, MF, or EUA has a "final" action, i.e., Cancelled, Closed, Exempted, Terminated, Voided, or Withdrawn with the FDA and closed with the IRB.

6. PROCEDURES

6.1 <u>Notification of IRA Transfer</u>

The Sponsor should first confirm the details of their departure and then immediately notify the Department Chair and Administrator of their pending employment transfer. The Sponsor should also initiate the FDA Administrative Action Checklist and submit to the UH CRC Research Support Core at Heather.Tribout@UHhospitals.org if using their services, otherwise it is the study regulatory coordinator's responsibility.

The Regulatory Coordinator or Research Support Core will schedule a meeting with the Sponsor-Investigator, the newly intended Sponsor (if it will remain open at UH) and their research team, and any applicable department or research personnel to discuss other pertinent information pertaining to the study.

6.2 <u>FDA Protocol Status Review</u>

The Regulatory Coordinator or Research Support Core will conduct a review of the FDA regulated protocol to ensure all regulatory, compliance, and financial matters with the FDA and local institution are up to date prior to making changes. The attendees of the review meeting will vary based on the findings of the review, which will include:

6.2.1 Regulatory Review

    6.2.1.1 Original approval letter

    6.2.1.2 Most recent annual report

    6.2.1.3 Upcoming tasks that would need to take place prior to the study transfer

6.2.2 Monitoring Status Review

    6.2.2.1 Monitoring findings

    6.2.2.2 Completion of monitoring findings

6.2.3 Data Analysis/Database Review

    6.2.3.1 Data collection

    6.2.3.2 How the data is being collected

    6.2.3.3 Where the data is being stored

    6.2.3.4 Has the data been queried during the study lifecycle

6.2.4 Data Safety Monitoring Board or Independent Safety Monitor

    6.2.4.1 DSMB Charter and DSMB meeting schedule

    6.2.4.2 DSMB meeting minutes

    6.2.4.3 DSMB members and affiliated institutions

    6.2.4.4 DSMB compensation for membership

    6.2.4.5 Programs, reports, etc. of what stat provides for the DSMB

6.2.5 Grants Accounting Review

    6.2.5.1 Confirmation of all paid invoices

6.2.6 Stock/Supply Review and Reconciliation
6.2.6.1 Drug/Device Stock reconciliation

6.2.7 If any of the listed items above are deemed incomplete or out of compliance, reconciliation of the noted item must be completed by the Sponsor to any transfer or closure of the research study.

6.3 Notification of pending transfer to all appropriate parties
6.3.1 The Sponsor will ensure that all appropriate parties including the Regulatory Coordinator or Research Support Core are notified of the pending study transfer within 10 business days of the transfer
6.3.1.1 FDA (formal written letter)
6.3.1.2 Existing IRB and transfer IRB (formal amendment)
6.3.1.3 Appropriate department personnel at both current and transfer site (email)
6.3.1.4 Principal Investigators if not the Sponsor, Co-Investigators listed on the FDA/IRB approved protocol at current site and Principal Investigator if not the Sponsor at transfer site (formal written letter/email)
6.3.1.5 Device Sponsor (if applicable- formal written letter/email)
6.3.1.6 Drug Sponsor, meaning manufacturer or funding agency (if applicable- formal written letter/email)
6.3.1.7 Data Safety Monitoring Board or Independent Safety Monitor (if applicable- formal written letter/email)

6.3.2 **The following information should be included in the notification by the Sponsor to all applicable parties listed above within 10 business days of notifying the Regulatory Coordinator or Research Support Core of the transfer from the day the PI notifies the institution after a scheduled meeting.**
6.3.2.1 Notice of transfer
6.3.2.2 Reason for transfer
6.3.2.3 Exact date of transfer
6.3.2.4 New transfer location for IRA
6.3.2.5 Sponsor's new contact information
6.3.2.6 Notify subjects by certified mail that the study will be ending at the current site and a new PI will follow up

6.3.3 This information applies to Sponsors who are transferring institutions and maintaining sponsorship of the IRA and Sponsors who are transferring the sponsorship to another individual outside of the originally approved research site.

6.4 Document/Data Transfer
6.4.1 Regulatory documentation required for the Sponsor to comply with applicable law at the new institution and associated with the FDA trial(s) is subject to be

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copied and taken to a new institution by the Sponsor. The documentation should not include any Protected Health Information, work conducted preparatory to research of any confidential information of University Hospitals. A data use agreement or other form of contract must also be executed and documented prior to the transfer of study materials. The contract should include a list of documents sent.

6.4.2 Oversight of the document copying and packing process must be overseen and approved by a current UH employee within the department. Shipment of all materials must be completed by a third party, independent, professional shipment company (i.e., cannot be transported by the Sponsor or a member of the current/new research team) to the new site of the Sponsor at the new site's expense. Documents should be shipped in a way that allows for verification of receipt (e.g., certified mail, return receipt requested).

6.4.3 All regulatory documentation must be stored in a secure, double locked location (i.e., locked cabinet, locked office) within the department prior to the transfer of the study.

6.5 IRB Notification of Closure and New Approval
6.5.1 If the IRA is being transferred to another institution, and will not continue at its current institution, the study protocol will need to be closed with the IRB by the research team within the department.

6.5.2 If the IRA is being transferred to another investigator at a different institution, but the conduction of research procedures will still take place at the current institution under the direction of a different PI, the IRB application will need to be amended appropriately by the research team within the department to reflect these institutional and personnel changes. All changes and transfers including study closure is to be completed prior to the departure of the investigator in order to ensure proper sign-off of the changes.

6.6 Final FDA Administrative Action Checklist
6.6.1 The final FDA Administrative Action Checklist should be completed by the Sponsor within 30 days of the final transfer or closure. The Research Support Core should be notified if they are contracted to conduct services, otherwise the PI and regulatory coordinator is responsible for completing the checklist. Any questions can be directed to Heather.Tribout@UHhospitals.org

7. REFERENCES
UH Clinical Research SOP GA-108 - Investigator-Initiated Research

8. FORMS OR ATTACHMENTS
FDA Administrative Action Checklist

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Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – July 17, 2023

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GA-107 – Investigator Training

1. PURPOSE:
The purpose of this SOP is to define the process for registering, completing, and documenting UH Investigator Training. Investigator training is required for all Principal Investigators (PI) of research studies conducted at UHHS or approved by the UH IRB.

2. SCOPE:
This SOP will set forth the procedure for registering, completing, and documenting UH Investigator Training.

3. RESPONSIBLE INDIVIDUALS:
University Hospitals (UH) investigators and UHCRC personnel.

4. RELATED TERMS AND DEFINITIONS:
Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
The University Hospitals Clinical Research Center (UHCRC) requires investigators to take the UH Investigator Training course in the UH GPS system prior to submitting to the UH IRB. Although not required, the UH Clinical Research Center highly recommends this training for all key personnel participating in research.

6. PROCEDURES:
UH Investigator Training serves as an introduction and overview of the research process at University Hospitals and highlights the essential information needed to be successful.

6.1   Watch a Series of Videos:
       The course is a series of five modules consisting of a collection of short videos:
       6.1.1 Getting Started
       6.1.2 Required Reviews and Approvals
       6.1.3 Study Start-Up
       6.1.4 Study Conduct
       6.1.5 Study Completion and closeout

6.2   Complete Assessments
       Investigators will log into UH GPS and complete all five assessments. Detailed instructions can be found on Investigator Training Instructions - PI and Team for both UH employees and non- employees. Credit for the course will be obtained from the UH GPS system.

6.3   Certificate of Completion Filing
       Upon completion of all five modules, the certificate of completion will automatically be emailed to ClinicalResearch@UHhospitals.org. The Certificate will be filed

appropriately within 7-10 days of training completion. If issues arise or persist past the 7-10 day window—please email ClinicalResearch@UHHospitals.org.

6.4 UH IRB Check for Completion
Completion of UH Investigator Training must be confirmed by the UH IRB before the IRB can process any new submissions (including new submissions, continuing reviews, and modifications).

6.5 Submission Process
Once the research database is updated, the investigator's submission to the IRB is processed. If investigators submit protocols to the IRB and the training is not yet complete, investigators will be notified through the SPARTA IRB Portal that their submissions will not be processed.

7. **REFERENCES:**
   - UH GPS Login

8. **FORMS OR ATTACHMENTS:**
   - Investigator Training Instructions - PI and Team
   - Investigator Training Flowchart

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – May 25, 2022

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Clinical Research
Standard Operating Procedure

University Hospitals Clinical Research Center

GA-108 - Investigator Initiated Research

1. PURPOSE:

This Standard Operating Procedure (SOP) describes the standards for conducting investigator-initiated research at University Hospitals (UH) and the requirements for ensuring the necessary oversight and compliance measures for an investigator-initiated protocol at UH. The UH CRC (CRC) has resources available, on a fee-for-service basis, to support Sponsor-Investigator research.

2. SCOPE:

This SOP provides instruction and sets minimum standards regarding the process for an investigator who is implementing an investigator initiated research protocol at UH. This SOP is not intended to supersede federal regulations set forth by the code of federal regulations but is intended to set a minimum standard for all investigators who wish to conduct investigator-initiated research.

3. RESPONSIBLE INDIVIDUALS:

This SOP applies to all investigators engaging in investigator-initiated research including those studies that are regulated by the Food and Drug Administration Code of Federal Regulations (FDA CFR) under an Investigational New Drug (IND- 21 CFR Part 312) or Investigational Device Exemption (IDE - 21 CFR Part 812) at UH. The Department Review Committee or Department Chair or designee is charged with ensuring that this review is complete and thorough. It is encouraged that other senior research members within the department be available as a mentor for anyone conducting investigator-initiated research within a particular department.

4. RELATED TERMS AND DEFINITIONS:

Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms found in this SOP.

5. POLICY STATEMENT:

All research protocols must be reviewed for scientific merit and ethical standards consistent with local, state and federal requirements and must be consistent with *Investigator Manual for IRB Submissions, Chapter 7 – Required Approvals*.

6. PROCEDURES:

6.1 Mentoring Young Investigators

If the investigator is not experienced in the conduct of clinical research at UH, the Department Chair or designee will identify a mentor in the applicable field; preferably during the study design phase.

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6.2 Project Feasibility Assessment
Before beginning a new research proposal at UH, investigators must complete a protocol feasibility assessment to ensure that there are adequate resources and potential participants to successfully conduct and complete the study. See UH Clinical Research SOP *SP-201 - Protocol Feasibility Process*.

6.3 Protocol Oversight/Sponsorship
The Sponsor-Investigator of an investigator-initiated study that is regulated by the FDA under an IND (21 CFR Part 312) or IDE (21 CFR Part 812) must be a UH attending physician (MD/PhD; MD; DO; OD). The FDA-regulated trial that is held by the sponsor must be within the sponsor-investigator's scope of practice. In addition, the acting sponsor-investigator must not delegate the primary responsibly of oversight, project implementation, and treatment oversight to a trainee or anyone else who is not an attending physician (i.e., MD/PhD, MD, DO, or OD).

The oversight and sponsorship of a clinical trial is critical to the successful outcome of a research study and the engagement and experience of the principal investigator (PI) is necessary.

6.4 Project Design/Protocol Creation
  6.4.1 Sponsor-Investigator creation of a protocol includes creation of:
    6.4.1.1 a project design that will meet scientific and ethical review;
    6.4.1.2 IRB-approved submission; and
    6.4.1.3 corresponding study budget and coverage analysis to ensure adequate funding to complete the study.

  6.4.2 Templates including all necessary elements for both protocols and consent forms are available on the CRC website and should be used prior to submitting for review by the local institutional review board and the Food and Drug Administration, if applicable. UH Research SOP *SP-202* describes the Coverage Analysis & Clinical Budget Development Process Flow.
  6.4.3 Certain investigational products must be added to the hospital charge master to assure compliant billing. Sponsor- Investigators must ensure proper monitoring of the investigation according to IND regulations and as such must establish the costs for routine monitoring or quarterly auditing through the Research Support Core or ORC, respectively. The investigator must engage the Research Finance Specialist core to assist in this process.
  6.4.4 The sponsor-investigator should also consult with a statistician to verify their statistical outcomes and ensure endpoints can be met based on the proposed patient number. Statistical services may be requested by contacting the Research Support Core.

6.5 Investigational Products
If the investigator-initiated research proposal includes the use of a drug, device, and/or biologic and the investigator is unsure if it's approved for use by the FDA for the study's therapeutic target, the investigator should contact the Research Support Core

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for assistance in helping to determine if the protocol needs to be reviewed by the FDA. Refer to the *Investigator Manual for IRB Submissions, Chapter 11 - Drugs* for additional information regarding instruction requirements. This includes the required use of Investigational Drug Services.

6.6   Study Funding
The sponsor-investigator must identify external funding or sufficient non-operating internal funding to support the research plan, in accordance with UH System Policy *R-41*.

6.7   Data Management
The FDA mandates that any study regulated under the Code of Federal Regulations must adhere to FDA 21 CFR Part 11 Compliance, or the electronic storage and entry of clinical research information. For more information, contact the Research Support Core. See *Investigator Manual for IRB Submissions, Chapter 26 – GDPR Requirements*.

Research that is not regulated by the FDA is not held to this standard, however, every measure should be taken to ensure all research information and data is stored in a secure location to minimize the risk.

6.8   Study Implementation and Oversight
Investigator-initiated research requires an increased level of regulatory and clinical coordination support. Each investigator should ensure that they have experienced regulatory and clinical support to help conduct the research study and maintain compliance throughout the course of the study.

The CRC strongly recommends that the individual responsible for the regulatory and clinical coordination duties is not a fellow, resident, or medical student, unless these trainees have undergone the necessary credentialing and training, including the completion of UH Investigator Training. If personnel are not available within a department to assist with an investigator initiated research study, the CRC has fee-for-service support available that can assist with any regulatory and clinical coordination duties.

6.9   Federal and Local Compliance
The Code of Federal Regulations (21 CFR Part 312 and 812) mandates that the sponsor of a drug, device, or biologic research trial provide independent monitoring of the information relating to their research trial (this is independent from the function of a Data Safety Monitoring Board or a Medical Monitor). The FDA acknowledges the responsibility of the placement of a monitor to be with sponsor-investigator.

Regular monitoring of sponsor-investigator research studies is expected. Fee-for-service monitoring services are available through the CRC Research Support Core upon request. If adequate monitoring oversight is not established the study will be subject to mandatory quarterly auditing, with associated fees, by the Human Research Protection Program. All studies at UH are subject to audit by the Human Research

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Protection Program; FDA; or other Regulatory bodies and those studies without an established monitoring oversight plan will be subject to mandatory audits. Contact the Human Research Protection Program for additional details.

7. **REFERENCES**
   - FDA 21 CFR Part 312 Investigational New Drug Application
   - FDA 21 CFR Part 812 Investigational Device Exemption
   - FDA 21 CFR Part 11 Electronic Records; Electronic Signatures – Scope and Application
   - UH Clinical Research SOP Manual
     - GA-106 - Transfer of Protocols out of UH
     - SP-201 - Protocol Feasibility Process
     - SP-202 - Coverage Analysis & Clinical Budget Development Process Flow
   - Investigator Manual for IRB Submissions
     - Chapter 7 – Required Approvals
     - Chapter 11 – Drugs
     - Chapter 26 – GDPR Requirements
   - UH System Policy R-41
   - Informed Consent Template
   - UH Investigator Training

8. **FORMS OR ATTACHMENTS**
   - Locally Held IND/IDE Agreement (HRP-602) (SpartaIRB Template)

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – January 8, 2021

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GA-109 – Departing Investigators

1. PURPOSE:
To integrate research responsibilities into the routine departmental off-boarding process by ensuring the proper transfer or closure of all active research studies conducted by a Principal Investigator employed by University Hospitals Health System, Inc. (UHHS), including any affiliate, or otherwise approved by the UHHS Institutional Review Board (IRB).

2. SCOPE:
All research protocols under the purview of the UHHS IRB including those conducted at UHHS or any facility affiliated with UHHS (Trial Site).

3. RESPONSIBLE INDIVIDUALS:
This SOP applies to Principal Investigators (PI) and Department Administrators of UHHS as well as the UHHS IRB/Human Research Protection Program (HRPP)

4. RELATED TERMS AND DEFINITIONS:
Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
The PI is responsible for the proper transfer or closure of the research study prior to his or her departure from UHHS. Once the UH Human Research Protection Program (HRPP) is notified that an investigator is leaving UH, the investigator is not permitted to start any new research at UH unless given permission by the HRPP Manager

6. PROCEDURES:
6.1 Faculty listed as Principal Investigators (PI) on Human Subjects Research studies must notify UHResearchCompliance@UHhospitals.org at least 60 days prior to departure to discuss the status and plan for all open studies, existing data, and records.

6.2 The UH Human Research Protection Program (HRPP) Core will provide a list of open studies that require action. This will be sent via email to the PI and other involved parties including the IRB Specialist assigned to that department.

6.3 The PI will communicate departure and collaborate with the Clinical Research Center (CRC) to define an acceptable action plan for each open study. Please note that some options may require additional contracts and/or pre-approval.
    6.3.1 Potential options for open studies
        6.3.1.1 Close study completely;
        6.3.1.2 Transfer study to new PI at UH and do not open at new Institution;
        6.3.1.3 Close study at UH and open at another Institution;
        6.3.1.4 Transfer study to new PI at UH and open at new Institution.

6.4 The PI is ultimately responsible for completing all of the items on the appropriate checklist applicable to each study. Checklists for each option presented in Section 6.3

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available in section 8 and in the [UH Clinical Research Toolbox](#).

    6.4.1   Failure to close or transfer of all research study processes (including ClinicalTrials.gov records) PRIOR to departure from UH, could result in a for-cause termination.

6.5   If a response to the initial request is not received, the HRPP will send a follow-up email reminder prior to the PI's departure with escalation to the PI's Department Chair/Chief, Administrator, and/or study team members.

6.6   If no response is received after the PI has left UH, the study(ies) will be referred to UH Research Compliance for a review. Studies without a UH-employed PI will be considered abandoned and may be suspended, terminated, or administratively closed by the UHHS IRB

6.7   <u>Data & Materials</u>

    6.7.1   All study data or study materials (including all samples), in any format, are the property of UHHS. No study data, materials or samples may be transferred outside of UHHS without the following:

        6.7.1.1 Permission from the department chair;

        6.7.1.2 Completion of study closure or transfer responsibilities as listed in this SOP (including the attached checklists);

        6.7.1.3 Outstanding account balances have been reconciled; and

        6.7.1.4 A contract, approved by the UHHS law department, in place for the transfer that has been approved by the UH IRB and CRC leadership.

    6.7.2   De-identified data or a Limited Data Set may be transferred using a data use agreement approved by the UHHS law department or the Grants & Contracts core office. Protected Health Information is generally not permitted to be transferred and would require specific approval on a case-by-case basis from the UHHS Law Department, the UH IRB, and the IRB of the institution receiving the data. To request the transfer of any data, please contact your designated IRB Specialist and Grants & Contracts Specialist.

6.8   <u>Equipment & Funds</u>
If any equipment has been purchased with grant funds and is required to be transferred for the sole purpose of completing the study, then approval is required from the department chair and the director of grants management. If any funds remain in the account and are required to be transferred for the sole purpose of completing the study, then approval is required from the department chair and the director of grants management. No funds will be transferred until all outstanding payments have been made. If a study has already been completed, then no funds or equipment should be transferred.

6.9   <u>Subject Notification</u>
In order to determine if subject notifications required, the PI should refer to the Investigator Manual for IRB Submissions. The Manual should be followed for all guidelines related to appropriate timelines of notification and requirements for obtaining consent from study subjects, if applicable. Please contact your designated IRB Specialist regarding any

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subject communications since IRB approval will be needed.

7. REFERENCES:
- [ICH-GCP E6 (R2)](#)
- [Investigator Manual for IRB Submissions (Ch. 5)](#)

8. FORMS OR ATTACHMENTS:
- [Transfer Study to new UH PI Checklist](#)
- [Transfer Study to new UH PI and open at another Institution Checklist](#)
- [Study Closure at UH Checklist](#)
- [Study Closure at UH and open at another Institution Checklist](#)

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – July 6, 2022

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GA-110 - Management of Clinical Research Expense Invoicing

1. PURPOSE:

To assure efficient communication, timely invoicing and payment of research-related recoverable expenses.

2. SCOPE:

This SOP applies to invoice management of externally-funded projects excluding those projects with Federal funding.

3. RESPONSIBLE INDIVIDUALS:

Principal investigators (PI), research nurses, research coordinators, departmental administration and other departmental research staff, Clinical Research Center (CRC) Core Offices: Post-Award Grants Accounting, Research Finance, Pre-Award Grants & Contracts, and Research Support Core.

4. RELATED TERMS AND DEFINITIONS:

Coverage Analysis (CA) – A systematic review of all patient care procedures listed in a study protocol to determine which are allowable to bill to third party insurance. Non-billable services are budgeted for payment by the research study sponsor.

Fixed Cost Charges – Business costs to be charged that are consistent whatever the quantity of goods or services to be produced. E.g. study start-up fees, monitoring visit fees, non-patient care supplies, salary support, and annual fees.

Grant Accountant (GA) – Individual who performs all post-award functions. E.g. award setup, fixed cost invoicing, salary/non-salary charges, adjustments and cash application, etc.

Grant Accounting Invoice Request Form (GAIRF) – Intake form which allows GA to invoice expenses that have been deemed recoverable.

Grants & Contracts Specialist (GCS) – Individual who provides oversight of the legal and budget aspects of grants, including negotiation of adequate study budgets.

Invoiceable – Billable item which requires an invoice to the sponsor.

Patient Care Charges – Expenses for items or services directly related to patient care.

Research Finance Specialist (RFS) – Individual who performs budgeting, billing reconciliation and invoicing of patient care charges. E.g. re-consent fees, as needed patient care charges, and serious adverse event reporting.

RFS IRF – Research Finance Specialist Invoice Request Form, similar to the GAIRF, and one of the methods end users can notify the RFS of patient care invoiceables.

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Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
The PI is ultimately responsible for the fiscal health of their project and to avoid residual grant deficit (UH Policy F-43 Grants Accounting Management). Departments (and the CRC Research Support Core if acting on behalf of the department) are responsible for knowing study contractual and payment terms, and to communicate invoice requests correctly and timely to GA and RFS teams to facilitate successful payment for services.

6. PROCEDURES:
  6.1   **Study Start-Up**
      6.1.1   Invoiceable fees will be negotiated by the GCS team and documented internally as follows:
         6.1.1.1   Fixed cost invoiced\able fees will be in the Industry Sponsored Research Budget Fees template for each research study record within Velos eResearch; this budget will be maintained by the GCS team
            6.1.1.1.1   This budget includes negotiated fees requested by the department via the Invoiceable Fees Checklist form

         6.1.1.2   Patient care invoiced\able fees
            6.1.1.2.1   Invoiced\able patient care costs associated with a fixed time point will be listed at that time point on the coverage analysis template under the purple "invoiceables" banner
            6.1.1.2.2   All invoiced\able fees with or without fixed time points will be summarized in a grid at the bottom left of the CA template
            6.1.1.2.3   Study teams will communicate event completion within each patient's unique schedule in Velos eResearch by documenting a status of "Done", "Coord Complete" or "Coord Reviewed" as appropriate.

         6.1.1.3   Investigational Drug Service (IDS) fees
            6.1.1.3.1   Upon IDS' receipt of a completed electronic Service Request from the department/division responsible party, IDS will generate an initial cost quote for services during study start-up, based upon established published fee rates.
            6.1.1.3.2   If a quote must be revised based upon negotiation with the sponsor, GCS will update the Invoiceable Fee Master and notify IDS via emailed PDF of the revised final fees the sponsor is willing to pay.
            6.1.1.3.3   IDS quote changes will be documented as follows:
                6.1.1.3.3.1   GCS will update the Sponsored Research Budget Fees template for each research study record in Velos eResearch.
                6.1.1.3.3.2   GCS will notify RFS regarding any required per patient changes and RFS will update the CA

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template accordingly.

6.1.2 Upon contract execution, the GCS will:
6.1.2.1 Send the final budget to the IDS manager with the subject: FINAL IDS FEES (see above at 6.1.1.3.2)
6.1.2.2 Distribute the final CTA via email, including final sponsor budget and the Velos Study Number.
6.1.2.3 Upload final CTA and final sponsor budget in the "Budget & Contract" category of the Documents tab for study record within Velos eResearch.
6.1.2.4 Distribute and save any contract amendments as above

6.2 **Invoicing**

6.2.1 It is department responsibility to know the contractual invoice terms, including any timeline parameters limiting the timeframe allowable for an invoice to be sent and/or paid

6.2.2 Initial study start-up fees do not require the submission of a GAIRF and will be invoiced by GA upon notice of contract execution. All other invoiced/able expenses incurred during the conduct of a study must have the department/division responsible party submit a GAIRF to the appropriate CRC business office as outlined below.

6.2.3 To determine charges to be invoiced, the department/division responsible party will refer to the 'Budget & Contract' Document category and/or the budget module for each specific study record in Velos eResearch
6.2.3.1 Review the study executed contract budget
6.2.3.2 Review the study Invoiceable Fee Master
6.2.3.3 Review the study per patient CA documentation

6.2.4 For non-patient care fixed cost invoicing, department will send GAIRF to GA and the GA will generate an invoice within 30 days as per protocol outlined in UH policy R-37
6.2.4.1 See Appendix A: "Invoice Responsibility List" for a detailed list of items to invoice by the GA team via GAIRF
6.2.4.2 GAIRFs should be submitted electronically on the form name "GAIRF_Grants Accounting Invoice Form" on the Forms tab of each specific research study record within Velos eResearch.

6.2.5 Patient care invoiced items will be sent to the RFS as per the below
6.2.5.1 See Appendix A: "Invoice Responsibility List" for a detailed list of invoiced items managed by the RFS
6.2.5.2 Invoiced/able fees associated with a fixed time point will be listed in the Velos calendar at the end of the visit
6.2.5.2.1 These invoiced fees do not require submission of an invoice request form
6.2.5.2.2 When such items have been performed, the study

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coordinator will mark a status of "Done","Coord Complete", or "Coord Reviewed" (as appropriate) with the DOS for that specific event within each patient's patient schedule in Velos eResearch.

    6.2.5.2.3 The RFS will invoice the sponsor based upon the department's completed patient schedule documentation

        6.2.5.2.3.1 Invoicing will be monitored monthly utilizing Velos reporting and follow-up on unpaid invoices will occur, and be documented in, Velos.

6.2.5.3 For services that occur at random time points or are not patient specific, the department must notify the RFS of occurrence by sending a completed RFS IRF on the Forms tab of the specific research study record within Velos eResearch.

    6.2.5.3.1 The department will need to clearly indicate which service is being invoiced by checking the correct description

6.2.5.4 Re-consent invoice notification will be communicated by the study coordinator via updating the patient status as "Re-consent signed"

6.2.5.5 Study specific invoiceable fees will be communicated by the department updating the study status by choosing status type "Study specific invoiceable fees" and selecting the correct study status **or** completing and submitting a RFS Invoice Request Form (RFS IRF)

6.2.6 Contracted Milestone Invoicing

    6.2.6.1 For trials with a CA, the RFS will invoice for patient care milestones based upon contractual terms set-up as milestones in the patient calendar. Additional requests may be submitted by the department using the options outlined in section 6.2.4

    6.2.6.2 For CA Exempt trials, the GA will invoice for milestones once a completed GAIRF has been received from the department

    6.2.6.3 Documentation of all GA study invoicing will be saved in an "Invoicing" file folder at the department level and RFS invoicing will be saved at the study level in S:\\Master Research\Research Billing\(Department Name)\(Study Name)

    6.2.6.4 Invoices will be sent to appropriate sponsor indicated email address, online submission portal or physical address with a copy to UHGrantInvoices@UHhospitals.org

6.3 **IDS, IRB, and CA Exempt Trial Invoicing**

6.3.1 IDS and IRB start-up costs will be automatically invoiced by the GA team and funds transferred to the appropriate account

6.3.2 For ongoing IDS study expenses, departments will provide GAIRF form to GA

6.3.3 For ongoing IRB study expenses, such as amendments, annual renewals and other fixed costs:

6.3.3.1 The study coordinator will file all amendments and renewal approvals in the appropriate study 'Invoice' folder

6.3.3.2 Department will include the IRB fees on their GAIRF form and submit to GA

6.3.4 Invoices will be sent to appropriate sponsor indicated email address, online submission portal or physical address with a copy to UHGrantInvoices@UHhospitals.org

7. REFERENCES:
- Velos eResearch 11.2: Requesting Invoicing
- Clinical Research Standard Operating Procedure
  - SS-314 Velos eResearch Data Entry / Access
- UH System Policies
  - F-43 Grants Accounting Management
  - R-37 Centralized Sponsor Invoicing/Billing

8. FORMS OR ATTACHMENTS:
- GAIRF
- Appendix A - Invoice Responsibility List

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Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center
– September 28, 2023

Appendix A – Invoice Responsibility List Event	Dept Communication	CRC Invoice Responsibility
Investigational Pharmacy Fees		
Pharmacy Start-up Fee	NA - automatic	GA
Pharmacy Annual/Monthly Maintenance Fee	GAIRF	GA
Pharmacy Destruction Fee	GAIRF	GA
Off Main Campus Delivery Fee & Transport Charge Fee	GAIRF	GA
Multiple Drug Order Set Review Fee	GAIRF	GA
Pharmacy Training Fee	GAIRF	GA
On-Site Destruction Fee	GAIRF	GA
After Hours or STAT Support Fee	GAIRF	GA
Addendum (IP Modification) Fee	GAIRF	GA
Remote Monitoring Fee	GAIRF	GA
Sponsor Compliance/FDA Audit Fee	GAIRF	GA
Sponsor Required Storage of Used Product Fee	GAIRF	GA
Special Equipment Fee	GAIRF	GA
Mandatory Compliance Audits for IDS Exception Study Fee	GAIRF	GA
DCRU Fees		
DCRU Start-up Fee	NA - automatic	GA
CRC Fees		
CRC Administration Fee	NA - automatic	GA
GA Administration Fee	NA - automatic	GA
Reliant Review Administration Fee	NA - automatic	GA
CRC Financial Management Fee	NA - automatic	GA
UB04 / 1500 / Economic / Healthcare Utilization Fee	NA - automatic	RFS
Office of Research Compliance Quarterly Audit Fee (Investigator held IND studies that are IDS exempted)	GAIRF	GA
Complion e-Regulatory System Fee	NA - automatic	GA
Clinical Trial Agreement Revisions Fee	GAIRF	GA
UH IRB Review Fees		
IRB Initial Review Fee	NA - automatic	GA
IRB Continuing Review Fee	GAIRF	GA
IRB Modification Fee	GAIRF	GA
IRB Study Closure Fee	GAIRF	GA
Departmental Fees		
Department Start-up Fee	NA - automatic	GA
PI Activation Fee	NA - automatic	GA
% Coordinator / Research Nurse Effort ~ Study Management	GAIRF	GA
Advertising Fee	GAIRF	GA
Annual Administrative Maintenance Fee	GAIRF	GA
Archiving/Record Retention Fee	GAIRF	GA
Investigator Meeting	GAIRF	GA
IRB Initial Review Submission Prep Fee	NA - automatic	GA
IRB Protocol Amendment Submission Prep Fee	GAIRF	GA
IRB Protocol Amendment w/ ICF Changes Submission Prep Fee	GAIRF	GA
IRB Continuing Review Submission Prep Fee	GAIRF	GA
IRB Termination Submission Prep Fee	GAIRF	GA
Sponsor Initiated Compliance/FDA Audit Fee	GAIRF	GA
Study Close Out Fee	GAIRF	GA
PI Close Out Fee	GAIRF	GA
Training Fee	GAIRF	GA
Patient Care		
Adverse Event Reporting Fee (Outside IND Safety Letters)	RFS IRF	RFS
Commercial Drug Acquisition Add-on Dispensing Fee *(Pharmacy)*	IDS spreadsheet	RFS
Monitoring Visits Fee	RFS IRF	RFS
Patient Care Not Performed On All Patients	RFS IRF	RFS
Patient Recruitment/Monthly Screening Fee	RFS IRF	RFS
Per Patient Pharmacy Administration Charges *(Pharmacy)*	IDS spreadsheet	RFS
Re-Consenting Fee	RFS IRF/GAIRF	RFS/GA* (*CA Exempt trials)
Re-Monitoring Fee	RFS IRF/GAIRF	RFS/GA* (*CA Exempt trials)
Remote Monitoring Fee	RFS IRF/GAIRF	RFS/GA* (*CA Exempt trials)
Re-Screening Fee	RFS IRF/GAIRF	RFS/GA* (*CA Exempt trials)
Research PFT Lab Charges	PFT Lab monthly invoice	RFS
SAE Reporting Fee	RFS IRF/GAIRF	RFS/GA* (*CA Exempt trials)
Screen Failure	RFS IRF/GAIRF	RFS/GA* (*CA Exempt trials)

SP-201 - Protocol Feasibility Assessment

1. **PURPOSE:**
   This Standard Operating Procedure (SOP) describes the process for obtaining a feasibility assessment of a research protocol through the UH Clinical Research Center's (UHCRC) use of the EMR Query Utilities. Feasibility assessment is optional prior to implementing a research protocol at University Hospitals. The intention of this service is to aide Investigators in protocol design.

2. **SCOPE:**
   This SOP provides instruction and sets minimum standards regarding the process for reviewing the recruitment feasibility of a research protocol throughout University Hospitals Health System (UHHS).

   Departments and/or Investigators may utilize and complete the UH Clinical Research Center (UHCRC) Protocol Feasibility assessment to aide in evaluating recruitment feasibility of a research protocol.

3. **RESPONSIBLE INDIVIDUALS:**
   This SOP applies to all Investigators who would like to implement a research study that prospectively enrolls human subjects. Investigators and study teams may work with UHCRC to evaluate patient recruitment feasibility and protocol design, specifically inclusion and exclusion criteria, to promote successful study recruitment.

   It is encouraged that senior research members within the department mentor any new Investigator conducting research.

4. **RELATED TERMS AND DEFINITIONS:**
   Requester - The REDCap user submitting the UHCRC Protocol Feasibility. This may be a study coordinator, department administrator, Investigator, etc.

   Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. **POLICY STATEMENT:**
   All research protocols detailed above are eligible to request an optional CRC Protocol Feasibility assessment. Studies are still required to follow internal study start-up processes prior to implementation at UH.

6. **PROCEDURES**
   Feasibility is completed in REDCap® and focuses on assessing the number of eligible participants available for recruitment within UHHS. To obtain the number of potentially eligible participants for the study, a query of the electronic medical record (EMR) is conducted through TriNetX Software or Epic SlicerDicer based on the information provided in feasibility review request by the Requester.

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6.1   UH CRC Protocol Feasibility Assessment
      Purpose: Information needed in this section pertains to study and site accrual goals and key inclusion and exclusion criteria as specified in the study protocol. To complete, the Requester populates information directly from the protocol relating to accrual requirements (i.e., study accrual, site accrual, estimated recruitment start and stop date) as well as inclusion and exclusion criteria.

   6.1.1   Requesters enter the study by submitting the feasibility review request by following this link
           https://redcap.uhhospitals.org/redcap/surveys/?s=AP7KJ97PTA

   6.1.2   Requesters enter the following information:
      6.1.2.1   Study Team Information
      6.1.2.2   Study Information
      6.1.2.3   Enrollment Information
         6.1.2.3.1   Three inclusion criteria and three exclusion criteria are encouraged for submission to improve results; more or fewer criteria may be entered as necessary.
      6.1.2.4   Requesters upload a Protocol or Protocol Synopsis (optional).
      6.1.2.5   Requesters Submit the Request.

   6.1.3   After submission, a notice is sent to the UHCRC through REDCap for a prompt to enter the information into a utility to query the EMR.

   6.1.4   A member of the CRC will enter information into an EMR query utility exactly as provided by the Requester to obtain the number of eligible participants within UHHS for the research trial.

   6.1.5   Query results are provided to the Requester and study team by the CRC within 3 business days; results include a query screenshot detailing outcomes from the UHHS database. UHCRC recommends that 5 times the number of required participants be available in the UH systems (5 x Anticipated Accrual at Local Site) to support successful study recruitment, although it is not required.

   6.1.6   Email notifications from the CRC alert Requesters regarding the outcome for the Feasibility review within three (3) business days:
      6.1.6.1   Meets Feasibility Recommendations (query returns ≥ 5 times Anticipated Accrual at Local Site) for implementation.
      6.1.6.2   Limited Patients Meet Criteria (query returns < 5 times Anticipated Accrual at Local Site) due to the low number of eligible participants in the UHHS database. The study team may proceed with Study Start-up Activities but are encouraged to schedule a consultation with the feasibility team to assist with protocol design with the aim to increase eligible participants.
         6.1.6.2.1   The requestor will receive an email from UHCRC with instructions to schedule a consultation if desired by the study team. If a response is not received within 2 weeks, UHCRC will consider the request complete.

7. REFERENCES:

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- Clinical Research SOP SS-314 – Velos eResearch – Access and Data Entry Requirements

8. FORMS OR ATTACHMENTS:
- Link to UH CRC Protocol Feasibility: https://redcap.uhhospitals.org/redcap/surveys/?s=AP7KJ97PTA

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – October 31, 2023

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Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SP-202 - Coverage Analysis & Clinical Budget Development Process Flow

1. **PURPOSE:**
   To standardize the UH Clinical Research Center's (UHCRC) process for research coverage analysis / clinical patient care budget development and approval.

2. **SCOPE:**
   All research projects that involve clinical patient care and are conducted within the University Hospitals Health System, must follow stated policy requirements for coverage analysis (CA). Process variations to implementing CA and clinical budget development may occur dependent upon the situation. This SOP addresses all trials, excepting those trials administratively managed by the Seidman Cancer Center (SCC) Clinical Trials Unit (CTU).

3. **RESPONSIBLE INDIVIDUALS:**
   UHCRC Personnel; Departmental Research Personnel

4. **RELATED TERMS AND DEFINITIONS:**
   Coverage Analysis (CA) – a uniform method of analyzing the items and services provided in a clinical trial to determine if that item or service can be appropriately billed to Medicare and other insurers. Such an analysis, when completed prior to study start and formally documented, can help provide a more accurate assessment of study costs for budgeting purposes; avoid submission of incorrect claims (protecting an institution from violations of the False Claims Act); identify non-covered study costs; and assist in the accurate coding of covered charges on billing claims.

   Local Coverage Determination (LCD) – specific payment decisions made by a regional Medicare Administrative Contractor (MAC) for their assigned states or a region of the country. Approval from the local MAC is required to bill for services related to the use of Category B devices.

   Medicare Qualifying Status – the determination whether a clinical trial may have services covered (paid) by Medicare. To qualify, trials must evaluate an item or service that falls within a Medicare benefit category; must have a therapeutic intent; enroll patients with a diagnosed disease plus have seven desirable characteristics or meet deemed status. See National Coverage Determination (NCD) for Routine Costs in Clinical Trials, manual section number 310.1.

   National Coverage Determination (NCD) – part of Center for Medicare and Medicaid Services Clinical Trial Policy; explains medical necessity, billing limitations and coding guidelines for services provided as part of a clinical trial. For approved clinical trials, defines the costs that Medicare will cover provided that the item or service is otherwise available to a Medicare beneficiary and specifies the claim format for billing such covered services.

Velos eResearch Clinical Trial Management System (CTMS) – a web-based application with capabilities to manage administrative data for studies throughout their lifecycle and manage patient enrollment and research patient billing.

Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. **POLICY STATEMENT:**
   Related to UH System Policies R-2, R-16, and R-39.

6. **PROCEDURES:**
   6.1   Notification of a new clinical trial requiring CA assessment will be sent to ResearchFinance@UHhospitals.org via:
       6.1.1   Automated Velos notifications for externally funded projects; which are generated once the department enters the project protocol, contract, and budget into the Velos study record
           6.1.1.1   In order for alert to trigger, above documents must be added using the correct document category (e.g. Protocol, Informed Consent, Budget & Contract)
       6.1.2   IRB specialist "Ancillary Review" notification for internally or federally funded projects
       6.1.3   ResearchFinance@UHhospitals.org will be monitored daily by the RFS team

   6.2   Upon notification, the Research Finance Specialist (RFS) will update the study status in Velos to "CA - Notification received"
   6.3   The assigned RFS will email the clinical department contact to initiate dialogue and schedule a meeting to review the CA and patient care budget development.

   6.4   Working in conjunction with the departmental clinical team, the RFS will validate whether the project is a qualifying clinical trial.
       6.4.1   Documentation for qualifying status will occur on the PI Information Form in Velos.
       6.4.2   Per federal regulations, PI attestation of qualifying status is required prior to the enrollment of patients on trial.
       6.4.3   To ensure completion prior to enrollment, automatic Velos reminders to complete the Qualifying Status attestation will be sent to the study coordinator, PI and Research Finance Director in escalation based upon study start-up statuses
   6.5   For all trials with billable patient care, the RFS will work with the clinical department to complete a CA and patient care budget which will include all of the required clinical care and billable items listed in the protocol.
       6.5.1   CPT coding for "Patient care" charges will be identified by the RFS and current charge master pricing with approved research discounts will be used.
       6.5.2   The RFS will document NCD, LCD or medical national standards in the following locations:

6.5.2.1 CA/budget draft excel template

6.5.2.2 On the "event" notes line in the Velos study calendar

6.5.3 Once patient care charges, sponsor personnel time detail, sponsor payment, and coverage determinations have been made, the RFS will update the Velos study status as "CA – RFS draft complete" and send to the department for review and personnel time input

6.5.4 The DCRU administrative team will provide any DCRU charges to the RFS for input into the budget. It is departmental responsibility to submit a DCRU Service Request form through Velos.

6.5.5 If the project is internally funded, an 'Internally Funded Research Project Request Form' will be provided to the clinical department contact.

6.5.5.1 The clinical department contact will complete the 'Internally Funded Research Project Request Form' and obtain the necessary clinical departmental/division approvals and signatures before returning to their RFS.

6.5.5.2 The RFS will then complete the form by reaching out to the appropriate department Finance Director to validate the balance in the identified account and obtain the clinical department Finance Director signature.

6.5.5.3 The RFS will upload and attach the completed form to the study "Documents" tab in Velos

6.5.6 The RFS will obtain PI (or designee) sign-off on the CA/budget final draft and upload the email documentation of approval in the Velos study record. They may also save in the department study specific CA folder in S:/Master Research/Research Billing.

6.5.6.1 The RFS will also update the study status of "CA – Draft/budget dept approval" in Velos eResearch.

6.6 For externally funded projects, once the CA/budget final draft has been approved by the department/PI, the RFS will notify Grants & Contracts Specialist (GCS).

6.7 For studies that do not have billable patient care, documentation of a waiver of CA will be added in the Research Finance Ancillary Review section of the project record in the IRB system and as study status "Study – CA exempt" in Velos, both with comments to include that a CA is not needed & the rationale why.

6.8 The GCS will collaborate with the department and RFS as needed during negotiation of the contract budget, and payment terms.

6.8.1 Once finalized, the GCS will generate a memo to the appropriate institutional official for sign-off of approval for the project.

6.9 Post Award communication

6.9.1 Internally funded trials – upon IRB approval, the Grant Accountant will set-up a PTAEO account specific to the project once a completed 'Internally Funded Research Project Request Form', and an approved CA / clinical budget has been verified.

6.9.1.1 Upon IRB approval, the RFS will forward, via email, a copy of the

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completed & signed 'Internally Funded Research Project Request Form' to the assigned Grant Accountant.

6.9.1.2 The Grant Accountant will follow the award set-up procedure and upon set-up will send a 'Notice of Grant Award' to the RFS, DCRU and clinical departmental contact and update the Velos Study Summary 'More Study Details' with the PTAEO number.

6.9.2 Externally funded trials – upon contract execution, the GCS will send an email to the clinical department and the Grant Accounting team.

6.9.2.1 The Grant Accountant will follow the award set-up procedure and upon set-up will send a 'Notice of Grant Award' to the RFS, DCRU and clinical departmental contact and update the Velos Study Summary 'More Study Details' with the PTAEO number.

6.9.3 Federally funded trials – the RFS will check for the project speed type from CWRU department administrators.

6.9.3.1 Once the CWRU project speed type & a department N award is available, the RFS will create a new task to add the new speed type to the appropriate patient care N award and enter the speed type number in the "description" field for the task. (Note: the grant award number will populate the "task name" field.)

6.9.3.2 RFS will add new information to "N Awards Res Pt Blg" spreadsheet located at path S:\\Center for Clinical Research\Research Patient Billing\N Award

6.9.3.3 If a department N award isn't set-up, the RFS will contact the Grant Accountant assigned to that department to request an award set-up.

6.9.3.4 The patient care N award number will be the PTAEO listed in the Velos Study Summary 'More Study Details'.

6.9.4 Epic Research Module Billing Protocol/Study Calendar – the RFS will ensure a study calendar/billing protocol is released in Epic, based on the Coverage Analysis, for use to create patient timelines to support encounter linking.

6.10 Managing Amendments

6.10.1 The department will notify their GCS when there is an amendment to existing clinical protocols.

6.10.2 For amendments that include changes to clinical care, the department will also contact their RFS.

6.10.3 The RFS will review the amendment and update the CA/budget template and Velos patient calendar as needed, informing the GCS when complete.

6.10.4 The RFS and GCS teams will update amendment study statuses in Velos: "CA-Amendment Draft Complete", "CA-Amendment Dept Approved", "CTA-Amendment Executed"

6.10.5 Coverage analysis updates will be completed in order of date of receipt of notification.

7. REFERENCES:

- National Coverage Determination for Routine Costs in Clinical Trials, section 310.1
- UH System Policies in UH PolicyStat

- R-2 – Research Patient Billing
        - R-16 – Grants Accounting: Development of Clinical Trials Budgets
        - R-39 – Clinical Research Investigation
        - R-41 – Internally Funded Research Policy
    - Training:
        - [Velos for Principal Investigators](#)
        - [Velos for Study Coordinators](#)

8. FORMS OR ATTACHMENTS: None

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – October 31, 2023

SP-203 – Radiology Research Review

1. PURPOSE:
To establish standards for the utilization and review of radiology services for clinical research projects conducted at University Hospitals of Cleveland, to be reviewed by the Department of Radiology to ensure applicable safety, compliance, feasibility, and effort requirements are met. The radiology review process is separate from the Radiation Safety Review. If Radiation Safety Review is needed in addition to the Radiology Research Review, please submit the separately to the Radiation Safety Committee.

2. SCOPE:
All research studies utilizing UHHS Radiology Services in the department of Radiology.

3. RESPONSIBLE INDIVIDUALS:
Clinical and research personnel who assist with initiating research projects.

4. POLICY STATEMENT:
Research studies which use radiology services require the approval of the Department of Radiology's Research Review Committee, unless they have a radiologist as a Principal Investigator or a funded Radiology Co-Investigator.

5. RELATED TERMS AND DEFINITIONS
Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

6. PROCEDURES:
  6.1 **Submitting Radiology Intake Form**
      6.1.1 Complete study start-up forms located in VELOS under Forms, Radiology Information and Review Form (If not already completed).
         6.1.1.1 Prior to completing the Radiology Intake form within Velos System, the *Summary Tab* must be completed.
         6.1.1.2 Applicable study documents needed for review should be uploaded to the Documents Tab. The required documents can be pending IRB approval or in template format. Documents include:
            6.1.1.2.1 Protocol (Required)
            6.1.1.2.2 Consent Form (Required)
            6.1.1.2.3 Imaging Manual (If Applicable)
            6.1.1.2.4 Other Study Documents (If Applicable)

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**If the documents listed above have already been uploaded to the Initial Study Documents form, documents do not need to be provided separately for the Radiology Review.

    6.1.1.3 Complete the form Radiology Information & Review form in Velos
        6.1.1.3.1 Select all applicable UH imaging locations for the study (If you do not select any additional sites, we will assume you are only completing study procedures at UHCMC).
        6.1.1.3.2 Select all applicable imaging requirements.
        6.1.1.3.3 Select the type of exam(s) for study (Appendix C).
        6.1.1.3.4 Estimated number of subjects to be enrolled each year
        6.1.1.3.5 Number of radiology exams per subject per year:
        6.1.1.3.6 Personnel Completing Radiology Request Form
        6.1.1.3.7 Upload a copy of the Sponsor's Imaging Capabilities Questionnaire (If Applicable).
        6.1.1.3.8 Upload any other study documents which are not already uploaded under the Protocol Information Form
        6.1.1.3.9 Ready to be reviewed by Radiology: Yes/No

    6.1.1.4 Once completed, verify that the question "Is this study ready to be reviewed by Radiology" has been selected. When this question is answered and the form status has been changed to "Completed", Velos will automatically send a notification Radiology to review.

6.1.2 Confirmation email will be sent to personnel completing the request within 2 business days. The email will confirm that all documents needed for review have been received. Based upon received documents, estimated category and fee will also be included within the confirmation email.

6.1.3 The review fee and turn-around time for completion are dependent on the category of the study. Studies which are internally-funded will be exempt from the Review Fee. Please see Appendix B for Radiology Review Categories. In addition, the review flow chart (Appendix C) explains the determination of the review process.

6.1.4 The radiology review team must have all required research related documents as mentioned above before review can begin. This review may be done in parallel to other study start-up processes such as contract/budget negotiation, or Radiation Safety Review and IRB review.

6.1.5 If there are urgent imaging capability questionnaires specific to Radiology or imaging services, email RadiologyResearchReview@UHhospitals.org for assistance before the review process. [NOTE: This is not required or a part of the review process, but can aid study teams in providing accurate information

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to Sponsors and coordinating centers].

6.2 **Radiology Research Review Process**

6.2.1 Requests for radiology services will be reviewed for safety, feasibility, effort and any special imaging guidelines that may impact the study and participants.

6.2.2 The radiology review team will be notified of the study and documents to be reviewed. The study will be reviewed by modality managers, radiology research team, Radiology IT (PACs), Chief Medical Physicist and the Vice Chair of Radiology Research and Chief Section Head.

6.2.3 Modality managers will be notified of the Sponsor's Imaging Capabilities Questionnaire that must be filled out during this process as well.

6.2.4 During the review process, questions from the review team may arise. Questions will be forwarded to the outside study team for clarification. If questions cannot be clarified in a timely manner or justifications cannot be made, please note this may delay the turn-around time for radiology review.

6.2.5 The radiology review process will also include collaboration with Research Finance and Grants & Contracts teams to ensure the coverage analysis includes the right procedures and CPT codes that may impact the study's budget.

6.2.6 Once all reviewers have approved the study, the Statement of Work (SOW) will be drafted and sent to the study team and cc: ResearchBiller@UHhospitals.org.

6.3 **Post- Radiology Research Review**

6.3.1 After the Radiology Research Committee has reviewed and approved the request, a SOW outlining the collaboration, to include fees, will be sent. This approval form will need to be reviewed and signed by the PI or receive Departmental Acknowledgement.

6.3.2 It is the responsibility of the study team to submit the SOW in SpartaIRB under Other Documents to complete the review process.

6.3.3 Sponsor's Imaging Capabilities Questionnaires will also be returned with the SOW. If questionnaires need to be returned in an early timeframe, please let the radiology team know. The questionnaires can be returned before the review has been completed.

6.3.4 The estimated turn-around time to receive a statement of work will be up to 10 business days depending on the complexity of the study and after all required information has been provided. Please keep these turn-around times in mind when sending your information.

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6.4 **Invoicing**

    6.4.1   Departments will be invoiced for Radiology Review fees based on the SOW and fees outlined in Appendix B.

6.5 **Additional Information**

    6.5.1   Radiology can also provide radiology specific imaging requisitions to the study team as applicable.

    6.5.2   Research IT will be notified of the study for review when a study submits a Radiology Intake Form, if applicable. It is the study team's responsibility to obtain Research IT approval for their study.

    6.5.3   Please inform the Radiology Research Office of any modifications in the study protocol that contain changes to imaging or radiology, or changes the terms of the finalized SOW by emailing to RadiologyResearchReview@uhhospitals.org.

7. REFERENCES:

- UH Clinical Research SOP
  - SP-201 - Protocol Feasibility Process
- UH CRC Research Study Database

8. FORMS AND ATTACHMENTS:

- Appendix A - Radiology Review Process Flow-Chart
- Appendix B - Radiology Review Categories
- Appendix C - Radiology Review Flow Chart

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – July 6, 2022

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Appendix A - Radiology Review Process Flow-Chart

Radiology Review Process
Complete the Radiology Information & Review in VELOS

↓

Complete the question "*Is this study ready to be reviewed by Radiology*" as "yes" and mark the form "Complete" to send an automatic submission to Radiology.

↓

Confirmation email will be sent by Radiology within 2 business days that all documents have been received. Email will include the estimated review category and fee.

↓

Radiology review time begins and documents are sent out to the committee.

↓

When the review is complete, the SOW will be processed.

↓

Radiology will send the signed SOW to the study contact for their signature.

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Appendix B - Radiology Review Categories

Service Level	Review Fee	Estimated Turn-Around Time
Category 1 (Minimal)	$0.00	1-3 Business Days
Category 2 (Basic)	$300.00	3-5 Business Days
Category 3 (Intermediate)	$600.00	5-8 Business Days
Category 4 (Complex)	$900.00	8-10 Business Days

Category 1: Minimal Review

- ☐ **Standard of Care scan/Clinically Indicated**
- ☐ **No picture upload or data handling/ manipulation**
- ☐ **No further Radiology involvement**

Category 2: Basic Review

- ☐ **Standard of Care scan/Clinically Indicated**
- ☐ **One Modality Only**
- ☐ **Coordination and scheduling assistance from radiology**
- ☐ **Data handling/ manipulation**

Category 3: Intermediate Review

- ☐ **Standard of Care Scan/Clinically Indicated or Research Indicated Scan**
- ☐ **Up to two modalities**
- ☐ **Scanner Qualifications at one site**
- ☐ **Review of Imaging Manual or Site Surveys/ Imaging Capabilities Questionnaires**
- ☐ **Coordination and scheduling from Radiology**
- ☐ **Technologist and Research Staff Training**
- ☐ **Study requires review of an Authorized User for the use of Radioactivity for research purposes**
- ☐ **Preparation of Research Requisition Form**

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Category 4: Complex Review

- ☐ **Standard of Care Scan/Clinically Indicated or Research Indicated Scan**
- ☐ **Three or more modalities**
- ☐ **Scanner Qualifications at two or more sites**
- ☐ **Review of Imaging Manual or Site Surveys/ Imaging Capabilities Questionnaires**
- ☐ **Coordination and scheduling from Radiology**
- ☐ **Technologist and Research Staff Training**
- ☐ **Set-up of Research Imaging Protocols at Scanner**
- ☐ **Study requires review of an Authorized User for the use of Radioactivity for research purposes**
- ☐ **Data handling/ manipulation**
- ☐ **Preparation of Research Requisition Form**

NOTE**Studies that are investigator-initiated, cooperative group, or have internal or federal funding will not be required to pay a review fee.
NOTE**Studies who do not meet the above criteria, will be reviewed and discussed internally. Please work with the outside study team to determine which category your study fits best.
NOTE** All required documents are needed to complete review in the estimated turn-around timeframe.

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Appendix C - Radiology Review Flow Chart

Radiology "Research" Exam

Clinically indicated — Standard of Care Imaging Protocol → Paid by patient's insurance → Use for clinical purpose and research purpose

Research indicated — Standard of Care Imaging Protocol → Paid by patient's insurance → Use for clinical purpose and research purpose

Research indicated — Research Imaging Protocol → Paid by Study Sponsor → Use for research purpose

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SP-204 - Research-Related Patient Education and Recruitment Materials

1. PURPOSE:
This Standard Operating Procedure (SOP) describes the process for UH Departments participating in clinical research that are interested in creating patient facing material pertaining to their research area(s). The goal of this SOP is to clarify the difference between general educational materials and study recruitment materials, and to provide guidance for UH Departments.

2. SCOPE:
This SOP provides instruction and sets minimum standards for UH Departments regarding the difference between general educational materials and study recruitment materials. General educational materials do not need to be submitted to the IRB for approval. In comparison, study recruitment materials require approval by the IRB. This material must be submitted with each study that could potentially recruit from it.

3. RESPONSIBLE INDIVIDUALS:
This SOP applies to staff involved in UH research and UHCRC staff members who may be involved in this process (e.g., Recruitment, Education, Compliance, IRB).

4. RELATED TERMS AND DEFINITIONS:
General Educational Materials - Materials created with the intent to provide general research education to patients, including (1) a definition of research; (2) what to expect when participating in research; (3) potential risks and benefits of participating in research; or (4) information about research the Department has conducted in the past. This material does not specifically intend to recruit patients and therefore, does not mention details or criteria of current research studies.

Study Recruitment Materials - Any items that target patients with the intent to enroll them into particular research studies. This type of material requires submission to and approval from the IRB prior to use. Types of materials that fall under this category are: flyers, verbiage, brochures, social media post content, posters etc.

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
This SOP is to help clarify the difference between general educational materials and study recruitment materials, as well as provide recommended content and language for general educational materials.

6. PROCEDURES:
6.1 General Education Materials may include:
    6.1.1 A description / definition of the term "research";
    6.1.2 What someone can generally expect when participating in research;

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6.1.3 General conditions or topics that are typically studied in the department (so long as language makes it clear that is it not a list of currently ongoing trials, or a promise that there will be an available trial on that topic);

6.1.4 Typical locations where research is conducted (so long as the language makes it clear that is it not a list of currently available locations, or a promise that that specific location will be an available);

6.1.5 Contact information for study teams or recruitment hotlines if people want to learn more about what trials are available; and

6.1.6 Names and information about researchers in the department.

6.2 General Education Materials may NOT include:

6.2.1 Specific study titles;

6.2.2 Specific eligibility information;

6.2.3 Specific participation benefits (e.g., a no-cost health examination);

6.2.4 Specific drugs, devices, or interventions to be studied;

6.2.5 Mention of whether financial compensation/reimbursement might be provided; or

6.2.6 A promise or implication of extra or better treatment if someone participates in research.

6.3 It is not permissible for either general education materials or recruitment materials to:

6.3.1 Include irrelevant, inappropriate, or misleading pictures or images;

6.3.2 Mention specific amounts of financial remuneration or overemphasize that remuneration is available;

6.3.3 Claim (explicitly or implicitly) that a study or intervention is safe or effective;

6.3.4 Claim (explicitly or implicitly) that a study is equivalent or superior to any other drug, biologic, device or intervention;

6.3.5 Include terms such as "new treatment," "new medication," or "new drug" without explaining that the test article is "investigational";

6.3.6 Use exculpatory language; or

6.3.7 State or imply a certainty of favorable outcome or benefits.

6.4 Please note that both general education materials and recruitment materials should only be distributed in appropriate and approved locations. For example, UH does not permit posting in elevators or bathrooms. It is also not appropriate to leave pamphlets in a waiting area that is not associated with the department without prior permission.

7. REFERENCES:
- UH System Policy GM-64 – Poster and Flyer Placement
- Investigator Manual for IRB Submission, Chapter 16 - Recruitment

8. FORMS OR ATTACHMENTS
None

APPROVALS
Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – August 26, 2022

SP-205 – IDS Exception Request

1. PURPOSE:
To standardize the process applicable for submitting an Investigational Drug Service (IDS) Pharmacy Exception Request as well as to outline minimum operational requirements for medical practice settings conducting research under an approved IDS Exception Request.

2. SCOPE:
This SOP applies to all clinical research projects requesting an exception to the policy requiring IDS control of Investigational Products (IP) as defined and outlined in MM-4.

An IDS exception will only be approved under limited circumstances, and only when it can be determined that there is an appropriate procedure in place for alternate handling.

3. RESPONSIBLE PARTIES:
The study principal investigator (PI) is responsible for submission of the IDS Exception Request, including all required supporting documentation. The Department Chair is responsible for the conduct of study operations under the Department IDS Exception SOP (as defined below). CRC Leadership is responsible for reviewing and rendering a final decision on an IDS Exception Request. For Specialized Practice Settings, CRC may require additional responsible parties on a case by case basis as required by law or UH policies.

4. RELATED TERMS AND DEFINITIONS:
Authorized Prescriber – As defined by the Ohio Board of Pharmacy 4729:5-1-02 is a licensed health professional authorized to prescribe drugs.

Qualified Prescriber – As defined in system policy MM-4 for Authorized Prescribers to order IP for IRB approved human-use clinical trials at University Hospitals (UH).

Investigational Product (IP) – As defined in system policy MM-4.

Dangerous Drug – As defined by the Ohio Board of Pharmacy, any drug or IP that requires a prescription for possession or administration to a patient.

Terminal Distributor License – As defined by the Ohio Board of Pharmacy 4729:5-1-01 as used in this policy means any person, other than a manufacturer, re-packager, outsourcing facility, third-party logistics provider, wholesale distributor, or pharmacist, who has possession, custody, or control of dangerous drugs for any purpose other than for that person's own use and consumption (TDDDL).

Regular Practice Setting – A medical practice that routinely prescribes/administers FDA approved dangerous drugs for patients (e.g. Doctors Office, Hospital or Office-based Clinic) receiving IP for a clinical trial as supplied by a sponsor, qualified third-party FDA registered manufacturer or commercial pharmacy holding an Ohio Board of Pharmacy

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(OHBP) TDDDL or otherwise in compliance with OHBP requirements.

Specialized Practice Setting – A laboratory that prepares or compounds IP under the Practice of Medicine for administration to human subjects in a clinical trial (e.g. in compliance with applicable regulations (e.g. USP Chapters <795>, <797>, <823> and/or FDA) as an FDA registered manufacturer or other entity holding an OHBP TDDDL.

Department IDS Exception Standard Operating Procedures (SOP) – Each IDS Exception Request must be submitted with a detailed Department SOP that specifies all aspects of the department's control of IP from receipt, preparation, ordering, dispensing, temperature control, etc. If a new protocol requires a deviation from the Department SOP, a protocol specific SOP may be submitted with a reference to the Department SOP, that designates responsibility for the conduct of the procedures that deviate from the Department SOP.

5. **PROCEDURES:**

   5.1 General
       5.1.1 Principal Investigator (PI) must hold an appropriate and current license to prescribe IP at the time of submission of an IDS Exception Request.
       5.1.2 The PI must submit the exception request via Velos and must include:
           5.1.2.1 Completed IDS Exception Request and Intake Form;
           5.1.2.2 Department SOP for the management of IP and the specialized practice, as needed, with Department Chair signature and date—reviewed and updated at least annually; and
           5.1.2.3 Protocol specific SOP whenever deviations from Department SOP are needed for a specific protocol with Department Chair signature and date.
           5.1.2.4 TDDDL number and expiration date for the conduct of each protocol
               5.1.2.4.1 If the PI does not hold the TDDL directly, the responsible party must provide attestation to the PI permission to conduct the research protocol under the responsible party's TDDL, for submission with the IDS Exception Request.
       5.1.3 After the IDS Request is received, the Request will be communicated with CRC Leadership for further review. CRC Leadership shall grant or deny the IDS Exception and the decision will be documented and communicated to the PI.
       5.1.4 The approval of an IDS Exception must be approved within one year of submission. If approval is not received in one year, a new submission will be required.
       5.1.5 Once an IDS Exception is granted, the PI accepts full responsibility for all aspects of the IP, including the following:
           5.1.5.1 Obtain and ensure all pertinent registrations and licensures, such as the Ohio Board of Pharmacy TDDDL remain current and active.
           5.1.5.2 The PI is responsible to have expertise and knowledge of practice specific regulations and prevailing authorities for the conduct of the

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study (e.g., USP and/or other registration/certifications), as a subject matter expert.

5.1.5.3 The PI is responsible to ensure that all study personnel working as delegated staff are adequately trained and have proper licensure to make them capable of managing secure drug supplies in compliance with MM-37 – Medication Storage, Security, Preparation, and Distribution and MM-47– Purchasing and Maintaining Pharmaceuticals and Related Supplies, Hospital and MM-4 Investigational Products and CRC Research SOP Manual. ORC will verify this during quarterly audits.

5.1.5.4 Control, preparation, monitoring and segregation of IP from commercial clinical supplies, drug accountability record forms, and dispensing records, etc. as required by the FDA, Ohio Board of Pharmacy, Joint Commission, and other regulatory bodies.

5.1.6 The signed IDS Exception approval must be provided to the IRB as part of the new study submission.

5.1.7 The department chair is responsible for ensuring the Department SOP is followed.

5.1.8 All approved IDS Exceptions that do not have an alternate source of monitoring acceptable to the CRC Leadership, are referred to the ORC for mandatory quarterly research compliance reviews. Fees are associated with mandatory reviews and are the responsibility of the PI. The ORC audits both Regular and Specialized Practice Setting compliance, per Department SOP, study protocol, study SOP, local requirements and associated regulations.

5.2 Third Party Verification Requirements

5.2.1 Departments requesting IDS Exception may be required to provide certification of compliance by a qualified third-party evaluator (as determined by CRC) for verification of compliance at the time the IDS Exception is submitted.

5.3 Amendments

5.3.1 In the event protocol amendments change the conditions that led to an IDS Exception approval, in addition to submitting to the IRB for review and approval, the PI will submit an update to IDS and CRC ORC reporting the change.

5.3.2 CRC Leadership will grant or deny the amendment request and shall communicate the decision to the PI and IRB.

5.3.3 Change in responsible party key personnel, pause in operations, change in facility or equipment must also be submitted to CRC ORC and the IRB for review and approval.

6. REFERENCES:

- UH Clinical Research Center Clinical Research Standard Operating Procedures Manual
- UH SOP MM-4 – Investigational Products
- UH SOP MM-37 – Medication Storage, Security, Preparation, and Distribution

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- [UH SOP MM-47](#)– Purchasing and Maintaining Pharmaceuticals and Related Supplies
- Ohio State Board of Pharmacy – [Terminal Distributor (TDDD) Licenses](#)

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – February 11, 2021

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University Hospitals
Clinical Research Center

SS-301 – Maintenance of Research Regulatory Binders

1. PURPOSE:
To describe the process for the collection and maintenance of research regulatory documents and other essential documents. To allow researchers to individually and collectively permit the evaluation of the conduct of a trial and the quality of data produced and to demonstrate their compliance with the standards of Good Clinical Practice and with all applicable regulatory requirements.

2. SCOPE:
This applies to all personnel who are delegated responsible for the collection and maintenance of research regulatory documents by the Principal Investigator (PI). This SOP does not supersede regulatory document maintenance required by sponsors in sponsored clinical trials.

This SOP does not address maintenance of participant research records.

3. RESPONSIBLE INDIVIDUALS:
The Principal Investigator and designated members of the study team are responsible for ensuring compliance with this procedure. The PI or designated member of the research team is responsible for the collection, review and maintenance of regulatory documents as required to the appropriate regulatory authorities.

4. RELATED TERMS AND DEFINITIONS:
Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
University Hospitals (UH) requires Investigators to maintain records of their human subjects' research activities. Regulatory documents will be maintained and up to date for all research studies conducted at UH.

6. PROCEDURES:
6.1 Collection and Maintenance
Collect and maintain in a secure location the following documentation. In general, the items below are required or recommended based on the following regulations and guidelines:

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	Items	Regulation or Guidance
1	Contact Information	Site Staff, Sponsor
2	Protocol and amendments: All versions should be numbered and dated.	ICH GCP Part 8.2.2, 8.3.11, and 8.3.2
3	Informed Consent Document / Assent Document / Information Sheet and all revisions	ICH GCP 8.2.3, 8.3.2, 8.3.12 45 CFR 46 21 CFR 50, 21 CFR 56
4	Investigator Brochure, Device Manual, Package Inserts	ICH GCP Part 8.2.1, 8.3.1
5	Delegation of Authority, Site Staff Signature Sheet: Documents the study-related procedures delegated by the Principal Investigator to the study staff.	ICH GCP Part 5.7, 4.1.5, 8.3.24
6	Training Documentation: Staff Training Log, Training Signature sheet(s)	
7	CV's / Resume / Biosketch signed and dated every two years to verify that the information is accurate and current.	ICH GCP Part 2.8, 4.1.1, 8.2.10, 8.3.5 21 CFR 312.53
8	Professional Licenses & Certifications Clinical, CREC, GCP, Credentialing, etc	
9	Screening Log: Capture all potential subjects who have been contacted, screened, or pre-screened for the study.	ICH GCP Part 8.3.20
10	Enrollment Log: Captures all subjects who have consented to the study and their Participant IDs / List of participant EMR records assessed	ICH GCP Part 8.3.22
11	Recruitment Materials Pamphlets, Posters, Flyers, Brochures, Phone and Email Scripts, Landing Pages	
12	Safety Reports: Documents adverse events reported to the IRB, sponsor, or regulatory groups, indicating severity and causality AE log, SAEs, Unanticipated Problems, Protocol Deviations, INDSRs.	ICH GCP Part 4.11, 4.11.3, 8.3.16-18
13	*Drug or Device Accountability Records: dispensing log, shipping and receiving records, randomization/blinding plans, return/destruction, temperature monitoring logs/reports. Note: May be maintained by Investigational Drug Services.	21 CFR 312 21 CFR 812 ICH GCP 4.6.3. 8.2.13-18, 8.3.23, 8.3.38-39, 8.4.1-2
14	Laboratory Certification and Documentation: These materials document the competency of all lab facilities being used in the study and support the reliability of test results. CLIA, CAP, normal laboratory and reference values and manuals, lab director's CV, IATA certifications, handling/storage/destruction plans, inventory/shipments, collection logs.	ICH GCP Part 8.2.11, 8.2.12, 8.3.6-7, 8.3.25
15	Case Report Forms, data collection sheets, questionnaires approved by the IRB; source document tools; electronic data capture (EDC) / remote data capture (RDC); operating guidelines	21 CFR 312 ICH GCP Part 8.3.14, 8.3.15, 4.9.3
16	IRB: Correspondence, submissions, approvals, FWA certificate	ICH GCP Part 8.2.7, 8.3.1, 8.3.2, 8.3.3, 8.3.11, 8.3.19
17	IRB Roster or IEC Committee Composition	
18	*FDA Forms: 1571, 1572, Financial Disclosure FDA 3455, Investigator Agreement, annual reports, and correspondence	21 CFR 312.23 and 312.53, 21 CFR 54 ICH GCP Part 4.1
19	Correspondence: Sponsor, NIH, staff, other	ICH GCP Part 8.3.11
20	*NIH grant applications	
21	Monitoring Log, Site Visit Signature Log, Reports, Letters: Documents any study-related activity performed to monitor study progress or the accuracy and completeness of study records	ICH GCP Part 8.2.19-20, 8.3.10, 8.4.5
22	*Data and Safety Monitoring Board / Committee / Plan: Approved charter, reports, minutes, recommendations.	ICH GCP Part 8.3.10, 5.19.3
23	Institutional Approvals	*Study Feasibility, Credentialing, Departmental Approval, PRMC, Investigational Drug Services, Radiology, Electrical Safety
24	*Sample Tracking	*Collection and processing *Storage, shipment, and disposition

*as applicable

6.1.1 A regulatory binder can be also known by other names: Reg Binder, Study Binder, Regulatory File, Investigator Binder, Administrative Binder, Investigator Site File (ISF), or Investigator's File.

6.1.2 Central binders can be used for storing and organizing essential regulatory documents that apply to multiple studies. The items can include, but are not limited to: CV, Clinical Licensure, Lab Certifications and Normal Range (CLIA/CAP), IRB Membership Lists, Training Records, and/or documentation of professional certifications.

6.1.3 The applicability of any item mentioned above is based on whether a research project is interventional, observational, a chart review, a repository, investigator initiated or FDA regulated. Research staff should maintain all of their essential regulatory documents as appropriate.

6.2 Electronic Records

6.2.1 It is acceptable to collect and store regulatory documents electronically.

6.2.2 Documents that are collected or stored electronically should have a note to file indicating that the documents are being maintained electronically and specifically stating where the electronic file is kept.

6.2.3 In all cases, electronic documents should be kept in a secure location and also password protected when appropriate.

6.2.4 Identifiable documents and documents containing subject IDs should not be kept in the same electronic location unless they are separately password protected.

6.3 Storage of Records

The following steps should be taken when the study is complete:

6.3.1 Review the documents of regulatory binders (both hard copy and electronic, if applicable) for completeness.

6.3.2 It is recommended that all electronic information is saved to an UH encrypted thumb/zip drive or other secure electronic media for long term storage.

6.3.3 Prior to archiving files, scan all documents so they are accessible electronically if needed.

6.3.4 Archive regulatory binders and storage media by labeling storage boxes for completeness.

6.3.5 Document inventory of storage boxes.

6.3.6 Store in a secure location for the specified amount of time according to institutional policies and federal regulations

6.3.7 Ensure regulatory binders are kept confidential and are stored in a secure, limited- access location.

6.4 Items NOT to be Included in the regulatory binder

The following information should not be included in the regulatory binder, but they should be maintained elsewhere and made available upon request.

6.4.1 Financial documentation (i.e. agreements, contracts , budgets, W-9s, participant compensation- voucher or gift card logs)

6.4.2 Identifiable patient information (PHI)

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6.4.3   Signed informed consent forms

6.5   <u>Access by Monitors or Auditors</u>
Prior to appointments scheduled by monitors, review the content of the regulatory files for completeness. Ensure that files are organized and up-to date.
6.5.1   See SOP GA-502 - Monitoring Visits for further guidance

7.   REFERENCES:

In general, the items are required by the FDA or recommended by ICH GCP (International Conference on Harmonisation Good Clinical Practice) guidelines based on the following regulations and guidelines:

FDA Requirements
- [21 CFR Part 50](#)—Protection of Human Subjects and Informed Consent
- [21 CFR Part 54](#)—Financial Disclosure by Clinical Investigators
- [21 CFR Part 56](#)—Institutional Review Boards
- [21 CFR Part 312](#) —Investigational New Drug Application
- [21 CFR Part 314](#)—Applications for FDA Approval to Market a New Drug
- [21 CFR Part 812](#)—Investigational Device Exemptions
- [21 CFR Part 814](#)—Pre-market Approval of Medical Devices
- [21 CFR Part 11](#)—Electronic Records; Electronic Signatures

8.   FORMS OR ATTACHMENTS:
- [UH Clinical Research Toolbox](#)
- Adverse Event Reporting:
  - [Internal Adverse Event Summary Log](#)
  - [External Adverse Event Summary Log](#)
- [Clinical Research Regulatory Binder Index](#)
- [Regulatory Binder Template and Tabs](#)
- [Delegation of Authority Log/Staff Signature Log](#)
- [Device Accountability Log](#)
- [Drug Accountability Log](#)
- [Monitoring Log](#)
- [Screening/Enrollment Log](#)

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – September 27, 2021

Clinical Research
Standard Operating Procedure

UNIVERSITY HOSPITALS
Clinical Research Center

SS-303 – Site Initiation Visit (SIV) or Study Start-Up Visit

1. PURPOSE:
To outline the protocol specific activities required to facilitate the research site initiation or study start-up process. This visit is usually conducted to assure that the site, facility, and staff are prepared to initiate, implement the research, and that appropriate training is completed.

2. SCOPE:
This SOP applies to all site personnel involved in the implementation and coordination of clinical research. Regardless of if a study involves participant interactions, utilizes PHI or collects medical or de-identified data, investigators should have a SIV or start-up meeting to ensure that the study staff understands the study objectives, the study procedures, and study roles and responsibilities.

3. RESPONSIBLE INDIVIDUALS:
The Principal Investigator, and when delegated by the Principal investigator, individuals involved with the research including, but not limited to Sub-Investigators/Co-Investigators, Research Nurses, Research Coordinators, Research Assistants, Regulatory Specialists, Data Specialists, and/or other pertinent staff.

4. RELATED TERMS AND DEFINITIONS:
Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
All research studies conducted at University Hospitals will complete a site initiation or study start-up visit prior to conducting any study related activities.

6. PROCEDURES:
6.1 The principal investigator or designee will schedule and arrange the site initiation or study start-up visit. Attendees will include all pertinent staff delegated responsibility for the study tasks by the PI.

6.2 Each meeting attendee will prepare by reviewing the IRB approved protocol and noting any areas of discussion or any questions. Study staff should utilize a FAQ's worksheet, as applicable in preparation.

6.3 The site initiation or study start-up visit should include discussion and review of the following:
6.3.1 Study objectives
6.3.2 Time and events schedule for the protocol
6.3.3 Participant recruitment/screening including the inclusion/exclusion criteria
6.3.4 Obtaining informed consent
6.3.5 Procedure for test article (investigational agent or device) accountability,

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storage, and documentation
- 6.3.6 Study logistics, inventory of supplies, and a study site(s)/facility tour, as applicable
- 6.3.7 Protocol-specific forms, manuals, and procedures
- 6.3.8 Data Management Plan that includes monitoring and process for team medical record access for data capture tools and systems, if applicable
- 6.3.9 Maintenance of essential study documents and the regulatory binder
- 6.3.10 Maintenance of the Velos eResearch worksheet, the Research Billing Notification Form (RBNF) completion and submission, and the study participant compensation process, as applicable
- 6.3.11 Adverse event reporting and the staff communication plan
- 6.3.12 Additional information from the Investigator's Meeting (if applicable)
  - 6.3.12.1 A site initiation or study start-up agenda should be generated and distributed to all pertinent research staff. Topics to include should be: protocol overview; participant recruitment, screening and enrollment; project timelines; regional sites and locations, if applicable; Informed Consent Process; data and data safety management; supplies and equipment; research staff responsibilities, etc.

6.4 Delegation of Authority Log is to be reviewed to ensure that responsibilities are clearly defined. If applicable, signature collection for all pertinent staff will occur.

6.5 Documentation of attendance during the initiation or study start-up visit will be maintained.

6.6 When protocol specific training occurs at the time of the site initiation or study start-up visit, documentation of this training will be retained. Subsequent training of any study staff will also be documented.

6.7 Verify that the study is marked as "Study - Active / Open to accrual" in Velos.

7. REFERENCES:
- 21 CFR 50, 54, 56, 312, 312.21, 312.32, 314, 600, 601, 812, and 814
- 45 CFR 46 Subparts A, B, C, and D
- FDA Guidance for Industry: Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects
- International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines
- GA-105 - Investigator Responsibility for Study Team Training and Documentation
- Velos Training Guide – eResearch Update a Study Status

8. FORMS OR ATTACHMENTS:

- Site Initiation/Study Start-Up Visit Tip Sheet
- Site Initiation Visit Checklist
- Site Initiation FAQs

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- [Site Initiation Agenda](#)
- [Template SIV Power Point Slide Deck](#)
- [Delegation of Authority Log](#)
- [Epic Workflow – Research Study Creation and Activation](#)
- [Epic Workflow – Slicer Dicer for Research Cohort Exploration](#)

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – October 31, 2023

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Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SS-304 - Investigational Drug Billing

1. PURPOSE:
To assure accurate and compliant billing of inpatient and outpatient research injectable and/or infusion investigational product (IP).

2. SCOPE:
All UH Cleveland Medical Center (UHCMC) inpatient and hospital outpatient (HOP) settings.

3. RESPONSIBLE INDIVIDUALS:
Investigators; study staff; Patient Access Services (PAS), investigational drug service IDS pharmacy personnel; corporate billing compliance; and UH Clinical Research Center (UHCRC) Research Finance Specialists (RFS).

4. RELATED TERMS AND DEFINITIONS:

Charge Description Master (CDM) – a comprehensive listing of items that could be billed to a patient or insurer by a healthcare provider. Its purpose is to develop an accurate summary of charges and services doctors and other healthcare professionals provide during the course of patient care.

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
Third-party payers will not be billed for items or services provided to subjects when funds have been secured to offset those expenses, for items when such items are provided by the sponsor at no cost for the study, or for items or services provided to subjects that are not considered covered or billable according to the applicable payer guidelines or current Medicare coverage policy, e.g., National Coverage Decision (NCD) Manual.

The PI is ultimately responsible for the accuracy of the billing plan for their project (UH System Policy R-2 - Research Patient Billing).

6. PROCEDURES:
6.1 For UH System inpatient, outpatient pharmacies, DO and OH based service provided by IDS, the IDS Pharmacy will receive, log, store, and distribute all IP unless an IDS Exception has been approved (per MM-4: Investigational Products).

6.2 The department will submit all new patient care trials in Velos eResearch including upload of all pertinent study documentation. To specifically notify IDS of a new drug trial, the department will complete an Investigational Drug Service (IDS) Request form in Velos eResearch.
6.2.1 Once an IDS service or exception request is submitted through Velos

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eResearch, a notification is sent to IDS and the pharmacy will review the provided protocol documentation.

    6.2.2 The pharmacist who receives the above notification will reach out to submitter for any additional details necessary to clarify IP acquisition and dispensing.

    6.2.3 The pharmacist will complete an IDS Fees Quote (according to the current approved & published IDS price list).

    6.2.4 Once complete, IDS will update the form status to "Signed Off", save a .pdf of the form in the Study Documents tab, and email the PI, Study Coordinator and RFS.

    6.2.5 **Note:** An IDS service charge will be generated for IDS services.

6.3 Licensed clinical study staff will enter patient specific orders in the EPIC EMR specific to the IP, including name, dose, route, and dates of administration, as defined by the protocol and approved by the PI. The UH Beacon Team (oncology) and the EPIC IT Team working with an IDS Pharmacist (non-oncology studies) endeavor to have EPIC Order Build Templates available for studies that may be accessed by the clinical staff. This includes assigning a CDM number and NO-cost to the IP.

    6.3.1 In some instances, EPIC order templates may not be available (e.g. Emergency Use). In those instances, the clinical staff will contact IDS and develop a collaboration plan to enable EPIC Order Build by the clinical staff: Link to Workfront request form: https://uhhospitals.my.workfront.com/requests/new?activeTab=tab-new-helpRequest&projectID=63d0137b000503e1fc83b1a10643fa2e&path

    6.3.2 Medication orders verified in EPIC are considered final orders and request for IDS dispensing activities to commence, that designates the study participant is properly consented for the clinical research study.

        6.3.2.1 The EPIC Informatic Teams set-up IP in the EMR by the completed EPIC order dispensed and/or administered to the study participant will cause Corporate Billing Compliance charge master analyst.

        6.3.2.2 If the investigational drug is provided free of charge by the sponsor, the cost of the drug will be loaded as $0.00 in the EMR and will pass to the billing system as a zero charge.

        6.3.2.3 If the study protocol requires the use of commercially available drug/s for use within FDA Package insert guidelines (e.g. usual and customary care), the drug will be entered in the EMR by licensed study staff/provider per protocol, and billed as research covered (Q1) treatment with standard charge mark-up applied.

        6.3.2.4 If the study protocol includes commercially available drug/s for use in the study not deemed a standard treatment in the protocol, the sponsor may provide the drug at no-charge to IDS for storage and dispensing. These drugs will be entered as IP and charged as $0.00 per section 6.3.2.4.

6.4 On the Research Date of Service

    6.4.1 Charges for patients associated with a research protocol in Epic will be routed to research charge review

6.4.1.1 Study teams are expected to maintain the patient study timeline and link encounters to their respective study timeline visit.

6.4.2 The provider/licensed clinical staff enter the study order in EPIC and IDS Pharmacy will verify the order.

6.4.3 Clinical or research staff administering the investigational drug will sign-off the order and document when care is provided.

6.4.4 To document IP administration, the nurse will select the patient specific order entered in EPIC EMR and sign off that it was administered. This will trigger charge entry (Note: This may be a zero charge).

6.5 Charge management

6.5.1 Charges associated with a research protocol in Epic will route to the RFS team for charge review and segregation according to the study coverage analysis.

6.5.2 Once charge segregation is completed by the RFS the charge will be research to revenue cycle for claim processing.

7. REFERENCES:
- UH System Policies
  - MM-4 - Investigational Products
  - R-2 - Research Patient Billing
  - SOP XV: IDS Billing Procedures

8. FORMS OR ATTACHMENTS:
None

APPROVALS

Signed by Grace A McComsey, MD, FIDSA, Director of the UH Clinical Research Center, University Hospitals Health System –
December 13, 2023

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SS-305 - Investigational Device Billing

1. **PURPOSE:**
   The purpose of this document is to assure a standard process for the financial management of research medical devices implanted or provided to patients to result in compliant billing and maximum appropriate reimbursement.

2. **SCOPE:**
   All UH Cleveland Medical Center (UHCMC) inpatient and hospital outpatient (HOP) settings.

3. **RESPONSIBLE INDIVIDUALS:**
   Clinical Research Center (UHCRC); Corporate Billing Offices (CBO) personnel; Departmental study staff; Investigators; OR and Procedure room staff; Patient Access Services (PAS); Legal; Supply Chain.

4. **RELATED TERMS AND DEFINITIONS:**
   CDM – "Charge Description Master" (or charge master) is a comprehensive listing of items that could be billed to a patient or insurer by a healthcare provider. Its purpose is to develop an accurate summary of charges and services doctors and other healthcare professionals provide during the course of patient care.

   CGS - Cigna Government Services

   Investigational device – Clinical devices that have not been cleared for marketing that involves an investigational plan approved by an institutional review board (IRB), informed consent from all patients, labeling stating that the device is for investigational use only, or is an approved device being used in a non-labeled indication.

   MAC - Medicare Administrative Contractor

   Operating Room (O.R.) – Facility where surgical operations are carried out in an aseptic environment. Includes the following areas: Mather Outpatient Surgery Center aka "MOSC" (outpatient), Humphrey (women's), Prentiss (pediatrics), and Mather (main O.R., adult).

   SUNRISE Surgical Care – Software system for the operating room which incorporates supply management, documentation, and billing capabilities.

   Procedure Room – Includes Cath Lab, EP Lab, as well as other departmental areas where devices may be implanted or provided to patients.

   UHCare – The electronic medical record system utilized by University Hospitals Health System. Also referred to as the electronic medical record (EMR).

   RBNF – Research Billing Notification Form

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Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:

Third-party payers will not be billed for items or services provided to subjects when funds have been secured to offset those expenses, for items when such items are provided by the sponsor at no cost for the study, or for items or services provided to subjects that are not considered covered or billable according to the applicable payer guidelines or current Medicare coverage policy, e.g., National Coverage Decision (NCD) Manual.

The PI is ultimately responsible for the accuracy of the billing plan for their project (UH System Policy R-2 - Research Patient Billing).

6. PROCEDURES:

6.1 Study Start-Up/Device Acquisition

    6.1.1 Contract negotiation with industry sponsors of investigational device trials will be managed by the CRC Grants & Contracts Office in conjunction with the Legal Department.

        6.1.1.1 A Grant & Contracts Specialist (GCS) will lead the negotiation of the Clinical Trial Agreement (CTA).

        6.1.1.2 If the Sponsor requires UH purchase of the investigational device, the GCS will alert Research Finance Specialist (RFS) and the Director, Corporate Value Analysis with the proposed device pricing information. The Director, Corporate Value Analysis will assign a Supply Chain Contract Administrator who will be handling the purchase agreement.

            6.1.1.2.1 Supply Chain will verify pricing to national benchmarks and contact the Sponsor if necessary to determine if there is room for purchase price, or other supply price, negotiation. Supply chain will collaborate and communicate with the requesting department and the Legal Department regarding the outcome of their discussions. Legal, GCS, and Supply Chain will work to finalize the language and execute the agreements.

            6.1.1.2.2 In about two weeks from the initiation of the supply agreement process, Supply Chain will forward a copy of the fully executed supply chain purchase agreement to ResearchBiller@UHhospitals.org and UHCRCGrantsContracts@uhhospitals.org once it is available so that the finalized device or supply price is included in the Coverage Analysis and the clinical research budget.

        6.1.1.3 The GCS will collaborate with the RFS to assure that the clinical research budget and coverage analysis have been finalized and approved prior to final contract execution.

            6.1.1.3.1 For projects that require UH purchase of the investigational device, the RFS/Research Finance Director will assess

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financial viability of the trial by engaging Finance Decision Support to determine the average cost, average Medicare payment and average total margin for predicate devices.

6.1.1.3.2 For device observational/outcome studies, the RFS will assess the need for implementation of this SOP to assure proper claim flow/billing.

6.1.1.4 During Clinical Trial Agreement negotiation, the department will submit an application for device and / or procedure coverage approval to our Medicare Administrative Contractor (MAC), Cigna Government Services (CGS).

6.1.1.4.1 Clinical Trial Agreements executed prior to obtaining Ohio MAC coverage approval must include language that states the prices quoted are subject to Ohio MAC CGS approval of a coverage determination and if not approved, that the Sponsor will pay any additional non-covered costs of the trial.

6.1.2 Upon supply chain purchase agreement execution the following will be completed:

6.1.2.1 For purchased investigational devices, a member of the clinical department's administration will submit a purchase order to Supply Chain via an I-procurement requisition.

6.1.2.2 The RFS will complete and submit a Service Catalog Request form (Appendix A).

6.1.2.2.1 RFS should contact the Supply Chain Contract Administrator if additional information is needed about the device.

6.1.2.2.2 RFS will obtain appropriate Department approval.

6.1.2.2.3 RFS will obtain appropriate Finance Director Approval for purchased items; the Research Finance Director will sign off on zero/penny charge items.

6.1.2.2.4 The Finance Director must type their name on the excel form and type "Approved" in their email

6.1.2.2.5 After approval is received, the RFS will send the completed Service Catalog Request form to the following people (See Appendix B) as an electronic excel file. RFS will keep approved copies for file.

6.1.2.2.5.1 Data Integrity Specialist, Material Distribution / Supply Chain

6.1.2.2.5.2 Sr. System Analyst, Revenue Integrity, Compliance

6.1.2.2.5.3 Perioperative Clinical Info Analyst, UHC Operative Services Admin

6.1.2.3 RFS will add the device information with a Pending status to the Active IDE's tab of the IDE Tracker in S:\Master Research\Research Billing Resources\Devices\IDE Tracker.xlsx

6.1.3 The Data Integrity Specialist, Material Distribution/Supply Chain will establish

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an Oracle Item Number for the devices and add it to the Service Catalog Request form. This needs to be completed before submission to the CDM.

6.1.4   The Sr. System Analyst, Revenue Integrity, Compliance will review the device requests with the Corporate Billing Compliance Director for approval and will add all approved submissions to the CDM.

6.1.4.1   An email will be sent back to the RFS who submitted the Service Catalog Request form if their request was denied.

6.1.4.2   Accepted requests will be entered into the CDM and include the IDE# in the description. If the device is investigational, it will be categorized to the 624 revenue code.

6.1.4.3   Corporate Billing Compliance will input a stop date and inactivate investigational device SPSI numbers in the service catalog for devices that become approved or for which the study has been terminated.

6.1.4.3.1   The individual requesting removal of the device from the CDM must submit a new Service Catalogue Request form requesting this change.

6.1.4.3.2   RFS will move the device to the Inactive IDE's tab of the IDE Tracker.

6.1.5   For purchased investigational devices, Supply Chain will receive and log the device shipment and deliver to the location provided on the I-procurement order.

6.1.5.1   When the Oracle item number and cost for the new investigational device are established, the device detail is interfaced to SUNRISE Surgical Care.

6.1.5.2   The O.R. Billing/Informatics team will confirm new investigational device information in SUNRISE Surgical Care, including the manufacturer information, catalog number, and the purchase price (or if provided free).

6.1.5.3   The staff responsible for Supply Chain within the user department will be contacted to discuss if there is a need for inventory/stocking of the related investigational device supply, separate from any commercial inventory/stock of the same device.

6.1.6   **Note:** Patients with Medicare or Medicare Advantage plans cannot be implanted with the investigational device until UH has received coverage determination authorization from our MAC.

6.1.6.1   To obtain such approval, the department must complete and submit Ohio's MAC Investigational Device Exemption Request Form.

6.1.6.2   Prior to submitting this form to the Ohio MAC, the department must contact UHHS Reimbursement to validate the hospital National Provider Identifier (NPI) number indicated.

6.1.7   RFS will update the device status on the IDE Tracker to Active and add any additional information if needed.

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6.2 <u>Device Implant</u>

   6.2.1 It is the responsibility of the Principal Investigator's department to educate the O.R. or procedure room staff about the study and investigational device prior to the start of the trial.

   6.2.2 Within 24 hours of the investigational device implant, the department research coordinator will complete the implant visit in Velos eResearch.

      6.2.2.1 When the RBNF Notification event line is changed to 'Done', a RBNF Notification will be sent to ResearchBiller@UHhospitals.org

      6.2.2.2 When the IDE event line is changed to 'Done', a notification will be sent to CMCOR.Billing@UHhospitals.org

   6.2.3 The department will also complete a Surgery Reservation Form (Appendix C) and include the short study name, device name, and IDE# in the "procedure information" section.

      6.2.3.1 This completed form will be emailed to the surgery scheduler, who will also forward to admitting/Patient Access Services (PAS) and Pre-operative Anesthesia Testing (PAT).

      6.2.3.2 Research patients will be registered with a research insurance type in the primary position.

   6.2.4 If the case will be performed in a procedure room, the research coordinator on the case will verify the study information from the form and assure the correct investigational product is pulled/charged for the case.

   6.2.5 On the DOS, the circulating O.R. nurse will enter a charge for the supply / device into SUNRISE Surgical Care and pull the appropriate investigational device for the case (Note: if departmental research staff are managing investigational device inventory, they will bring the device to the O.R. rather than having it pulled by the O.R. staff).

      6.2.5.1 The O.R. nurse will document the investigational device as "generic supply/implant" with a notation of research in SUNRISE Surgical Care or use the Oracle number if one has been assigned.

      6.2.5.2 The O.R. Billing / Informatics team will document "Research" in the comments if it is entered as a generic supply/implant and enter the cost provided by the vendor.

      6.2.5.3 It is critical that the procedural area O.R. circulating nurse, or the procedure room staff, chooses the correct device listing from the CDM for billing.

         6.2.5.3.1 Investigational devices are assigned to revenue code 624 and will have the IDE number imbedded in the description.

   6.2.6 The O.R. Billing / Informatics team will review and validate that the correct investigational device information has been entered in SUNRISE Surgical Care. RFS will be contacted if there are any questions or issues.

   6.2.7 The procedure room manager will review the charge ticket information on the case prior to entry in Soarian to assure that the correct device is being billed.

   6.2.8 At the end of the case, the physician will document in the procedure notes that the patient is enrolled on a research protocol and had an investigational device implanted per UH Clinical Research SOP SC-403 - Research Documentation.

      6.2.8.1 Documentation will be conducted through Heartlab software for the

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Cath Lab, Cardiolab software for the EP Lab, and in SUNRISE Surgical Care for the O.R.

6.2.8.2 **Note:** For appropriate coding to occur, the words "enrolled on a research protocol" must be included in the procedure documentation.

6.2.8.3 Research O.R. documents that are recorded on paper will be scanned into the EMR by medical records.

6.2.8.4 Health Information Services coders will add the Z00.6 research diagnosis code in the secondary position only upon confirming the presence of the required research documentation per UH Clinical Research SOP SC- 403 - Research Documentation.

6.3 Post Procedure

6.3.1 The department research coordinator will update the patient specific Calendar in Velos eResearch with the date of service and the study procedures completed throughout the participant's involvement with the study.

6.3.2 Once charges are entered into the hospital billing system and the claim is created, the claim will route to the RFS queue based upon the presence of a Z00.6 dx code, 624 revenue code, or research payer.

6.3.2.1 The RFS will review the claim for, and indicate, covered and non-covered charges.

6.3.2.2 The RFS will add the NCT number to the claim if it is not already present.

6.3.2.3 The RFS will add the IDE # to the investigational device line if it is not already present, and follow-up with the department and OR Billing/Informatics team or Cath Lab/EP Lab Billing team to determine why IDE # was missing on the claim.

6.3.2.4 Once the claim review is complete, the RFS will forward the claim to the CBO revenue cycle team that manages research billing.

6.3.3 The CBO research billing revenue cycle team will process claims according to federal guidance (National Coverage Decision, Medicare Claims Processing Manual, CMS Transmittals), and assure all other research claim requirements are met prior to releasing the claim to be billed.

6.3.4 Quality monitoring and claim review will be performed by the RFS after 1 - 2 patients have been implanted on a new device trial to assure that all components of the process are working smoothly. Additional assessment will be performed if an issue is identified, and continued until claims are correct.

6.3.4.1 For large trials (expected enrollment of ≥ 30), additional assessment will occur after every 10 patients are enrolled.

7. REFERENCES:

- UH System Policy
  - R-2 - Patient Billing
- UH Research SOP
  - SC-403 - Research Documentation

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8. FORMS OR ATTACHMENTS:
- Appendix A - [Service Catalog Request Form](#)
- Appendix B - [Service Catalog Request Contact List](#)
- Appendix C - [Surgery Reservation Form](#)

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – January 15, 2021

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Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SS-307 - Obtaining an Identified Patient List Through the UH Clinical Research Center's TriNetX Export ID Feature

1. PURPOSE:
This Standard Operating Procedure (SOP) describes the process for obtaining an identified patient list for recruitment purposes through the UH Clinical Research Center's (UHCRC).

2. SCOPE:
This SOP provides instruction and sets minimum standards regarding the process for submitting, reviewing, and releasing patient lists containing PHI for recruitment purposes.

Prior to requesting patient lists, the project and recruitment plan must be approved by the Institutional Review Board (IRB) and a waiver of HIPAA authorization must be granted.

3. RESPONSIBLE INDIVIDUALS:
This SOP applies to University Hospitals (UH) Principal Investigators (PI) who are interested in identifying potential study participants for purposes of increasing recruitment for an under enrolling study or identifying potential participants for a new study. This process is only available to UH PI's who have submitted to the UH IRB.

4. RELATED TERMS AND DEFINITIONS:
TriNetX – A global health research network that brings together healthcare organizations, biopharmaceutical companies, and contract research organizations to optimize clinical research and enable discoveries through the generation of real-world evidence. UHCRC has contracted with TriNetX to provide the ability to query the UH electronic medical record

Export ID – A TriNetX feature for re-identifying a de-identified patient list for recruitment.

Epic SlicerDicer – A self-service reporting tool in Epic.

UH Honest Broker – The person from the UHCRC who will receive the UH PI's request for identification, re-identify the patients via TriNetX ExportID or Epic SlicerDicer, and release the list to the investigator.

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
UH PIs seeking patient lists for identifying eligible research participants must have IRB Approval and a waiver of HIPAA authorization. The release of PHI through the UH Honest Broker mechanism will be based on IRB approval of this method of recruitment for the specific study of interest. The UH PI will collaborate with the IRB to include this recruitment method in the protocol of interest. The release of PHI is intended to be used solely to identify prospective research participants. UH PIs and study teams must recruit subjects in an ethical manner by following the IRB approved recruitment plan and all requirements

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outlined in the Investigator Manual.

6. PROCEDURES:

Export ID through TriNetX is a process where a UH designated Honest Broker can download a de-identified dataset and re-identify the patient cohort for recruitment purposes. The procedures below list the responsibilities of the UH PI and of the CRC Honest Broker. Alternatively, the CRC Honest Broker may utilize Epic SlicerDicer to obtain a patient list directly from the EMR.

6.1   The UH PI confirms that *Part 1* of the UHCRC Feasibility Process has been completed before sending an Export ID request.

6.2   The UH PI confirms that the study has received IRB approval and a waiver for HIPAA authorization.

6.3   The UH PI and study team shall also confirm that obtaining a list of prospective research participants aligns with the IRB approved recruitment methods.

6.4   If the requirements above have been met, then the UH PI meets the criteria to send an electronic request for a patient list. The UH IRB Number and the approved UHCRC Feasibility Review form must be included in the request in order to retrieve the dataset.

6.5   The UHCRC Honest Broker will confirm IRB approval and waiver of HIPAA authorization.

6.6   The UHCRC Honest Broker will utilize TriNetX or Epic SlicerDicer to identify the number of eligible participants within UH for the research trial.

6.7   The UHCRC Honest Broker will request de-identified patient data from TriNetX and match synthetic IDs to medical record numbers behind the UH Firewall utilize TriNetX or Epic SlicerDicer to identify.

6.8   The UHCRC Honest Broker will match the medical record number to only the data elements authorized by the IRB on the HIPAA waiver.

6.9   The CC Honest Broker will send the patient list results to the Principal Investigator via UH e-mail within 3-5 business days. The email may not be forwarded to any other non-UH email address or to anyone that is not part of the study team. Results will include an excel file containing the data elements requested and approved by the IRB. The excel file will not exceed 5x anticipated accrual at local site and/or 500 patients, whichever is less. The email subject must include the term "SECURE" to ensure the email message is encrypted and protect against unintended delivery to a non-UH email address.

6.9.1   By obtaining a patient list for recruitment through the process, the UH PI and study team attest that no patient will be contacted without prior approval from the providing physician, unless your recruitment plan specifically authorizes

another process.

6.9.2 Patient lists received through this mechanism are confidential. PIs must agree that the patient list will not be shared with anyone outside of the IRB approved study team or sent to any non-UH email.

| Investigator Responsibilities | Submit for feasibility assessment | Submit to IRB | Receive committee approval | Electronic request for Patient ID |

| UHCRC Honest Broker Responsibilities | Confirm IRB Approval & Waiver of HIPAA Authorization | Review Query and Export ID from TriNetX | Match synthetic ID's to MRN | Match MRN to data elements requested on HIPAA waiver | Release patient list to UH Investigator |

7. REFERENCES
- Link to *Part 1* UH CRC Protocol Feasibility
- UH Clinical Research SOP SP-201 - Protocol Feasibility Assessment
- UH System Policy R-3 - Uses and Disclosure of Protected Health Information (PHI for Research)

8. FORMS OR ATTACHEMENTS:
None

APPROVALS

Signed by Grace A McComsey, MD, FIDSA, Director of the UH Clinical Research Center,
University Hospitals Health System –
December 13, 2023

Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SS-308 - Obtaining De-identified Data and Performing Online Analysis Using TriNetX

1. PURPOSE:

This Standard Operating Procedure (SOP) describes the process for obtaining de-identified data to aid in research studies through the UH Clinical Research Center (UHCRC) and obtaining limited access to TriNetX to perform online analysis and building study feasibility queries without direct dataset access through the use of the global health research network, TriNetX.

2. SCOPE:

This SOP provides instruction and sets minimum standards regarding the process for submitting, reviewing, and releasing de-identified data for protocol creation through the UHCRC. Additionally this SOP provides instructions and expectations for privileged users to request limited access to TriNetX for the purposes of online analysis and building study feasibility queries without direct access to a dataset. This SOP also addresses limitations on the use of that data. Any requests for data from TriNetX not intended to be used for research purposes must comply with all UH policies including but not limited to IS-22.

3. RESPONSIBLE INDIVIDUALS:

This SOP applies to all University Hospitals (UH) or Case Western Reserve University (CWRU) personnel who are interested in obtaining de-identified data for purposes of applying for grants, creating protocols, conducting research with de-identified data, or for other needs preparatory to research. This SOP also applied to all University Hospitals (UH) or Case Western Reserve University (CWRU) personnel who are interested in obtaining limited access to TriNetX to perform online analysis and building study feasibility queries without direct dataset access.

4. DEFINITIONS:

TriNetX - A global health research network that brings together healthcare organizations, biopharmaceutical companies, and contract research organizations to optimize clinical research and enable discoveries through the generation of real-world evidence. UHCRC has contracted with TriNetX to provide the ability to query the UH electronic medical record and the larger de-identified HCO network.

UH Privileged User - An individual external to UHCRC who is granted limited access to TriNetX for the purpose of online analysis of data without direct dataset access. This user agrees not to attempt to download data from the TriNetX environment or attempt to re-identify patients from their online analysis or feasibility query. UH Privileged Users will be restricted to the full TriNetX research network, access to sub-networks will not be granted.

CWRU Privileged Partner – An individual employed by Case Western Reserve University who is granted limited access to TriNetX for the purpose of online analysis of data without direct dataset access. This user agrees not to attempt to download data from the TriNetX environment or attempt to re-identify patients from their online analysis or feasibility query.

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CWRU Privileged Partners will be restricted to the full TriNetX research network, access to sub-networks will not be granted. CWRU Privileged users must have a UH sponsor and must be UH Research Credentialed with active status. Accounts for CWRU Privileged Partner must be configured with a UH email address.

UH Sponsor – An employee of University Hospitals Health System, with managerial privileges, who is responsible for a non-UH employee (i.e., ensuring the non-employee completes requirements that allow granting access to UH data and systems).

UH Honest Broker - The person from the UHCRC who will receive the UH PI's request for information and ensures that datasets are completely de-identified prior to release.

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:

The UHCRC must approve user access to TriNetX, those permitted will not have the ability to obtain patient-level data.

Federal regulations prohibit the conduct of human subject research (45 CFR 46.102(f)) without appropriate IRB review. As such, any researcher who wishes to use identifiable patient data must obtain IRB approval prior to the collection and use of this information.

When seeking de-identified patient data (meaning no elements of PHI are included) IRB approval is not necessary because obtaining de-identified data without a link to identifiers does not meet criteria for human subject's research.

The UH IRB considers the use of de-identified data obtained from the TriNetX system through the UHCRC Honest Broker to meet criteria for a determination of not human subjects research (NHR). In addition, UH IRB has determined that use of this de- identified patient data does not require a HIPAA waiver as no elements of PHI will be included.

The UH IRB considers the use of the TriNetX system's online analytics feature by use of a UH Privileged User or CWRU Privileged Partner, without direct dataset access, to meet criteria for a determination of not human subjects research (NHR). In addition, UH IRB has determined that use of this online analytics feature does not require a HIPAA waiver as no elements of line level data, including PHI, will be accessible to the user.

UH and CWRU personnel using TriNetX for the sole purpose of obtaining de-identified patient data under this SOP are not required to submit a "Research Determination" form in the electronic IRB system when requesting data through the UH Honest Broker within UHCRC.

UH and CWRU personnel using TriNetX for the sole purpose of deriving results and outcomes using the online analytics feature or performing study feasibility analysis using the

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query builder without direct dataset access under this SOP are not required to submit a "Research Determination" form in the electronic IRB system when performing analysis using the TriNetX platform as a UH Privileged User or CWRU Privileged Partner.

If you are obtaining de-identified patient data from any other source, in any other manner, you must submit a "Research Determination" form in the electronic IRB system.

The UHCRC will review and approve all UH Privileged User and CWRU Privileged Partner access requests. The total number of system users, including CRC users, shall not exceed 500 accounts. The UHCRC may periodically review and suspend unused account to free licenses for other users to access the platform.

UH and CWRU personnel must follow all other UH policies related to research, record retention and IT&S policies related to use of UH electronic systems, data storage and data security.

6. PROCEDURES:

Please note that this process should only be used by individuals who seek to obtain strictly de-identified data, with no link, and no need to ever re-identify patient data. If you require a link to identifiers, or you may need to re-identify patient data in the future, please contact the IRB and submit a Human Subjects Research protocol in advance of your project. This process may also be used to request UH Privileged User or CWRU Privileged Partner access to the TriNetX environment for the purposes of study feasibility query building and online analysis of data without direct dataset access.

6.1 UH Privileged User Access Requests

6.1.1 To initiate the process of requesting limited access to the TriNetX environment, a request should be submitted in the form of an email from the UH requestor, describing the reason for requesting access, whether access is permanent or temporary and how being given access will benefit research within the requestor's therapeutic division or department. The email should contain at least the following details:
- The purpose for granting the requestor access
- The therapeutic division or department of the requestor
- The intended usage of TriNetX access should have a positive impact on research within the therapeutic division or department
- The duration or time period access is requested

6.1.2 The access request email must be sent to CRCResearchDevelopment@UHhospitals.org and UHIRB@UHhospitals.org, after which it will be reviewed by the UH CRC Research Development team and UH IRB. All requests must be received from a UH email address.

6.1.3 Requestors will be provided with TriNetX training modules to be completed and sent a Usage Attestation form, which must be signed by the Requestor and kept on file with the CRC Research Development Core and CRC Human Research Protection Program Core. This Usage Attestation must be renewed annually to

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maintain access to the TriNetX environment.

6.1.4 Following receipt of the Usage Attestation form and completion of TriNetX training module, UHCRC shall grant the requestor limited access to the TriNetX platform.

6.2 CWRU Privileged Partner Access Requests

6.2.1 To initiate the process of requesting limited access to the TriNetX environment, a request should be submitted in the form of an email from the CWRU requestor and UH Sponsor, describing the reason for requesting access, whether access is permanent or temporary and how being given access will benefit research within the requestor's therapeutic division or department. The CWRU requestor must have active UH Research Credentialing and must identify a UH sponsor prior to submitting. At each credentialing renewal cycle, requestors must obtain UH sponsor approval and request an extension of TriNetX access *(see SOP GA – 103 – UH Research Credentialing for credentialing renewal information)*. The email should contain at least the following details:
- The purpose for granting the requestor access
- The therapeutic division or department of the requestor
- The intended usage of TriNetX access should have a positive impact on research within the therapeutic division or department
- The duration or time period access is requested
- The UH sponsor

6.2.2 The access request email must be sent to CRCResearchDevelopment@UHhospitals.org and UHIRB@UHhospitals.org, after which it will be reviewed by the UH CRC Research Development team and UH IRB. All requests must be received from a UH email address.

6.2.3 Requestors will be provided with TriNetX training modules to be completed and sent a Usage Attestation form, which must be signed by the Requestor and a UH sponsor then kept on file with the CRC Research Development Core and CRC Human Research Protection Program Core. This Usage Attestation must be renewed annually to maintain access to the TriNetX environment.

6.2.4 Following receipt of the Usage Attestation form and completion of TriNetX training module, UHCRC shall grant the requestor limited access to the TriNetX platform.

6.3 UH Privileged User/CWRU Privileged Partner – Performing Study Feasibility using Query Builder

6.3.1 Using a web browser, navigate to https://live.trinetx.com and login with your credentials.

6.3.2 Select "Create New Study" box in TriNetX to begin your query.

6.3.3 Name your project and select "Assess Feasibility of Clinical Trial" as the

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Research Purpose.

    6.3.4 Search for inclusion and exclusion criteria by entering the corresponding billing code or the term itself.

    6.3.5 Filter by age at event or current age

    6.3.6 Create a New Group to add a Time Constraint using Relative Time or Specific Dates.

    6.3.7 Set a Relationship within the new group if terms have a temporal relationship.

    6.3.8 Count Patients when query is complete.

6.4 UH Privileged User/CWRU Privileged Partner – Performing Analysis using the Online Analytics Feature

    6.4.1 Please note that Section 6.3 is a required pre-component that must be completed prior to analysis.

    6.4.2 To initiate an online analysis of queried patient population(s), select the "Analytics" tab on the left-hand menu and click on "+ New Analysis" in the top right corner. Analyses that are currently available to the UH Privileged User or CWRU Privileged Partner will be selectable. If the desired analysis is not available, request access by emailing CRCResearchDevelopment@UHhospitals.org. Requesting access does not guarantee access to the analysis.

    6.4.3 After selecting the desired analysis, follow the steps as presented in the left-hand menu, starting with "Cohort(s)." If assistance is required, please review the available TriNetX training modules, or request assistance by emailing CRCResearchDevelopment@UHhospitals.org and BiostatsSupport@UHhospitals.org

    6.4.4 To export a summary of results from an online analysis, select "Results" in the left-hand menu, then "Export" in the top right corner.

    6.4.5 If assistance is required in selecting or performing the online analysis, or in interpreting the findings of the online analysis, request assistance by emailing CRCResearchDevelopment@UHhospitals.org and BiostatsSupport@UHhospitals.org. By receiving biostatistical assistance, the UH Privileged User or CWRU Privileged Partner agrees to include the UH Clinical Research Biostatistician(s) as an author on any poster, presentation or publication for their contributions to the study.

    6.4.6 Any poster, presentation or publication submission using findings sourced from TriNetX must include an acknowledgement of the UH Clinical Research Center by citing: *This publication was made possible through the support of the Clinical Research Center of University Hospitals Cleveland Medical Center (UHCMC) and the Case Western Reserve University Clinical and Translational Science Collaborative (CTSC) 4UL1TR000439. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of UHCMC or NIH.*

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6.5 **Requesting a De-identified Dataset for Analysis by UHCRC**

6.5.1 To initiate the process of requesting data and data analysis by UHCRC, submit a request via our Request Survey at https://redcap.uhhospitals.org/redcap/surveys/?s=YMNNNFXRNN4K8DJ8. If difficulty is encountered using the survey, please contact CRCResearchDevelopment@UHhospitals.org or BiostatsSupport@UHhospitals.org.

6.5.2 Datasets will not be released to the requestor. Any requested dataset will be maintained and controlled by UHCRC on a secure network drive to ensure compliance with the TriNetX usage agreement.

6.5.3 By receiving biostatistical assistance, the requestor agrees to include the UH Clinical Research Center Biostatistician(s) as an author on any poster, presentation or publication for their contributions to the study.

6.5.4 Any poster, presentation or publication submission using findings sourced from TriNetX <u>must include an acknowledgement</u> of the UH Clinical Research Center by citing: *This publication was made possible through the support of the Clinical Research Center of University Hospitals Cleveland Medical Center (UHCMC) and the Case Western Reserve University Clinical and Translational Science Collaborative (CTSC) 4UL1TR000439. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of UHCMC or NIH. Failure to comply with this will result in termination of access to the TriNetX platform.*

7. REFERENCES
- 45 CFR 46.102(f)
- UH System Policy IS-22 - Sharing of UH Clinical or Business Data with Third Parties
- UH TriNetX Webpage
- SOP GA – 103 UH Research Credentialing

8. FORMS OR ATTACHMENTS
- BioStats Request Survey

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – March 29, 2023

Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SS-309 – REDCap Project Access for UH Employees

1. **PURPOSE:**
   The purpose of this SOP is to define University Hospitals' standard for use of UH REDCap to support research or clinical operations functions and protect UH patient data or proprietary business intelligence data.

   1.1 REDCap (Research Electronic Data Capture) is a secure web platform used to build and manage online surveys and projects. It may be used to collect almost any type of data, but is intended to support online or offline data capture for research studies and operations.
      1.1.1 REDCap is hosted on the secure UH Network within UH firewalls. It includes an audit trail function that allows UH IT to track project user activities, including data downloads.

2. **SCOPE:**
   This SOP applies to all UH employees.

3. **RESPONSIBLE INDIVIDUALS:**
   All UH employees conducting clinical research at UH who have UH REDCap access, UH employees who sponsor non-employees, and UH IT staff supporting UH REDCap.

4. **RELATED TERMS AND DEFINITIONS:**
   Employee – An individual under the direction and control of UH who receives full or partial salary from UH.

   - **Data Use Agreement**
   - **HIPAA**
   - **Institutional Review Board (IRB)**

   Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. **POLICY STATEMENT:**
   All UH employees will follow best practices for roles and responsibilities outlined in this SOP for:

   5.1 Initiating REDCap access;
   5.2 REDCap project maintenance; and
   5.3 Terminating REDCap access.

6. **PROCEDURES:**

   6.1 Initiating REDCap Access for UH Employees:
      6.1.1 Existing Project

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6.1.1.1 Project owner must request access through the UH REDCap User Access Request Form at: https://redcap.uhhospitals.org/ by providing:

6.1.1.1.1 Requestor's name and e-mail address;

6.1.1.1.2 Existing REDCap project title; and

6.1.1.1.3 New user's name, UH e-mail address, UH username, primary institution, and confirming whether or not the user is a student.

6.1.2 New Project

6.1.2.1 UH employee may request access through the UH REDCap New Project Request Form at: https://redcap.uhhospitals.org/ by providing:

6.1.2.1.1 Name, e-mail address, UH username, department;

6.1.2.1.2 Purpose of project;

6.1.2.1.3 Confirmation whether project will include Protected Health Information (PHI);

6.1.2.1.4 Whether the project is a student project (if so, name of student, information about school, department, and year in school);

6.1.2.1.5 Whether the trial is FDA-regulated; and

6.1.2.1.6 Title of new REDCap project.

6.1.3 UH Research IT

6.1.3.1 UH Research IT will process all new requests.

6.1.3.1.1 New requests require submission of a SailPoint request to add REDCap to the user's list of applications.

6.2 REDCap Project Maintenance

6.2.1 All UH employee project owners and users must:

6.2.1.1 Adhere to UH's IT policies on data security and protection of PHI when entering data or downloading and securely storing downloaded data from a REDCap project, including, but not limited to:

6.2.1.1.1 Sole use of an UH e-mail address to sending surveys from REDCap or sharing data via e-mail;

6.2.1.1.2 Downloading data from REDCap to a secure (encrypted, password-protected) storage device only;

6.2.1.1.3 Downloading and sharing de-identified data only; and

6.2.1.1.4 Termination of a non-employee's access to a project when the non-employee's participation has ended.

6.2.1.2 Review list of project users regularly to confirm all users should still have access.

6.2.1.2.1 If user no longer requires access, the project owner or UH Sponsor can:

6.2.1.2.1.1 Directly terminate a user's access to their specific projects, or

6.2.1.2.1.2 Contact REDCap@UHhospitals.org to request termination.

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6.3 Terminating REDCap Access for UH Employees
    6.3.1 UH employees transferring to another department or leaving UH
        6.3.1.1 Clinical research or business operational data within a REDCap projects remains the property of the UH department.
        6.3.1.2 If UH PI terminates their relationship with UH, oversight responsibility for protocol-specific UH REDCap project(s) will transition according to SOP GA-109 - Departing Investigators.

    6.3.2 Terminated UH employees
        6.3.2.1 Even though the UH employee termination process will remove access to REDCap projects, the department administrator or project owner should enter an expiration date within the specific project(s) that the terminated UH employee had access to or remove the user from the project. An alternative is to request access termination at REDCap@UHhospitals.org.
            6.3.2.1.1 This will prevent UH rehires from having automatic access to those projects if hired in another department or capacity and the UH e-mail address, username, and associated IT applications are reassigned.

    6.3.3 Internal Transfers
        6.3.3.1 Prior to transfer, the employee's manager must contact: REDCap@UHhospitals.org to:
            6.3.3.1.1 Request access to the project and terminate the transferring employee's access to any UH REDCap project; and
            6.3.3.1.2 Review the project for department proprietary information and reassign to another department employee.

    6.3.4 Non-employee No Longer Collaborating on a Clinical Project
        6.3.4.1 UH Sponsor or project owner will either terminate access:
            6.3.4.1.1 In the projects User Rights section, or
            6.3.4.1.2 By contacting REDCap@UHhospitals.org.

6.4 Downloading Data
    6.4.1 Prior to Access Termination
        6.4.1.1 If a UH employee wants to download data (identified or de-identified) prior to access termination, they need to request approval from their Department Chair or Administrator for business operations or research data. If the data is research data, the UH employee must request approval from the Vice President, Research, by contacting the UH CRC Research Grants & Contracts liaison at: UHCRCGrantsContracts@UHhospitals.org or Research Legal Services at 216-767-8216 to execute a UH Data Use Agreement.

    6.4.2 After Access Termination

6.4.2.1 If a UH employee wants to access an existing REDCap project or download data following access termination, they need to request approval from the Department Chair or Administrator for business operations or research data. If the data is research data, the individual with prior access must request approval from the Vice President, Research, and enter into a UH Data Use Agreement by contacting either: the Department's Research Grants & Contracts liaison at: UHCRCGrantsContracts@UHhospitals.org or Research Legal Services at 216-767-8216 to execute a UH Data Use Agreement.

7. REFERENCES:
- REDCap.UHhospitals.org
- UH System Policies
  - IS-1 – Internet Use
  - IS-7 – Remote Computer Access
  - IS-12 – Access to Electronic Records and Computers for Inquiries and Investigations
  - IS-14 – Acceptable Use of UH Electronic Assets
  - IS-15 – UH Network and Systems Access
  - IS-22 – Sharing of UH Clinical or Business Data with Third Parties
  - R-40 – Research Misconduct
- UH Clinical Research SOPs
  - GA-102 – Use and Disclosure of Protected Health Information Preparatory to Research
  - GA-103 – UH Research Credentialing
  - GA-109 – Departing Investigators
  - SS-301 – Maintenance of Research Regulatory Documents

8. FORMS & ATTACHMENTS:
None

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – October 31, 2023

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Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SS-310 – REDCap Project Access for Research Credentialed Users

1. **PURPOSE:**
   The purpose of this SOP is to define the University Hospitals standards for use of REDCap to support research or clinical operations functions, protect UH patient data and/or proprietary business intelligence data by research-credentialed users.

2. **SCOPE:**
   This SOP applies to all use of UH REDCap for project access and to all external, research credentialed users of with access to UH REDCap.

   All individuals from affiliated or non-affiliated institutions who request access to UH REDCap must receive a copy of this SOP for reference.

3. **RESPONSIBLE INDIVIDUALS:**
   This SOP applies to:
   3.1 UH Principal Investigator (PI), authorized UH Study Personnel as delegated by the PI
      3.1.1 UH PI or authorized UH Study Personnel must ensure compliance with this SOP as it relates to collection, use and maintenance of data associated with a specific research protocol, and access given to external institutions or personnel.

   3.2 UH Research IT Department
      3.2.1 UH Research IT Department is responsible for implementing REDCap processes to support this SOP and supporting UH PIs in managing access of external institutions.

   3.3 UH Legal Department
      3.3.1 UH Legal Department is responsible for legal activities described in this SOP.
   3.4 External institutions/personnel given access to UH REDCap projects

      3.4.1 External institutions or personnel given access to UH REDCap projects are responsible for knowledge of and adherence to the best practices described in this SOP.

   The PI is responsible for protecting UH PHI and other confidential proprietary research or business information. Failure to follow these procedures may result in disciplinary action.

4. **RELATED TERMS AND DEFINITIONS:**
   External, affiliated institution/research-credentialed personnel – Personnel with a legal affiliation to UH (e.g. employee, medical student) with any institution listed in SOP GA-103 Research Credentialing, including: UH-affiliated hospitals (i.e. Southwest General, Lake Health, and Firelands Regional Medical Center), Case Western Reserve University (CWRU), Kent State University (College of Nursing), Ursuline College (Breen School of Nursing), and Cleveland State University (School of Nursing). This list may be expanded by

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UH legal counsel.

UH Project Owner – UH employee (e.g. PI or authorized study member) who has access to UH REDCap and privileges to add research-credentialed personnel to an existing or new project.

- **Data Use Agreement**
- **HIPAA**
- **Institutional Review Board (IRB)**

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
This SOP will be used by UH PIs to grant research-credentialed users access to UH's REDCap projects and for sharing UH data with external, non-affiliated institutions.

    5.1 Procedures are described for initial REDCap access, REDCap project maintenance, and termination of REDCap access for research-credentialed, affiliated institutions/personnel.

6. PROCEDURES:
    6.1 <u>Initial REDCap Access for Research Credentialed, Non-Employee</u>
        6.1.1 Existing Project
            6.1.1.1 UH Project Owner must request access through UH REDCap User Access Request Form at: https://redcap.uhhospitals.org/. UH Project Owner must provide:
                6.1.1.1.1 Requestor's name and e-mail address;
                6.1.1.1.2 Existing REDCap project title; and
                6.1.1.1.3 New user's name, UH e-mail address, primary institution, and whether the user is a student.
                    6.1.1.1.3.1 Project access is usually granted approximately one (1) to two (2) business days after request is made.

        6.1.2 New Project
            6.1.2.1 Only the UH Sponsor or UH PI can request access for a research credentialed non-employee through the UH REDCap New Project Request Form.
            6.1.2.2 UH Research IT will process all new requests requiring:
                6.1.2.2.1 Submission of a SailPoint request to add REDCap to new user's list of applications.
            6.1.2.3 After project access is granted, UH Research IT will send the UH Sponsor and research credentialed non-employee a request every 90 days to review and confirm whether the non-employee should still have access to and be a user on the project.

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6.1.2.3.1 If no response is received from the UH Sponsor, the research credentialed non-employee user's access will be terminated.

6.2 REDCap Project Maintenance
    6.2.1 All UH employee project owners and users must:
        6.2.1.1 Adhere to UH's IT policies on data security and protection of PHI when entering data or downloading and securely storing downloaded data from a REDCap project, including, but not limited to:
            6.2.1.1.1 Sole use of an UH e-mail address to sending surveys from REDCap or sharing data via e-mail;
            6.2.1.1.2 Downloading data from REDCap to a secure (encrypted, password-protected) storage device only;
            6.2.1.1.3 Downloading and sharing de-identified data only; and
            6.2.1.1.4 Termination of a non-employee's access to a project when the non-employee's participation has ended.

        6.2.1.2 Review list of project users regularly to confirm all users should still have access.
            6.2.1.2.1 If user no longer requires access, the project owner or UH Sponsor can:
                6.2.1.2.1.1 Directly terminate a user's access to their specific projects, or
                6.2.1.2.1.2 Contact REDCap@UHhospitals.org to request termination.

6.3 Terminating UH REDCap Access for Research-credentialed, non-employees
    6.3.1 Non-employee No Longer Collaborating on a Clinical Project
        6.3.1.1 UH Sponsor or project owner will either terminate access:
            6.3.1.1.1 In the projects User Rights section, or
            6.3.1.1.2 By contacting: REDCap@UHhospitals.org.

6.4 Downloading Data
    6.4.1 Prior to Access Termination
        6.4.1.1 If a research credentialed, non-employee wants to download data (identified or de-identified) prior to access termination, they need to request approval from their Department Chair or Administrator for business operations or research data. If the data is research data, the UH employee must request approval from the Vice President, Research, by contacting the UH CRC Research Grants & Contracts liaison at: UHCRCGrantsContracts@UHhospitals.org or Research Legal Services at 216-767-8216 to execute a UH Data Use Agreement.

    6.4.2 After Access Termination
        6.4.2.1 If a research credentialed, non-employee wants to access an existing

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REDCap project or download data following access termination, they need to request approval from the Department Chair or Administrator for business operations or research data. If the data is research data, the individual with prior access must request approval from the Vice President, Research, and enter into a UH Data Use Agreement by contacting either: the Department's Research Grants & Contracts liaison at: UHCRCGrantsContracts@UHhospitals.org or Research Legal Services at 216-767-8216 to execute a UH Data Use Agreement.

7. REFERENCES:
- REDCap.UHhospitals.org
- UH System Policies
  - IS-1 – Internet Use
  - IS-7 – Remote Computer Access
  - IS-12 – Access to Electronic Records and Computers for Inquiries and Investigations
  - IS-14 – Acceptable Use of UH Electronic Assets
  - IS-15 – UH Network and Systems Access
  - IS-22 – Sharing of UH Clinical or Business Data with Third Parties
  - R-40 – Research Misconduct
- UH Clinical Research SOPs
  - GA-102 – Use and Disclosure of Protected Health Information Preparatory to Research
  - GA-103 – UH Research Credentialing
  - GA-109 – Departing Investigators
  - SS-301 – Maintenance of Research Regulatory Documents

8. FORMS & ATTACHMENTS:
None

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – February 3, 2023

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Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SS-311 – REDCap Project Access for External, Non-Research Credentialed Users

1. PURPOSE:
The purpose of this SOP is to define the University Hospitals standards for use of REDCap to support research or clinical operations functions, protect UH patient data and/or proprietary business intelligence data by external, non-research credentialed users.

2. SCOPE:
This SOP applies to all use of UH REDCap for project access and to all external, non-research credentialed users of with access to UH REDCap.

All individuals from affiliated or non-affiliated institutions who request access to UH REDCap must receive a copy of this SOP for reference.

3. RESPONSIBLE INDIVIDUALS:
This SOP applies to:
3.1   UH Principal Investigator (PI), authorized UH Study Personnel as delegated by the PI
    3.1.1   UH PI or authorized UH Study Personnel must ensure compliance with this SOP as it relates to collection, use and maintenance of data associated with a specific research protocol, and access given to external institutions or personnel.
3.2   UH Research IT Department
    3.2.1   UH Research IT Department is responsible for implementing REDCap processes to support this SOP and supporting UH PIs in managing access of external institutions.
3.3   UH Legal Department
    3.3.1   UH Legal Department is responsible for legal activities described in this SOP.
3.4   External institutions/personnel given access to UH REDCap projects
    3.4.1   External institutions or personnel given access to UH REDCap projects are responsible for knowledge of and adherence to the best practices described in this SOP.

The PI is responsible for protecting UH PHI and other confidential proprietary research or business information. Failure to follow these procedures may result in disciplinary action.

4. RELATED TERMS AND DEFINITIONS:
External, non-affiliated institution/non-research credentialed personnel – Personnel with a legal affiliated with any institution not listed in SOP GA-103 - Research Credentialing.

UH Project Owner – UH employee (e.g. PI or authorized study member) who has access to UH REDCap and privileges to add research-credentialed personnel to an existing or new project.

- **Data Use Agreement**
- **HIPAA**
- **Informed Consent Document (ICD)**
- **Institutional Review Board (IRB)**
- **Protected Health Information (PHI)**

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
This SOP will be used by UH PIs to grant individuals from external, affiliated and non-affiliated institutions, access to UH's REDCap projects and for sharing UH data with external, non-affiliated institutions.

5.1   Procedures are described for initial REDCap access, REDCap project maintenance, and termination of REDCap access for non-research-credentialed, non-affiliated institutions/personnel.

6. PROCEDURES:
6.1   Research Credentialing Not Required
This section details procedures for all research studies where a UH REDCap project is used as a centralized repository for collection and management of data from UH and/or affiliated institutions.

6.1.1   Research credentialing is not required for personnel from external, non-research credentialed institutions if personnel:

6.1.1.1   Will not be conducting protocol-specific activities at UH-affiliated sites/properties;

6.1.1.2   Will not require access to PHI/UH patients;

6.1.1.3   Will not receive a UH username/e-mail address;

6.1.1.4   Access to UH REDCap will use the external user's official institutional e-mail address;

6.1.1.5   And an appropriate agreement is in place (see below).

6.2   UH PI Responsibilities
6.2.1   UH Research Legal Department requires confirmation of scope of UH Data Use Agreement by individual's external institution/personnel prior to execution of agreement.

6.2.2   UH PI must not permit data uploads to occur until UH Data Use Agreement is executed.

6.2.2.1   To enter into a UH Data Use Agreement, contact either the Department's Research Grants & Contracts liaison at UHCRCGrantsContracts@UHhospitals.org or Research Legal Services at 216-767-8216.

6.2.3   UH PI should review and respond to REDCap@UHhospitals.org 90-day requests to confirm external, non-research-credentialed, non-affiliated

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personnel still require access to UH REDCap. Failure to respond to requests will result in termination of access for the external personnel.

    6.2.4 UH PI must notify REDCap@UHhospitals.org and UH Research Legal Department when an external, non-research-credentialed, non-affiliated user:

        6.2.4.1 Changes (i.e. changes access) or completes role in study;

        6.2.4.2 Changes institution; and/or

        6.2.4.3 Is added to the study.

6.3 <u>Initial REDCap Access for Research</u>

    6.3.1 UH PI must be the project owner for the UH REDCap project they are seeking to provide access to for the external, non-research-credentialed, non-affiliated user.

        6.3.1.1 Existing Project

            6.3.1.1.1 After UH Data Use Agreement is fully executed, UH PI or designated UH study personnel will request access to existing UH REDCap protocol-specific project(s) for external, non-research-credentialed, non-affiliated personnel. IRB approval must be in place.

            6.3.1.1.2 UH PI or designated UH study personnel will request access for the user via UH REDCap User Access Form at: https://redcap.uhhospitals.org/redcap/surveys/?s=KCHECL 98KE

            6.3.1.1.3 One form will be completed per approved personnel.

            6.3.1.1.4 External user's official institutional e-mail address will be used as listed in the executed UH Data Use Agreement. No personal or generic e-mail address will be permitted.

6.4 <u>REDCap Project Maintenance</u>

    6.4.1 All UH employee project owners and users must:

        6.4.1.1 Adhere to UH's IT policies on data security and protection of PHI when entering data or downloading and securely storing downloaded data from a REDCap project, including, but not limited to:

            6.4.1.1.1 Sole use of an UH e-mail address to sending surveys from REDCap or sharing data via e-mail;

            6.4.1.1.2 Downloading data from REDCap to a secure (encrypted, password-protected) storage device only;

            6.4.1.1.3 Downloading and sharing de-identified data only; and

            6.4.1.1.4 Termination of a non-employee's access to a project when the non-employee's participation has ended.

        6.4.1.2 Review list of project users regularly to confirm all users should still have access.

            6.4.1.2.1 If user no longer requires access, the project owner or UH Sponsor can:

                6.4.1.2.1.1 Directly terminate a user's access to their specific projects, or

                6.4.1.2.1.2 Contact REDCap@UHhospitals.org to request

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termination.

6.5 <u>Data Use Agreement Executed Before Data Upload into UH REDCap</u>
   6.5.1 A UH Data Use Agreement must be executed before any data is uploaded into a UH REDCap project. Original, fully-executed Data Use Agreements will be maintained by the UH Research Legal Department. A copy of the Data Use Agreement must be filed in the Regulatory Binder.
       6.5.1.1 To enter into a UH Data Use Agreement, contact either the Department's Research Grants & Contracts liaison at UHCRCGrantsContracts@UHhospitals.org or Research Legal Services at 216-767-8216.
   6.5.2 UH PI will provide UH Research Legal Department with requirements for personnel access to UH REDCap project. Examples of access levels include:
       6.5.2.1 Data upload, management, access to, download of their institution's de-identified/limited data or identifiable dataset (as specified) only—no further access.
       6.5.2.2 Data management of aggregate dataset (which may include upload and download/export of de-identified/limited dataset or identifiable dataset).
   6.5.3 Access to aggregate PHI (identifiable data) requires:
       6.5.3.1 UH Data Use Agreement with investigator's institution; and
       6.5.3.2 Written permission from UH VP, Research, to UH Research Legal Department, approving potential increased access to UH PHI and/or proprietary information.

6.6 <u>Terminating UH REDCap Access for External, non-research-credentialed, non-employees</u>
   6.6.1 Non-employee No Longer Collaborating on a Clinical Project
       6.6.1.1 UH Sponsor or project owner will either terminate access:
           6.6.1.1.1 In the projects User Rights section, or
           6.6.1.1.2 By contacting: REDCap@UHhospitals.org.

6.7 <u>Downloading Data</u>
   6.7.1 Prior to Access Termination
       6.7.1.1 If a non-research-credentialed non-employee wants to download data (identified or de-identified) prior to access termination, they need to request approval from their Department Chair or Administrator for business operations or research data. If the data is research data, the UH employee must request approval from the Vice President, Research, by contacting the UH CRC Research Grants & Contracts liaison at: UHCRCGrantsContracts@UHhospitals.org or Research Legal Services at 216-767-8216 to execute a UH Data Use Agreement.
   6.7.2 After Access Termination
       6.7.2.1 If a non-research-credentialed non-employee wants to access an existing REDCap project or download data following access

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termination, they need to request approval from the Department Chair or Administrator for business operations or research data. If the data is research data, the individual with prior access must request approval from the Vice President, Research, and enter into a UH Data Use Agreement by contacting either: the Department's Research Grants & Contracts liaison at: UHCRCGrantsContracts@UHhospitals.org or Research Legal Services at 216-767-8216 to execute a UH Data Use Agreement.

6.8 Research Protocol Review and Approval

    6.8.1 All research studies in which a UH REDCap project is used as a centralized repository for data collection and management from external, non-affiliated institutions requires review and approval of the research protocol by the UH IRB unless the UH IRB has agreed to cede review to an external IRB.

    6.8.2 Each external, non-affiliated institution must provide:

        6.8.2.1 IRB approval letter from its institution (including personnel approved to have access to data) or in cases of reliant review, documentation of reliance on UH IRB from the local IRB and/or executed IRB authorization agreement.

            6.8.2.1.1 Any external IRBs relying on UH IRB retain oversight over their local study personnel.

        6.8.2.2 Approved Informed Consent Document listing UH and/or other institutions as having access to patient data in the HIPAA Authorization.

        6.8.2.3 Documentation that HIPAA waivers, if required, were granted by the other IRB, or that the other IRB has agreed to rely on UH to approve HIPAA waivers.

    6.8.3 IRB approval letters and Informed Consent Documents from external, non-affiliated institutions must be filed in the Regulatory Binder.

7. REFERENCES:

- REDCap.UHhospitals.org
- UH System Policies
  - IS-1 – Internet Use
  - IS-7 – Remote Computer Access
  - IS-12 – Access to Electronic Records and Computers for Inquiries and Investigations
  - IS-14 – Acceptable Use of UH Electronic Assets
  - IS-15 – UH Network and Systems Access
  - IS-22 – Sharing of UH Clinical or Business Data with Third Parties
  - R-40 – Research Misconduct
- UH Clinical Research SOPs
  - GA-102 – Use and Disclosure of Protected Health Information Preparatory to Research
  - GA-103 – UH Research Credentialing
  - GA-109 – Departing Investigators
  - SS-301 – Maintenance of Research Regulatory Documents

8. FORMS & ATTACHMENTS:
None

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – February 3, 2023

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SS-312 - Veeva SiteVault Free Account Access & Management

1. **PURPOSE:**
   This procedure describes the process of requesting user accounts, managing a clinical trial within Veeva SiteVault Free, and user security at University Hospitals (UH). Use of Veeva SiteVault Free, electronic Investigator Site File (eISF), is optional.

2. **SCOPE:**
   This procedure describes how to set up a new Veeva SiteVault Free account for a department and a short description of the features included with the system.

3. **RESPONSIBLE INDIVIDUALS:**
   This SOP applies to University Hospitals (UH) Principal Investigators (PI), their research staff members who choose to conduct remote monitoring visits using Veeva SiteVault Free, and external users with a business need to view documentation.

4. **RELATED TERMS AND DEFINITIONS:**

   External User – Personnel, not within the clinical trial team, including, but not limited to: an auditor, monitor, Sponsor, CRO, or CRA. The user is granted view-only access within a specific time-frame to maintain compliance with the monitoring review contract. External users should only be viewing de-identified information per UH IT permissions

   eISF (Electronic Investigator Site File) – A computer system that may be used to house Essential Regulatory Documents required for the conduct of clinical research by the Investigator.

   Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. **POLICY STATEMENT:**
   University Hospitals offers Veeva SiteVault Free as an option for remote monitoring and as an eISF. Users must comply with all procedures to keep their account active in the system, including not uploading PHI into the system. Veeva SiteVault Free is compliant with 21 CFR Part 11 and HIPAA requirements.

6. **PROCEDURES:**
   6.1 Requesting User Account Access for a New Site/Department:
       6.1.1 Complete Veeva SiteVault Free Sign-up form.
       6.1.2 After completing, a Veeva SiteVault Free representative will add your site (named after your UH Department), to the University Hospitals Organization.
           6.1.2.1 You will have access to add documents and users.
       6.1.3 Once you have a site created, email ClinicalResearch@UHhospitals.org to have a representative from the UH Research Integration & Education added to your site in Veeva SiteVault Free.

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6.1.3.1 Access is granted to one representative to ensure compliance with SOP and to better improve the system for UH users.

6.2 Creating and Managing a Study:
    6.2.1 Please refer to "Creating Studies" in the Getting Start Guide on Veeva SiteVault.
        6.2.1.1 In order for a study to be reviewed by an External User, the study must be in an "Active" stage.

6.3 Managing Users and Roles:
    6.3.1 Please refer to "Managing Users, System Roles, and Add-on Permissions".

6.4 Uploading Source Documentation for a Study Participant to a Study:
    6.4.1 Please refer to "Upload Source Files" in the Quick Start Guide.
        6.4.1.1 The Study Participant's folders field should be the participant's assigned de-identified Subject ID for the specific trial.
        6.4.1.2 **All source files uploaded must be properly redacted. No PHI may be uploaded in Veeva SiteVault Free.**

6.5 Uploading Regulatory Documents for an eBinder for a Study:
It is pertinent to select the correct type of document when uploading Regulatory Documents. These Regulatory documents are automatically filtered into the eBinder within eISF.
    6.5.1 Please refer to "Managing Study Documents" in the Quick Start Guide.

6.6 Other Features of Veeva SiteVault Free:
    6.6.1 Refer to the Overview of SiteVault and the Veeva SiteVault Free GPS Training, to see additional features of Veeva SiteVault Free.

7. REFERENCES:
- Veeva SiteVault Getting Started (Videos)
- FDA Part 11, Electronic Records; Electronic Signatures - Scope and Application, 2003
- ICH GCP E6 (R2): Harmonized Tripartite Guidelines for Good Clinical Practice
- Veeva SiteVault Free GPS Training

8. FORMS OR ATTACHMENTS:
- Veeva SiteVault Free Document Types Spreadsheet (Direct Download)

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – April 25, 2022

Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SS-313 – Research Participant Compensation and Travel Reimbursement

1. PURPOSE:
To standardize the process for research participant compensation and travel reimbursement for clinical trials/research, sponsored or investigator initiated, within UH, system-wide.

2. SCOPE:
This policy and procedure applies to all clinical trials/research, sponsored or investigator initiated, within the UH system.

3. RESPONSIBLE INDIVIDUALS:
Principal investigator (PI) and when delegated by the PI, individuals involved with the research including, but not limited to: sub-investigators, Research Nurse, Study Coordinator, Regulatory Coordinator, Grants and Contracts Specialists, and other pertinent research staff.

4. RELATED TERMS AND DEFINITIONS:
Research Participant Compensation - Sponsor/Investigator approved monetary payment to research participants for their time, inconvenience, discomfort, or some other consideration as they relate to participation in a clinical trial.

Travel Reimbursement - Sponsor/Investigator approved reimbursement for travel expenses to and from the clinical trial site and associated costs such as mileage reimbursement, parking, transportation, meals, and lodging.

Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
All research personnel responsible for the conduct of the clinical trial are required to adhere to this policy and procedure, institutional policies, local regulations, and Federal regulations as applicable.

6. PROCEDURES:
6.1 The study team will review the study visits and procedures with the PI to ensure research participant compensation and travel reimbursement is appropriate for the research participant's time, inconvenience, discomfort, and other considerations as they apply to the participation in the clinical trial. The frequency and duration of study visits and procedures will be compared to standard-of-care visits and procedures for the patient population.
   6.1.1 Study visits and procedures that fall outside standard-of-care frequency and duration are classified as research and research participants may be offered compensation for their time, inconvenience, and discomfort.

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6.1.1.1 For research studies enrolling minors, every effort should be made to compensate the research participants or their caregiver according to the following institutional guidelines listed below. (*Refer to the Investigator Manual for IRB Submissions for more information*).

Research Participant Age	Research Participant Compensation	Caregiver Compensation
Up to 6 years old	*	100%
7-13 years old	50%	50%
14 years or older	100%	0%

* Age-appropriate toys or gifts of nominal value may be offered to children as compensation based on the complexity or frequency/duration of the research visits or procedures as long as the IRB has approved this.

6.1.1.2 Sponsor approved study compensation and travel reimbursement will follow local policies and third-party vendor policies and procedures as applicable. For third-party vendor who require cardholders to be 18 years of age or older, 100% of the compensation and travel reimbursement will be issued to the research participant's caregiver and the research participant who is a minor may be offered a small gift, toy, or gift card of nominal value for their participation.

6.1.2 Travel reimbursement to and from the site may be offered to research participants or their caregivers when the study visits and procedures fall outside standard-of-care frequency and duration. This includes: mileage reimbursement, parking passes, public transportation (taxi, Lyft/Uber, bus, airfare, etc.), and lodging, as applicable. The FDA does not consider reimbursement for travel to and from the clinical trial site and associated costs to raise issues regarding undue influence.

6.2 Study personnel responsible for preparing and submitting the informed consents and assents to the IRB will ensure all information concerning proposed research participant compensation and travel reimbursement, including the amount and schedule of payment(s), are detailed in the informed consent documents. The documents must be reviewed and approved by the IRB prior to implementing.

6.3 The IRB of record will review both the amount of payment and the proposed method and timing of disbursement to assure that neither are coercive nor present undue influence [21 CFR 50.20].

6.4 PAYMENTS:
6.4.1 Payment methods should be approved by site and sponsor/investigator and included in the IRB application. Methods can be third-party vendors such as

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ClinCard, cash/check through FoxPro, & cash/gift cards from study grant, funding source, or department funds when applicable. The institution responsible for managing the grant funds is considered the "payor" and responsible for collecting, maintaining, and reporting financial information per IRS regulations, as applicable.

6.4.2 Cash/check through FoxPro: Grants Accounting team's role in the context of patient reimbursement is to – (1) request access to Patient Reimbursement System (PSR) through Sailpoint, (2) provide training to study coordinators, (3) create a study in PSR, (4) support study coordinators with issues during stipend creation, (5) support study coordinators when a payment is not received by the research participant in collaboration with Corporate Finance etc.

6.4.3 Electronic payments through UH ClinCard: study teams can submit a request to use the UH ClinCard platform to issue participant compensation, reimbursements, and to schedule transportation through Lyft. The UH ClinCard administrator will provide users with access to the platform, training, and create study-specific payment milestones. The UH CRC will be responsible for sending electronic W-9s and participant compensation information to the UH Supplier Correspondence per system policies. Study teams are responsible for securely storing W-9's and emailing them to SupplierCorrespondence@UHhospitals.org per system policies.

6.4.4 Study personnel should create a participant compensation log, **if this information cannot be reconciled elsewhere**, that details the dispensation of any participant compensation or travel reimbursement provided e.g. cash, checks, gift cards, meal vouchers or parking vouchers. The details of this log should include the date dispensed, participant IDs, dispensed by whom, etc.

6.4.5 A W-9 will be completed by the study participant in order to gain payment for study activities- as required by IRS regulations.
6.4.5.1 W-9s for related to payments issued through UH systems and/or funds managed by UH will be e-mailed by a designated study team member to SupplierCorrespondence@UHhospitals.org (as seen on the FoxPro Study Add Change form) for UH Finance records and IRS reporting requirements.
6.4.5.2 W-9s for payments issued through CWRU systems and/or funds managed by CWRU will be managed by your Grants Support staff.

6.4.6 All financial information and documents should be kept in a secure, limited access location and separate from any regulatory binders maintained by study personnel.

7. REFERENCES:
- University Hospitals Clinical Research Center: Investigator Manual for IRB Submissions

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- [FDA Office of Good Clinical Practices: Information Sheet; Payment and Reimbursement to Research Subjects - Guidance for Institutional Review Boards and Clinical Investigators, January 2018](#)
- [F-43 Grants Accounting Management](#)
- [F-32 Petty Cash Reimbursement](#)
- UH ClinCard [Request Form](#)
- UH GPS - [Greenphire ClinCard Coordinator Training](#)

8. **FORMS OR ATTACHMENTS:**
   - [FoxPro Study Add Change form](#)

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APPROVALS

Signed by Grace A McComsey, MD, FIDSA, Director of the UH Clinical Research Center, University Hospitals Health System –
December 13, 2023

</div>

Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SS-314 - Velos eResearch – Access and Data Entry Requirements

1. **PURPOSE:**
   To define the UH Clinical Research Center's (UHCRC) access control and data entry requirements within Velos eResearch, the Clinical Trial Management System (CTMS) used to manage human subjects research projects.

2. **SCOPE:**
   This SOP describes how to obtain access, enter data, and maintain accurate data in Velos eResearch. In order to set up a grant award, obtain certain agreements, and other financial aspects of a human subjects research project, Velos forms must be completed to have sign-off by the appropriate team.

3. **RESPONSIBLE INDIVIDUALS:**
   UHCRC Personnel, Departmental Research Personnel, Delegated Study Staff

4. **RELATED TERMS AND DEFINITIONS:**
   Velos eResearch Clinical Trial Management System (CTMS) – a web-based application with capabilities to manage administrative data for studies throughout their lifecycle and manage patient enrollment and research patient billing.
   Project-Task-Award-Expenditure-Organization (PTAEO) – the unique Oracle account string for management of expenses and invoices
   Electronic Case Report Form (eCRF) – an electronic data form employed by sponsors to collect study and subject visit data.
   Electronic Data Collection System (EDC) – an electronic system used by sponsors to collect study and subject information.
   Research Finance Services Invoice Request Form (RFS IRF) – a paper and electronic form utilized to capture invoiceable patient care expenses for invoicing.
   Grants Accounting Invoice Request Form (GAIRF) – a paper and electronic form utilized to capture invoiceable fixed fees expenses for invoicing.
   Radiology Information and Review Form – a form utilized to request review of any study that will utilize radiology services within the study.
   Investigational Pharmacy (IDS) Request Form – a combined form utilized to submit both investigational drug dispensing service requests and investigational drug exemption requests.
   Invoiceable Fees Checklist – a form utilized to submit the initial request for assessment of incidental fees requested by departments for industry sponsored studies. Final negotiated fees are available in the fixed fees budget in eResearch.

5. **POLICY STATEMENT:**
   This SOP supports the attainment of policy R-1: Clinical Research Investigation, by providing a centralized, secure, accessible and auditable data repository for required legal, fiscal, ethical, scientific and regulatory reviews. All human subjects research projects under the purview of UH IRB should be in Velos eResearch. Data requirement variations will occur depending on study type and funding source.

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6. PROCEDURES:

6.1 <u>Accessing the Velos eResearch environment</u>
Velos eResearch is a restricted access environment. Training must be completed prior to being granted access to Velos eResearch.

    6.1.1 Training can be accessed and completed in UH GPS.

        6.1.1.1 Velos for Study Coordinators is recommended for study staff and other departmental staff.

        6.1.1.2 Velos for Principal Investigators is recommended for UH Principal Investigators.

        6.1.1.3 Those who feel they do not fit into one of these categories may reach out to VelosSupport@UHhospitals.org for training guidance to be granted access to the application.

    6.1.2 After completion of required training and signed attestation, access to Velos eResearch will be granted.

        6.1.2.1 Velos eResearch must be accessed from a UH computer at a UH location, a UH portable computer via Cisco AnyConnect VPN, or through UH Virtual Desktop (VDI).

            6.1.2.1.1 Please see "Links and Resources" attachment for internal links to Virtual Desktop or VPN guidance.

        6.1.2.2 Use Google Chrome to navigate to Velos eResearch: https://uhvelosprdapp01.uhhs.com

        6.1.2.3 Sign into the application using UH network credentials. The user name field is case sensitive; if your UH network ID has capital letters you must type your username with capital letters.

            6.1.2.3.1 Velos eResearch is Imprivata Single Sign On compatible, username and password will be auto-filled by Imprivata for users with Single Sign On when accessing Velos using Google Chrome.

6.2 <u>Study and Data Access Permissions</u>

    6.2.1 General users must be listed on the study team tab in Velos and under the Contacts tab in SpartaIRB, to view and work with data belonging to a specific study. Existing study team members will have access to modify the study team.

        6.2.1.1 Study team roles must be assigned to users with respect to the SpartaIRB contact list. New study team members must be granted access to a study by an existing study team member or by Velos Support.

            6.2.1.1.1 Study team change requests may be sent to VelosSupport@UHhospitals.org if existing study team members are unable to make changes to the study team

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list. This should not be the primary method used to update study team lists.

6.2.1.2 Study team changes are required to comply with the approved IRB submission and HIPAA regulations.

6.2.1.3 Changes to the study team are audited and validated against the SpartaIRB contact list by Velos Support and Research Compliance.

6.2.1.4 If you are unable to find the user you are searching for, email VelosSupport@UHhospitals.org to have the user added to the application. *This new user will not have access to sign into the application until they complete training.*

6.2.1.5 Requests for changes to security group assignment must be submitted to VelosSupport@UHhospitals.org. Users assigned to departmental security groups must be added to the study team list, in addition to security group assignment, if they are associating patients with studies or updating patient status and billing information due to EMR integration.

6.2.2 Employee Transfers or Terminations
6.2.2.1 The department may notify VelosSupport@UHhospitals.org upon the transfer or termination of an employee to remove previously granted permissions, and refer to Clinical Research SOP GA-109 – Departing Investigators if the departing employee is an Investigator.

6.3 Data Entry Requirements
6.3.1 The department study team will enter and maintain a study summary, containing general study information, for their human subject research studies.
6.3.1.1 **Required fields:**
6.3.1.1.1 Principal Investigator
6.3.1.1.2 Study Contact
6.3.1.1.3 Short Title (should match IRB submission)
6.3.1.1.3.1 Studies of sensitive nature may wish to use a masked Short Title as this field is interfaced as a banner note on a patient chart within the EMR when associated with the study.
6.3.1.1.4 IRB Approved Full Protocol Title
6.3.1.1.5 Description and Contact Information for Epic
6.3.1.1.6 NCT Number (if applicable)
6.3.1.1.7 Department
6.3.1.1.8 Division
6.3.1.1.9 Local Accrual Target
6.3.1.1.10 Phase (if applicable)
6.3.1.1.11 Origin of Protocol

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6.3.1.1.11.1 Investigator initiated studies must indicate if the study is initiated by a UH PI or an external party.

6.3.1.1.11.2 Studies flagged as Investigator initiated will trigger notifications to Investigational Drug Services and appropriate CRC Core Offices for additional review.

6.3.1.1.12 Study Type

6.3.1.1.13 Funding Source (if Other you must specify)

6.3.1.1.14 IRB number (once available)

6.3.1.1.15 IDE number (only for IDE studies)

6.3.1.2 Recommended Optional Fields

6.3.1.2.1 Study Scope

6.3.1.2.2 Blinding (if applicable)

6.3.1.2.3 Randomization (if applicable)

6.3.1.3 Department management is responsible for monitoring compliance with the above data entry requirements, at minimum on a quarterly basis, by utilizing the Velos "Study Summary Audit" report. Management will ensure that missing required data entry is completed.

6.3.2 End users will be responsible for entering and maintaining an accurate listing of study statuses throughout the lifecycle of their study

6.3.2.1 Users must enter study statuses that pertain to their job role with respect to the study.

6.3.2.2 Status dates must reflect the actual date a status was first valid, not the date the status was documented in Velos eResearch.

6.3.2.3 "IRB – Initial Approval" is a start-up timeline management status, the IRB remains the source of record for actual approval determinations.

6.3.3 All prospectively enrolling research studies must have patient enrollment tracked in Velos eResearch. Patients must be associated with their study the day of consent, or prior, to support Research Billing.
Patient lists must have current patient statuses (see *Appendix A*: Velos Study and Patient Statuses).

6.3.3.1 Patients must be associated with studies by utilizing the patient search function using a UH MRN.

6.3.3.1.1 Patients must be registered with a UH MRN, any patient without a UH MRN must not be associated with a study due to EMR integration.

6.3.3.1.2 Patients must not be added by using the Add New Patient function.

6.3.3.1.3 Failure to complete this step may result in incorrect billing of study procedures or inaccurate placement of study information on an EMR patient chart.

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6.3.3.1.4 If a patient is unable to be located using patient search, reach out to VelosSupport@UHhospitals.org.

6.3.3.2 Users are prohibited from altering the Velos ID or Patient ID field, these must contain the patient's UH MRN.

6.3.3.3 Patient demographics updates must be made in the EMR, changes should not be made directly in Velos. Any EMR demographic changes, ADT (Admit, Discharge, Transfer) and scheduling events will overwrite demographic changes made directly in Velos.

6.3.3.4 Patient Study ID must be recorded in the Patient Study ID field.

6.3.3.5 Study Teams must document the following patient statuses for patients:
6.3.3.5.1 Informed Consent Signed
6.3.3.5.2 Enrolled/Randomized or Screen Failure (for Interventional Studies)
6.3.3.5.3 Lost to Follow-Up or Withdrawn or Completed / Off Study

6.3.3.6 Additional Statuses for Interventional Studies: Active / On Treatment, Off Treatment and In Follow-Up

6.3.3.7 Status dates must reflect the actual date a status was first valid, not the date the status was documented in Velos eResearch.

6.3.3.8 Additional statuses may be required by other CRC Cores to support internal business practices.

6.3.4 All research studies with clinically billable patient care must utilize a patient calendar to manage research patient billing in accordance with Policy R-2.
6.3.4.1 Velos eResearch supports Policy R-2 by housing coverage analysis template, the patient list and patient specific coverage analysis documentation.
6.3.4.1.1 Newly consented patients must be added to their research study in Velos eResearch during the consenting/screening visit before the encounter closes in Epic. Failure to complete this step will result in patient charges failing to flow through the Research Charge Review process.

6.3.4.1.2 Existing patients must have their encounters linked to their study in Epic to facilitate Research Charge Review. Encounters can be linked at the time of scheduling, during the visit or from reporting available in Epic. Encounters must be linked before they close. Encounters cannot be linked in Epic after the encounter closes.

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6.3.4.1.3 Velos eResearch automates the Research Billing Notification process by electronically notifying Research Finance when a patient visit has the RBNF Notification line(s) marked as done.

6.3.5 Invoiceable expenses that occur must be recorded in Velos eResearch via Study Status Documentation, Patient Status Documentation, or completion of a RFSIRF or GAIRF as directed by the responsible Research Finance Specialist and Grant Accountant with respect to Clinical Research SOP GA-110 – Management of Clinical Research Expense Invoicing.

6.3.6 <u>Study Entry Timeline and CRC Administrative Support Data Entry</u>
   6.3.6.1 Study Entry Into IRB and Velos eResearch

   6.3.6.2 Study Startup Form Entry in Velos as applicable
      6.3.6.2.1 Startup - Coordinator Workflow Job-Aid
         6.3.6.2.1.1 Reference form that provides contact information for departments that provide services for research.

      6.3.6.2.2 Startup - Invoiceable Fees Checklist Form
         6.3.6.2.2.1 The study team completes this form for studies that require an agreement that is managed through UHCRC Grants and Contracts to direct the Grant and Contract specialist which fixed fees should be included in the agreement budget.

      6.3.6.2.3 Startup - PI Compensation_Qualifying Study Status Form
         6.3.6.2.3.1 The Principal Investigator completes this form and signs with a form status "PI Approved" to indicate any conflicts of interest, select their allocation for the PI compensation program if applicable and attests to Medicare Qualifying Status for patient care related to the study.

      6.3.6.2.4 IDS Request Form
         6.3.6.2.4.1 The study team completes this form for studies requiring dispensing of investigational drugs to request a quote or exception approval from Investigational Pharmacy Services.

      6.3.6.2.5 DCRU Service Request Form
         6.3.6.2.5.1 The study team can complete this pass-through form for studies in which they would like to

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engage DCRU services.
*Note: Data entered in this pass-through form is saved in Redcap and will not be visible in Velos after submission.

  6.3.6.2.6 Radiology Information and Review Form
    6.3.6.2.6.1 The study team can complete this form for studies in which they would like to engage Radiology services.

  6.3.6.2.7 Submit for Trial Finder Review
    6.3.6.2.7.1 The study team can complete this form for studies they would like to have advertised on the UH Clinical Trial Finder App.

  6.3.6.2.8 RIE – Clinical Trial Finder Submission Review
    6.3.6.2.8.1 The Research Integration & Education team will complete this form after reviewing study information before publishing the study to the Clinical Trial Finder App.

6.3.6.3 Pre-Award Grants & Contracts Team Documentation for Industry Funded Studies
  6.3.6.3.1 Wellspring Number, Industry Sponsor Name, Budget and Contract Development and Execution Timeline
  6.3.6.3.2 Fixed Fee Schedule
  6.3.6.3.3 Invoicing and Payment Terms

6.3.6.4 Post-Award Grants Accounting Documentation for Industry Funded Studies
  6.3.6.4.1 Award Account String "PTAEO" and Grant Setup Date
  6.3.6.4.2 Review and Management of Velos eResearch GAIRF forms
  6.3.6.4.3 Milestones for Management of Fixed Fee Invoiceables
  6.3.6.4.4 Invoicing of Manually Collected Receivables
  6.3.6.4.5 Review of Outstanding Manual and Auto-triggered receivables

6.3.6.5 Research Patient Billing – Research Finance Documentation for Trials with Clinically Billable Patient Care
  6.3.6.5.1 Coverage Analysis Development and Approval Timeline
  6.3.6.5.2 Coverage Analysis/Patient Calendar Template
  6.3.6.5.3 Patient Charge Segregation Documentation
  6.3.6.5.4 Milestones for Management of Patient Care Invoiceables
  6.3.6.5.5 Milestones for Management of Patient Care eCRF/EDC triggered receivables
  6.3.6.5.6 Invoicing of Manually Collected Receivables

6.3.6.5.7   Review of Outstanding Manual and Auto-triggered
receivables

6.4   Velos and Epic EHR Integrations
6.4.1   The Velos eResearch environment and Epic EHR system are integrated to
facilitate data transfer between the two systems
6.4.1.1   Patient demographics from Epic to Velos, provides patient information
for easy and accurate lookup of patients in the Velos eResearch
environment as well as updates to existing patients when
demographics are updated in Epic.
6.4.1.2   Study Records from Velos to Epic, provides functionality to create
Research Study Records (RSH Records) in Epic, as well as updates to
those records as data is updated in Velos eResearch. This enables
functionality within the research module in Epic
6.4.1.3   Patient Study Associations from Velos to Epic, provides functionality to
link patients to studies from the Study Records integration. Patients are
linked to their respective studies in Epic when added to their study in
Velos. Updates to patient statuses are also pushed from Velos to Epic
as added in Velos.
6.4.1.4   Study Calendar/Billing Protocols from Velos to Epic, provides
functionality to create patient timelines and link encounters to study
calendar visits to support Research Billing Workflows

6.4.2   Creating and Updating a Research Study Record in Epic from Velos
6.4.2.1   Study records can be created or updated in Epic by adding certain
study statuses. Only those statuses denoted with an asterisk (*) may
be used multiple times if updates to the study record are needed.
6.4.2.1.1   Study / Active – Open to accrual
6.4.2.1.2   Study / Active – Closed to accrual
6.4.2.1.3   Study – Closed / Completed
6.4.2.1.4   Study – Withdrawn
6.4.2.1.5   Study – Terminated
6.4.2.1.6   Send to Epic – Active*
6.4.2.1.7   Send to Epic – Not Recruiting*

6.4.3   Linking Patients to Studies and Updating Patient Status in Epic from Velos
6.4.3.1   Patients will be automatically associated/linked to their study record in
Epic when patients are added to a study in Velos
6.4.3.2   Patient statuses will be automatically updated in Epic when their
patient status is updated in Velos.
6.4.4   Study Calendar/Billing Protocol Creation in Epic from Velos
6.4.4.1   Research Finance and the Seidman Budget Analyst teams must
release Billing Protocols in Epic for use to create patient timelines.

7. **REFERENCES:**
- [UH System Policies](#) in the Digital Workplace (DWP)

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- o R-1 – Clinical Research Investigation
- o R-2 – Research Patient Billing
- UH Clinical Research SOPs
  - o GA-109 – Departing Investigators
  - o GA-110 – Management of Clinical Research Expense Invoicing
  - o SP-202 – Coverage Analysis & Clinical Budget Development Process Flow
  - o SP-203 – Radiology Research Review
  - o SS-304 – Investigational Drug Billing
- Virtual Desktop (VDI) Resource Link
- Velos eResearch (Must use Google Chrome Browser)
- Velos eResearch Resource Center on the Digital Workplace (DWP)
- Velos for Study Coordinators Training
- Velos for Principal Investigators Training

8. FORMS OR ATTACHMENTS:
- Appendix A: Velos Patient and Study Status Definitions
- Appendix B: Velos to Epic Data Integration Definitions

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – September 28, 2023

Appendix A – Velos Patient and Study Status Definitions

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Departmental Study Statuses – To Be Entered by Departmental Study Team:

Radiology Process Review Requested: requested by users. Entry by department upon submission of request to Radiology.

Research IT Review: requested by users. Entry by department upon submission of request to Radiology.

IRB – Initial Approval: To be entered by department upon reciept of initial approval letter from IRB.

Study Active / Open to accrual: Study is open to enrollment.

Study Active / Closed to accrual: Study is closed to enrollment. Patients may still be on study and the study is still active with the IRB.

Study – Closed / Completed: Study activity is completed, data analysis completed, no additional research activities and study is closed with IRB

Study – On Hold: Study is placed on hold during study activation activities

Study – Suspended: Study is activated and study enrollment is halted

Study – Terminated: Terminated by sponsor, FDA or other external entity.

Study – Withdrawn: Withdrawn from study start-up process; will not proceed to opening

Patient Statuses:

Screen Failure: patient failed to meet enrollment/inclusion criteria

Re-Screened: patient is evaluated again for potential enrollment

Informed Consent Signed: patient signed informed consent

Enrolled/Randomized: active on trial*

Active/On Treatment: patient is actively on treatment

Off Treatment: patient is off treatment, but still on study

In Follow-Up: patient is off treatment and in follow up phase of study

Lost to Follow-Up – lost to follow-up / off study

Withdrawn – no further study care will be provided

Completed / Off Study: all study visits performed

Reconsent Signed: patient signed new consent form

Serious Adverse Event: patient experienced a Serious Adverse Event

Adverse Event: patient experienced an Adverse Event

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Appendix B – Velos to Epic Data Integration Definitions
General Study Fields Sent to Epic

Velos Field Name	Epic Field Name	Data Type
Study Number	Study Code	Exact Match
Short Title	Study Name	Exact Match
Description and Contact Information for Epic	Description	Exact Match
Study Type	Study Type	Mapped
Study Status	Study Status	Mapped
IRB Number	Approval Number	Exact Match
NCT Number	NCT Number	Exact Match
IDE Number	IDE #	Exact Match
Grant {Project, Task, Award, Expenditure, Organization}	PTAEO	Exact Match
DCRU Number	DCRU #	Exact Match

Study Type Mappings

Velos Study Type	Epic Study Type
Companion Correlative Diagnostic Epidemiological Feasibility Interventional / Therapeutic Interventional / Device Prevention Screening or Early Detection Supportive Care Others Tissue Banking or Laboratory Collection	Interventional
Chart Review (Retrospective) Observational Questionnaire or QoL	Observational
Compassionate Use Registry	Expanded Access

Study Status Mappings

Velos Study Status	Epic Study Status
Study – Active / Open to accrual	Recruiting
Send to Epic – Active	Recruiting
Study – Active / Closed to accrual	Active, not recruiting
Send to Epic – Not Recruiting	Active, not recruiting
Study – Closed / Completed	Completed
Study – Terminated	Terminated
Study – Withdrawn	Withdrawn

Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SC-401 - Registration of Clinical Trials in ClinicalTrials.gov

1. PURPOSE:

This Standard Operating Procedure (SOP) describes the creation of an account and registration of a clinical trial on ClinicalTrials.gov.

This process involves two distinct steps:
Step 1 of 2: Creation of a ClinicalTrials.gov Account
Step 2 of 2: Registering a Clinical Trial

For questions or more detailed help, please email UHResearchCompliance@UHhospitals.org.

Please refer to SOP *SC-406 - Results Reporting of Clinical Trials in ClinicalTrials.gov* regarding the entry of clinical trials results within the ClinicalTrials.gov system.

2. SCOPE:

This SOP will provide instruction and promote consistency among all departments within University Hospitals Cleveland Medical Center (UHCMC) regarding the requirement of registering applicable clinical trials with ClinicalTrials.gov. The U.S. Food and Drug Administration (FDA) is the government agency that requires registration of clinical trials. Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA 801 or US Public Law 110-85) passed on September 27, 2007 requires mandatory registration and results reporting for certain clinical trials of drugs, biologics, and devices of all applicable clinical trials initiated on or before September 27, 2007, and is ongoing as of December 27, 2007. This legislation coupled with the Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11) creates the regulatory requirements and procedures for ClinicalTrials.gov.

The International Committee of Medical Journal Editors (ICMJE) member journals require, as a condition of consideration for publication in their journals, registration in a public trials registry. The ICMJE does not advocate one particular registry, but its member journals require authors to register their trial in a registry that meets several criteria.

According to the Food and Drug Administration Amendments Act of 2007:
- Penalties may include civil monetary penalties up to $12,462 fine for failing to submit or for submitting fraudulent information to ClinicalTrials.gov.
  - **NOTE:** fines increase annually to reflect inflation
- After notification of noncompliance, the fine may go up to $12, 462 per day until resolved.
  - **NOTE:** fines increase annually to reflect inflation
- For federally funded grants, penalties may include the withholding or recovery of grant funds.

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2.1   Registration Requirements:
      Ultimately, all interventional studies need to be registered.

      2.1.1   FDA Regulated Research Requirements:
              FDAAA requires registration and results reporting of 'Applicable Clinical Trials
              (ACTs)'. An ' (ACT)' is defined as:
              2.1.1.1 Interventional studies;
              2.1.1.2 Studies that require an IND or IDE;
              2.1.1.3 Studies where AT LEAST ONE or more of the following applies:
                       2.1.1.3.1   at least one site in the US or one of its territories, or
                       2.1.1.3.2   study is conducted under an IND or IDE
                       2.1.1.3.3   the product is manufactured in and exported from the US or
                                   one of its territories.
              2.1.1.4 Studies that evaluate at least one drug, biological, or device product
                       regulated by the FDA
              2.1.1.5 Studies that are not Phase 1 (drug and biological products)* or not
                       Device Feasibility (device products)**
              2.1.1.6 Clinical trials must be submitted for registration with ClinicalTrials.gov
                       within 21 days after the enrollment of the first patient.'
      *Phase 1 studies of new drugs are usually the first that involve people. Phase 1 studies
      are done **to find the highest dose of the new treatment that can be given safely
      without causing severe side effects.**Device Feasibility are usually **10 or fewer**
      people to test the safety/efficacy of the device, has to meet very specific criteria to fit
      feasibility.

      2.1.2   For more information regarding 'Applicable Clinical Trials', see Elaboration of
              Definitions of Responsible Party and Applicable Clinical Trials. ClinicalTrials.gov
              also provided the Checklist and Elaboration for Evaluating Whether a Clinical
              Trial or Study is an Applicable Clinical Trial
              (https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf) as a reference.

      2.1.3   While Phase I trials or device feasibility studies are not considered 'Applicable
              Clinical Trials' under the FDAAA regulations, they do need to be registered if the
              study will be published, use Medicare or receive funding from NIH, as described
              below.

2.2   ICMJE Requirements:
      The ICMJE requires, and recommends that all medical journal editors require,
      registration of clinical trials in a public trials registry before the time of first patient
      enrollment as a condition of consideration for publication. Editors requesting inclusion
      of their journal on the ICMJE website list of publications that follow ICMJE guidance
      should recognize that the listing implies enforcement by the journal of ICMJE's trial
      registration policy.

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http://icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html

2.3 <u>Medicare Requirements:</u>
Effective January 1, 2015, all Medicare qualifying trials, including some Phase 1 and device feasibility trials, are required to be registered into the ClinicalTrials.gov database. NCT numbers are required on clinical research related claims in order to receive payment. Patients should not be enrolled on a trial unless the NCT registration number is in place.

2.4 <u>NIH Requirements:</u>
The National Institutes of Health (NIH) Policy on Dissemination of NIH-Funded Clinical Trial Information requires registration and results reporting, and applies to all clinical trials funded by NIH, regardless of whether they are subject to the FDAAA 801 and the Final Rule effective January 18, 2017. The Policy is effective for competing applications and contract proposals submitted on or after January 18, 2017 and states that all NIH-funded awardees and investigators conducting clinical trials will register and report the results of their clinical trials in ClinicalTrials.gov. Please refer to the following grants policy information from NIH's Office of Extramural Research to learn more about ensuring compliance with NIH's implementation of FDAAA 801: https://grants.nih.gov/policy/clinical-trials/reporting/index.htm

To help answer the question, "Does your human subjects research study meet the NIH Definition of a clinical trial?" Please go to https://grants.nih.gov/ct-decision/index.htm.

3. RESPONSIBLE INDIVIDUALS:
3.1 <u>FDA Regulated Research Requirements:</u>
According to federal law, the 'Responsible Party' is responsible for registering and reporting results to ClinicalTrials.gov and is defined as:
3.1.1 The IND/IDE holder of the trial, or
3.1.2 For studies not conducted under an IND/IDE
3.1.2.1 The study sponsor or the grantee institution,
3.1.2.2 Principal Investigator, if there is no external funding agreement

3.1.3 <u>Situations in which Institution/PI is the Responsible Party</u>
For trials being conducted under a funding agreement, grant (e.g. NIH awards) or department/internal funding, the funding recipient is considered the Responsible Party. Because the PI is in best position to understand the research protocol study results and adverse events, the institution will designate the Principal Investigator to assume the role of the Responsible Party.

In situations where UH serves as the primary site for a clinical trial and the institution is determined to be the "Responsible Party," the Institution will designate this responsibility to the Principal Investigator.

3.1.4 <u>Situations in which Institution/PI is NOT the Responsible Party</u>

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For most industry sponsored trials, the sponsor will be the Responsible Party, and, as such, the institution and PI will NOT have to manage submissions to ClinicalTrials.gov. Similarly, for multi-center and academic center trials, only the lead site (overall PI) typically bears responsibility for ClinicalTrials.gov reporting; site PIs typically do not have to do additional reporting.

    3.1.5 <u>What are the criteria for designating the Principal Investigator as the "Responsible Party" for registering and reporting results?</u>
According to federal law, the Principal Investigator can serve as a Responsible Party if that individual:
3.1.5.1 Is responsible for conducting the trial
3.1.5.2 Has access to and control over the data from the clinical trial
3.1.5.3 Has the right to publish the results of the trial

3.2 <u>ICMJE Requirements</u>
Anyone involved in the clinical trial could register the trial, in practice this responsibility usually falls with the individual submitting the publication to the ICMJE journal, which is usually the Principal Investigator.

3.3 <u>Medicare Requirements:</u>
In order to ensure proper research billing compliance, it is the responsibility of department research personnel to communicate the NCT number to their Research Finance Specialist (RFS) during administrative study start-up and prior to any patient enrollment on the trial. It is the responsibility of the RFS to associate the appropriate NCT number with study related claims and assure this communication to the appropriate parties in revenue cycle management.

3.4 <u>NIH Requirements:</u>
The trial's "responsible party" is responsible for two basic elements of compliance:
3.4.1 The registration of the ACTs in ClinicalTrials.gov, and
3.4.2 The reporting of summary results information (including adverse events)

3.5 All NIH grantees, regardless of whether or not they are the "responsible party" under FDAAA are responsible for:
3.5.1 Certification in the grant application and progress report forms that the responsible party has made all required submissions to ClinicalTrials.gov for ACTs funded in whole or in part by the NIH.

4. DEFINITIONS:
ACT - Applicable Clinical Trial
CCCC - Case Comprehensive Cancer Center
ICMJE - International Committee of Medical Journal Editors
NCT Number - National Clinical Trial (NCT) number, another term for the ClinicalTrials.gov registry number unique to each record. The format for the ClinicalTrials.gov registry number is "NCT" followed by an 8-digit number (*e.g.*, NCT00000419).

PRS (Protocol Registration and Results System) - A quality control and reviewing body to ensure all aspects of a clinical trial are entered according to federal regulations.

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:

All applicable clinical trials must be registered in ClinicalTrials.gov. All studies must be registered no later than 21 days after enrollment of the first participant. In addition, failure to register applicable trials by an investigator could delay future research approvals.

The ICMJE clinical trial registration policy requires prospective registration (i.e., registration prior to first person enrolled) of all interventional clinical studies. Please see References below for additional information.

6. PROCEDURES:

6.1 **Step 1: Creation of a ClinicalTrials.gov Account**
To establish an account with the ClinicalTrials.gov Protocol and Registration System email your request to UHResearchCompliance@UHhospitals.org. An account will be created within 2 business days.

6.2 **Step 2: Registering a Clinical Trial**
Registration of a study will take approximately one (1) hour, you can save and come back as needed. It will be helpful to have the following:
- The protocol
- Informed consent document
- IRB approval date and number (if available)

6.2.1 Login at https://register.clinicaltrials.gov/ with the information from your account registration using your username, password, and one-word organization name assigned by PRS (UHClevelandMC) Emailed UHResearchCompliance@UHhospitals.org if you need your password re-set.

6.2.2 Click on "**New Record**" in the Quicklinks dialogue box on the left or add a record in the "**Records**" drop down menu. A "**Create New Records**" page will be displayed.
Organization's Unique Protocol ID: use the assigned UHCMC IRB number.
Brief Title: [DO NOT ENTER THE OFFICIAL STUDY TITLE NOR THE IRB NUMBER IN THIS FIELD]
Acronym (If Required): [CONDITIONAL, MAY BE LEFT BLANK]
Study Type: Select the appropriate type – (1) Interventional, (2) Observational, or (3) Expanded Access

6.2.3 Select "**Continue**" to proceed followed by "Okay" in the next dialogue box.

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6.2.4 An "**Edit Study Identification**" page will appear. Complete as follows:
Organization's Unique Protocol ID: use the assigned UHCMC IRB number.
Brief Title: [DO NOT ENTER THE OFFICIAL STUDY TITLE NOR THE IRB NUMBER IN THIS FIELD]
Acronym (If Required): [CONDITIONAL, MAY BE LEFT BLANK]
Official Title: [ENTER STUDY'S FULL TITLE HERE SHOULD MATCH OFFICAL TITLE SUBMITTED TO IRB]
Secondary IDs: [IF ANY, e.g., the grant number, funding agency number or other funding source number] **NOTE:** sometimes it can take a while for a grant number to show up in the system. If you get an error message, leave blank and try entering again in a few weeks. It is okay to submit the record if the grant number in not yet available, you will just need to make sure to add it the next time you are in the record making edits.

6.2.5 Select "**Continue**" to proceed.

6.2.6 An "**Edit Study Status**" page will appear. Complete as follows:
Record Verification Date: [ENTER MONTH AND YEAR] This date should be updated to the current MONTH and YEAR each time you are in the record. Records are required to be verified annually and this is the date they track that by.
Overall Recruitment Status: [CHOOSE FROM DROP DOWN MENU]
Study Start Date: [ENTER MONTH, DAY, YEAR, AND TYPE]
Primary Completion Date: [ENTER MONTH, DAY, YEAR, AND TYPE]Should reflect **DATA COLLECTION ONLY.** Reference time frames listed in primary outcomes for this date.
Study Completion Date: [ENTER MONTH, DAY, YEAR, AND TYPE] Should reflect **DATA COLLECTION ONLY.** Reference time frames listed in secondary outcomes for this date.
NOTE: if you have the same time frames for both primary and secondary outcomes your completion dates SHOULD BE THE SAME.

6.2.7 Select "**Continue**" to proceed.

6.2.8 An "**Edit Sponsor/Collaborators**" page will appear. Complete as follows:
Responsible Party: [SELECT SPONSOR-INVESTIGATOR OR PRINCIPAL INVESTIGATOR]
Investigator Name (Username): [SELECT NAME FROM THE DROP DOWN MENU]
Investigator Official Title: [INPUT THEIR TITLE]
Sponsor: [ENTER SPONSOR IF NOT PREPOPULATED BY SYSTEM]
Collaborators: [ENTER ORGANIZATION NAME OF ANY SUPPORTING, FUNDING, IMPLEMENTATION, DATA ANALYSIS, OR REPORTING ORGANIZATIONS]

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6.2.9 Select "**Continue**" to proceed.

6.2.10 An "**Edit Oversight**" page will appear. Complete as follows:
U.S. FDA Regulated Drug: Enter "Yes" or "No".
U.S. FDA Regulated Device: Enter "Yes" or "No".
    If you select YES the following fields will appear, fill out as appropriate:
    Unapproved/Uncleared Device: "Yes" or "No"
        NOTE: if you select "No" this will not satisfy ICMJE requirements
        since it will delay the posting on ClincialTrials.gov and may cause
        publication issues.
Pediatric Postmarket Surveillance: "Yes" or "No"
U.S. FDA IND/IDE: Enter "Yes" or "No".
    If you select "Yes" the following fields will appear, fill out as appropriate:
    FDA Center: Select from drop down
    IND/IDE Number: IND/IDE number assigned by the US FDA
        NOTE: if you have not yet received your IND/IDE number mark US
        FDA IND/IDE "No" and update later once the number has been
        received.
    IND Serial Number: 4 digit number entered on the US FDA application,
    Form 1571, if any
Human Subjects Protection Review: Board Status: [ENTER THE
APPROPRIATE RESPONSE (E.G., EXEMPT; SUBMITTED, PENDING;
SUBMITTED, APPROVED; ETC.)]
NOTE: Exempt should only be chosen for studies deemed exempt by the IRB.
ClinicalTrials.gov will request your exemption letter.
    If you select "Submitted, Approved" it will ask for an Approval Number-
    enter your IRB assigned number here.
Board Name: University Hospitals Cleveland Medical Center Institutional Review
Board
Board Affiliation: University Hospitals Cleveland Medical Center
Phone: (216)844-1529
Email: UHIRB@UHhospitals.org
Address: 11100 Euclid Avenue, Cleveland, OH 44106
Data Monitoring Committee: Select "Yes" or "No".
FDA Regulated Intervention: Select "Yes" or "No".
If you mark "Yes" another field will populate, this is in reference to applicable
clinical trial status:
Section 801 Clinical Trial: Select "Yes" or "No"

6.2.11 Select "**Continue**" to proceed.

6.2.12 An "**Edit Study Description**" page will appear. Complete as follows:
NOTE: There are character limits with this section
Brief Summary: [INPUT BRIEF SUMMATION OF THE STUDY.]

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NOTE: this should be in lay terms, you can use language in consent form for ease. ClinicalTrials.gov does not like the use of pronouns so make sure to edit as appropriate.
Detailed Description: [INPUT A SPECIFIED OVERVIEW OF THE STUDY, NOT THE ENTIRE PROTOCOL.] Not required to be filled out.

6.2.13 Select "**Continue**" to proceed.

6.2.14 An "**Edit Conditions**" page will appear. Complete as follows:
Conditions or Focus of Study: [SEARCH FOR TAGS RELATED TO THE DISEASE OR CONDITION INTO THE FIELD SPACE. THIS WILL QUERY THE DATABASE ON THE SITE FOR MATCHING TAGS.]
Keywords: [ENTER KEY TERMS HERE. THIS WILL HELP USERS FIND YOUR CLINICAL TRIAL.]

6.2.15 Select "**Continue**" to proceed.

6.2.16 An "**Edit [Observational/Interventional/Expanded Access] Study Design**" page will appear. Complete as follows:
Study Type: Select either:
A) Interventional,
B) Observational, or
C) Expanded Access.

Follow the guided prompts below (A-C) for the appropriate fit for your trial.

A) INTERVENTIONAL

   a. *PART I: STUDY DESIGN (Interventional Only)*
   Primary Purpose: Select, "Treatment, Prevention, Diagnostic, Supportive Care, Screening, Health Services Research, Basic Science, Device Feasibility, or Other".
   Study Phase: Select, "N/A, Early Phase 1 (Phase 0), Phase 1, Phase 1/Phase 2, Phase 2, Phase 2/Phase 3, Phase 3, Phase 4".
   NOTE: Study Phase should ONLY be used for drugs and biologicals.
   Interventional Study Model: Select, "Single Group, Parallel, Crossover, Factorial, or Sequential".
   Model Description: [NOT A REQUIRED FIELD, BEST FOR COMPLICATED DESIGN EXPLANATIONS.]
   Number of Arms: [ENTER APPROPRIATE NUMBER PER TRIAL DESIGN.] Arms should correlate with how the data is being reported for the study.
   Masking: Check one, "Participant, Care Provider, Investigator, Outcomes Assessor, or None (Open Label)."
   Masking Description: [NOT A REQUIRED FIELD, BEST FOR COMPLICATED DESIGN EXPLANATIONS.]

Allocation: Select, "N/A, Randomized, or Non-Randomized."
Enrollment: [ENTER NUMBER OF SUBJECTS AND TYPE (ANTICIPATED OR ACTUAL).]

b. *PART II: ARMS AND INTERVENTIONS (Interventional Only)*
Arm Title: [ENTER DESCRIPTIVE TITLE FOR ARM.]
Arm Type: Select from, "Experimental, Active Comparator, Placebo Comparator, Sham Comparator, No Intervention, or Other".
Arm Description: Open field text box [DESCRIBE THE INTERVENTION(S) TO BE ADMINISTERED].
Interventions
Intervention Type: Select, "Drug, Device, Biological/Vaccine, Procedure/Surgery, Radiation, Behavioral, Genetic, Dietary Supplement, Combination Product, Diagnostic Test, or Other".
Intervention Name: [ENTER NAME OF INTERVENTION IN FIELD.]
Other Intervention Names: [ENTER ANY OTHER NAMES OF INTERVENTIONS.]
Intervention Description: [WRITE DESCRIPTIVE SUMMARY OF THE INTERVENTION(S).]
CROSS-REFERENCE: This field appears if there are more than 1 arm and/or more than 1 intervention.

c. *PART III: OUTCOME MEASURES (Interventional Only)*
NOTE: ALL primary and secondary outcomes listed in the protocol are **REQUIRED** to be entered in the record.
Outcome should be formatted in a very specific format: What you are measuring and How, no description or narration. Only ONE measure per outcome. Try to be as numerical as possible.
Title: [ENTER TITLE FOR OUTCOME]
Description: [WRITE A DESCRIPTION FOR THE OUTCOME TO BE MEASURED.]
Time Frame: [PICK AN ADEQUATE/APPROPRIATE TIME FRAME.]
Time frame should reflect specific time point of data collection FOR THAT OUTCOME MEASURE. For example, if you are collecting data via a survey, the time frame should be length of time it takes participants to complete the survey, ie. Up to 45 mins.
Only ONE time point should be included in the time frame, unless you are measuring a change. If you are measuring a change "Change" has to be included in your title.
NOTE: Additional Outcomes may be added, as needed.
Secondary Outcome Measures:
Title: [ENTER TITLE FOR OUTCOME]
Description: [WRITE A DESCRIPTION FOR THE OUTCOME TO BE MEASURED.]
Time Frame: [PICK AN ADEQUATE/APPROPRIATE TIME FRAME.]
NOTE: Additional Outcomes may be added, as needed.

Other Pre-Specified Outcomes
NOT required to be entered. You should list any exploratory outcomes listed as such in the protocol here. Only outcomes listed as EXPLORATORY or TIRTIARY are allowed to be listed here.
Title: [ENTER TITLE FOR OUTCOME]
Description: [WRITE A DESCRIPTION FOR THE OUTCOME TO BE MEASURED.]
Time Frame: [PICK AN ADEQUATE/APPROPRIATE TIME FRAME.]
NOTE: Additional Outcomes may be added, as needed.

d. *PART IV: ELIGIBILITY (Interventional Only)*
Sex: Select, "Male," "Female," or "All".
Gender Based: Select, "Yes" or "No".
Age Limits: [DETERMINE THE MINIMUM AND MAXIMUM VALUES.]
Accepts Healthy Volunteers: Select, "Yes" or "No".
Eligibility Criteria: [ENTER THE INCLUSION CRITERIA AND THE EXCLUSION CRITERIA IN THE TEXT BOX].

e. *PART V: CONTACTS/LOCATIONS (Interventional Only)*
Central Contact Person: [COMPLETE FIELDS: FIRST, MI, LAST NAME, AND DEGREE, PHONE & EXT, & EMAIL.]
Central Contact Backup: Not a required field.
Overall Study Officials: [COMPLETE FIELDS: FIRST, MI, LAST NAME, AND DEGREE, ORGANIZATIONAL AFFILIATION, & OFFICIAL'S ROLE.] Required per ICMJE
Add Locations
Facility: [COMPLETE FIELDS: NAME, CITY, STATE/PROVINCE, ZIP/POSTAL CODE, AND COUNTRY.]
Site Recruitment Status: Select, "Not Yet Recruiting; Recruiting; Enrolled by Invitation; Active, Not Recruiting; Completed; Suspended; Terminated (Halted Prematurely); or Withdrawn (No Participants Enrolled)".
Facility Contact: [COMPLETE FIELDS: FIRST, MI, LAST NAME, AND DEGREE, PHONE & EXT, & EMAIL.]
Add Investigator: Add investigators as necessary.

f. *PART VI: IPD SHARING (Interventional Only)*
NOTE: This is individual participant level data, no aggregate data sets. If you have plans to share this level of data your plan has to be submitted to the IRB for their review and approval. Mark this as "No" until IRB has review and approved your plan. Undecided is not accepted per ICMJE policies. Please mark either "Yes" if your plan has been submitted and approved by IRB, or "No" if you do not have plans to share this level of data.

Plan to Share IPD: Select "Yes", "No", or "Undecided". [COMPLETE ACCORDING TO THE PREPOPULATED DROP DOWNS.]

g. *PART VII: REFERENCES (Interventional Only)*
Citations: Not required.
Links: Not required.

B) OBSERVATIONAL

a. *PART I: STUDY DESIGN (Observational Only)*
NOTE: An optional patient registry button appears but is not a requirement.
Observational Study Model: Select either, "Cohort, Case-Control, Case-Only, Case-Crossover, Ecologic or Community, Family-Based, Other".
Time Perspective: Select either, "Retrospective, Prospective, Cross-Sectional, or Other".
Biospecimen Retention: Select either, "None Retained, Samples with DNA, or Samples without DNA".
Enrollment: [ENTER NUMBER OF SUBJECTS AND TYPE (ANTICIPATED OR ACTUAL).]
Number of Groups/Cohorts: [ENTER THE CORRECT NUMBER PER THE TRIAL DESIGN.]

b. *PART II: GROUPS AND INTERVENTIONS (Observational Only)*
Group/Cohort Label: [ENTER LABEL FOR THE GROUP/COHORT.]
Group/Cohort Description: [COMPLETE WITH A BRIEF DESCRIPTION OF THE GROUP/COHORT.]
NOTE: Groups may be added as necessary
Interventions/Exposures
NOTE: Only applies when there are 2 or more groups and 1 or more interventions/exposures.
Intervention Type: Select, "Drug, Device, Biological/Vaccine, Procedure/Surgery, Radiation, Behavioral, Genetic, Dietary Supplement, Combination Product, Diagnostic Test, or Other".
NOTE: not common to have interventions with observational studies
Intervention Name: [ENTER NAME FOR THE PLANNED INTERVENTION.]
Other Intervention Names: Complete as needed.
Intervention Description: [DESCRIBE THE PLANNED INTERVENTION.]
NOTE: Interventions may be added as necessary.
Cross-Reference
NOTE: This field appears if there are more than 1 arms and/or more than 1 intervention.

c. *PART III: OUTCOME MEASURES (Observational Only)*
NOTE: ALL primary and secondary outcomes listed in the protocol are **REQUIRED** to be entered in the record.
Outcome should be formatted in a very specific format: What you are measuring and How, no description or narration. Only ONE measure per outcome. Try to be as numerical as possible.

Title: [ENTER TITLE FOR OUTCOME]
Description: [WRITE A DESCRIPTION FOR THE OUTCOME TO BE MEASURED.]
Time Frame: [PICK AN ADEQUATE/APPROPRIATE TIME FRAME.]
Time frame should reflect specific time point of data collection FOR THAT OUTCOME MEASURE. For example, if you are collecting data via a survey, the time frame should be length of time it takes participants to complete the survey, ie. Up to 45 mins.
Only ONE time point should be included in the time frame, unless you are measuring a change. If you are measuring a change "Change" has to be included in your title.
NOTE: Additional Outcomes may be added, as needed.
Secondary Outcome Measures:
Title: [ENTER TITLE FOR OUTCOME]
Description: [WRITE A DESCRIPTION FOR THE OUTCOME TO BE MEASURED.]
Time Frame: [PICK AN ADEQUATE/APPROPRIATE TIME FRAME.]
NOTE: Additional Outcomes may be added, as needed.
Other Pre-Specified Outcomes
NOT required to be entered. You should list any exploratory outcomes listed as such in the protocol here. Only outcomes listed as EXPLORATORY or TIRTIARY are allowed to be listed here.
Title: [ENTER TITLE FOR OUTCOME]
Description: [WRITE A DESCRIPTION FOR THE OUTCOME TO BE MEASURED.]
Time Frame: [PICK AN ADEQUATE/APPROPRIATE TIME FRAME.]
NOTE: Additional Outcomes may be added, as needed.

d. *PART IV: ELIGIBILITY (Observational Only)*
Sex: Select, "Male," "Female," or "All".
Gender Based: Select, "Yes" or "No".
Age Limits: [DETERMINE THE MINIMUM AND MAXIMUM VALUES.]
Accepts Healthy Volunteers: Select, "Yes" or "No".
Eligibility Criteria: [ENTER THE INCLUSION CRITERIA AND THE EXCLUSION CRITERIA IN THE TEXT BOX].

e. *PART V: CONTACTS/LOCATIONS (Observational Only)*
Central Contact Person: [COMPLETE FIELDS: FIRST, MI, LAST NAME, AND DEGREE, PHONE & EXT, & EMAIL.]

Central Contact Backup: Not a required field.
Overall Study Officials: [COMPLETE FIELDS: FIRST, MI, LAST NAME, AND DEGREE, ORGANIZATIONAL AFFILIATION, & OFFICIAL'S ROLE.] Required per ICMJE
Add Locations
Facility: [COMPLETE FIELDS: NAME, CITY, STATE/PROVINCE, ZIP/POSTAL CODE, AND COUNTRY.]
Site Recruitment Status: Select, "Not Yet Recruiting; Recruiting; Enrolled by Invitation; Active, Not Recruiting; Completed; Suspended; Terminated (Halted Prematurely); or Withdrawn (No Participants Enrolled)".
Facility Contact: [COMPLETE FIELDS: FIRST, MI, LAST NAME, AND DEGREE, PHONE & EXT, & EMAIL.]
Add Investigator: Add investigators as necessary.

f. *PART VI: IPD SHARING (Observational Only)*
NOTE: This is individual participant level data, no aggregate data sets. If you have plans to share this level of data your plan has to be submitted to the IRB for their review and approval. Mark this as "No" until IRB has review and approved your plan. Undecided is not accepted per ICMJE policies. Please mark either "Yes" if your plan has been submitted and approved by IRB, or "No" if you do not have plans to share this level of data.

Plan to Share IPD: Select "Yes", "No", or "Undecided". [COMPLETE ACCORDING TO THE PREPOPULATED DROP DOWNS.]

g. *PART VII: REFERENCES (Observational Only)*
Citations: Not required.
Links: Not required.

C) **EXPANDED ACCESS**

a. *PART I: STUDY DESIGN (Expanded Access Only)*
NOTE: An optional patient registry button appears but is not a requirement.
Type: Check the appropriate box(es): "Not Applicable, Individual Patients, Intermediate-Size Population, or Treatment IND/Protocol."

b. *PART II: INTERVENTIONS (Expanded Access Only)*
Interventions/Exposures
NOTE: Only applies when there are 2 or more groups and 1 or more interventions/exposures.
Intervention Type: Select, "Drug, Device, Biological/Vaccine, Procedure/Surgery, Radiation, Behavioral, Genetic, Dietary Supplement, Combination Product, Diagnostic Test, or Other".

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Intervention Name: [ENTER NAME FOR THE PLANNED INTERVENTION.]
Other Intervention Names: Complete as needed.
Intervention Description: [DESCRIBE THE PLANNED INTERVENTION.]
NOTE: Interventions may be added as necessary.
Cross-Reference
NOTE: This field appears if there are more than 1 arms and/or more than 1 intervention.

c. *PART III: ELIGIBILITY (Expanded Access Only)*
Sex: Select, "Male," "Female," or "All".
Gender Based: Select, "Yes" or "No".
Age Limits: [DETERMINE THE MINIMUM AND MAXIMUM VALUES.]
Accepts Healthy Volunteers: Select, "Yes" or "No".
Eligibility Criteria: [ENTER THE INCLUSION CRITERIA AND THE EXCLUSION CRITERIA IN THE TEXT BOX].

d. *PART IV: CONTACTS/LOCATIONS (Expanded Access Only)*
Central Contact Person: [COMPLETE FIELDS: FIRST, MI, LAST NAME, AND DEGREE, PHONE & EXT, & EMAIL.]
Central Contact Backup: Not a required field.
Overall Study Officials: [COMPLETE FIELDS: FIRST, MI, LAST NAME, AND DEGREE, ORGANIZATIONAL AFFILIATION, & OFFICIAL'S ROLE.]
Add Locations
Facility: [COMPLETE FIELDS: NAME, CITY, STATE/PROVINCE, ZIP/POSTAL CODE, AND COUNTRY.]
Site Recruitment Status: Select, "Not Yet Recruiting; Recruiting; Enrolled by Invitation; Active, Not Recruiting; Completed; Suspended; Terminated (Halted Prematurely); or Withdrawn (No Participants Enrolled)".
Facility Contact: [COMPLETE FIELDS: FIRST, MI, LAST NAME, AND DEGREE, PHONE & EXT, & EMAIL.]
Add Investigator: Add investigators as necessary.

e. PART V: REFERENCES (Expanded Access Only)
Citations: Not required.
Links: Not required.

6.2.17 Select "Continue" to proceed if all information is final. A second dialogue box will populate. To confirm completion, select "OK".

6.2.18 If there are any outstanding "ERROR(S)" these will be noted in red font and require correction or additional information to be addressed to complete the entry/registration of your trial in the ClinicalTrials.gov system. Once all outstanding "ERROR(S)" are addressed, the registration process includes review and approval.

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6.2.19 <u>Helpful Tips:</u>
    6.2.19.1 The system offers the option to save data if you do not have time to complete the entire process

    6.2.19.2 Be aware of fields marked with the following:

*	Required by ClinicalTrials.gov
FDAAA	Required to comply with US Public Law 110-85, Section 801

6.2.20 Once the registration of the study is released by the Responsible Party, it will be reviewed by personnel at ClinicalTrials.gov. Any comments are posted on the Responsible Party's account at ClinicalTrials.gov alongside an email. Comments are REQUIRED to be addressed **within 15 calendar days.** Corrections to trial registration can be made, as needed, and the trial can be re-released. If there are no review comments the trial is released to the public website within 7 business days with the assigned NCT #. This number should be kept on file in the study records, and the IRB application must be updated with the NCT# on or before the continuing review. The NCT # is required to be on the title page of the protocol, including a summary of amendments submitted when results are reported.

6.3 **<u>Updating Your Registered Study</u>**
Once a trial is registered, both the FDA and ICMJE require that registrations be updated as follows:

6.3.1 **FDA** updating requirements:
    6.3.1.1 Information must be updated at least once every 12 months, to do this make sure to update the Record Verification Date to the current month and year
    6.3.1.2 If changes affect human subjects via a protocol amendment, the information must be updated within 30 days of the IRB's approval
    6.3.1.3 The record must be updated within 30 days of any changes in recruitment status or completion of study*
    6.3.1.4 Summary results (including adverse event information) need to be submitted no later than 1 year after the trial's primary completion date. ALL RESULTS must be submitted no later than 1 year after the study completion date.
    6.3.1.5 The record must be updated within 15 days of change in approval or clearance status of drugs and devices not previously approved by FDA

6.3.2 The UH Human Research Protection Program will notify the Responsible Party (or designee) which trials are due for updates.

6.3.3 For the most up-to-date information or to cross reference the requirements for ClinicalTrials.gov please visit: https://clinicaltrials.gov/ct2/manage-recs/faq. Also see Clinical Research SOP Number SC-406 - Results Reporting of Clinical Trials in ClinicalTrials.gov.

7. REFERENCES:
- ICMJE Obligation to Register Clinical Trials - http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html
- NIH Guidance on Clinical Trials Registration in ClinicalTrials.gov - http://grants.nih.gov/clinicaltrials_fdaaa/
- ClinicalTrials.gov public website - http://clinicaltrials.gov
- ClinicalTrials.gov registration site - https://register.clinicaltrials.gov
- Registration at ClinicalTrials.gov: Fact Sheet - http://prsinfo.clinicaltrials.gov/
- Definitions of Responsible Party and Applicable Clinical Trial - https://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf
- Protocol Data Element Definitions - http://prsinfo.clinicaltrials.gov/definitions.html
- ClinicalTrials.gov Training Materials - http://clinicaltrials.gov/ct2/manage-recs/present
- Learning Module 1: ClinicalTrials.gov Overview and PL 110-85 Requirements - http://prsinfo.clinicaltrials.gov/WebinarSlidesBasicResults.pdf
- Frequently Asked Questions - https://clinicaltrials.gov/ct2/manage-recs/faq
- UHCMC Research SOP Number: SC-406 Results Reporting of Clinical Trials in ClinicalTrials.gov
- 42 CFR 11 https://www.govinfo.gov/content/pkg/CFR-2019-title42-vol1/xml/CFR-2019-title42-vol1-part11.xml
- https://prsinfo.clinicaltrials.gov/prs-users-guide.html

8. FORMS OR ATTACHMENTS:
- Appendix A: Creation of a ClinicalTrials.gov Account (Visual Guide)

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – May 11, 2022

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SC-402 – Transportation of Specimens

1. **PURPOSE:**
   To standardize and describe the process for safely transporting human research participant specimens within, to or from University Hospitals (UH) facilities.

2. **SCOPE:**
   This SOP applies to all personnel who are responsible for transporting human research participant specimens for research purposes within or to UH facilities.

   This SOP covers transport of Biological Substances Category B only. Category A Infectious Substances should not be transported using this SOP. Individuals planning to transport Category A Infectious Substances should contact: Department of Hospital Safety: Safety@UHHospitals.org.

3. **RESPONSIBLE INDIVIDUALS:**
   Principal Investigator (PI) and when delegated by the PI, individuals also involved with the research including but not limited to sub-investigators, Research Nurse, Study Coordinator, and/or other pertinent research staff.

4. **RELATED TERMS AND DEFINITIONS:**
   Patient Specimens – Human or animal materials, collected directly from humans or animals, including but not limited to excreta, secreta, blood and its components, tissue and tissue fluid swabs, and body parts being transported for purposes such as research, diagnosis, investigational activities, and disease treatment and prevention. Anything that is a therapeutic product is not considered a specimen, e.g., stem cells collected for treatment purposes.

   - **Clinical Research Specimens** – (A subcategory of the definition of patient specimens developed for purposes of this SOP) Specimens collected directly from humans including, but not limited to excreta, secreta, blood and its components, tissue and tissue fluid swaps, and body parts being transported for the purposes of research and investigational activities.

   Department of Transportation (DOT) – The US federal agency working under the authority of Congress to regulate the safe transportation of hazardous materials in intrastate, interstate, and foreign commerce.

   International Air Transport Association (IATA) – Publishes the Dangerous Goods Regulations, which are instructions for transporting dangerous goods by air and are based on the International Civil Aviation Organization's (ICAO) Technical Instructions.

   Infectious Substances (Class 6.2) – Substances which are known or are reasonably expected to contain pathogens. Pathogens are defined as micro-organisms (including bacteria, viruses, rickettsiae, parasites and fungi) and other agents such as prions, which can cause disease in humans and animals. Infectious substances are further categorized

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into:

- Infectious Substance Category A – An infectious substance is one that is in a form that, when exposure to it occurs, is capable of causing permanent disability, life threatening or fatal diseases to humans or animals. These are subject to the strictest shipping requirements (special paperwork, labels, containers), whether in cultures or in human or animal specimens. Examples include, but aren't limited to, Ebola virus, Hepatitis B virus (cultures only) and West Nile virus (cultures only).
- Biological Substance Category B – All other infectious substances are classified as Category B infectious substances. These are still subject to the shipping regulations but with lesser requirements in terms of shipping papers and quality of containers.

Exempt Human Specimen – According to DOT and IATA regulations, patient specimens for which there is minimal likelihood that pathogens are present are not subject to these regulations if the specimen is packed in a packaging which will prevent any leakage and which is marked "Exempt human specimen". These materials must be deemed non-infectious before they are classified as an exempt specimen. If there is suspicion that the material being transported contains a pathogen, it must be classified as an infectious material (either Category A or Category B). *While patient specimens are exempt from shipping requirements, packaging requirements must still be met (triple packing). See below for packaging requirements.*

Hazardous Materials (HM) – Materials capable of posing an unreasonable risk to health and safety and property when transported in commerce.

Pipeline and Hazardous Materials Safety Administration (PHMSA) – Division within DOT responsible with coordinating a national safety program for the transportation of hazardous materials by air, rail, highway and water.

Dangerous Goods (DG) – Articles or substances capable of posing a significant risk to health, safety or to property when transported by air.

Occupational Safety and Health Administration (OSHA) – The main US federal agency charged with the enforcement of safety and health legislation.

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. **POLICY STATEMENT:**
   All research personnel responsible for transporting participant specimens for a UHCMC IRB approved protocol are required to adhere to this SOP. This may include, but is not limited to, transporting specimens between other University Hospitals sites and University Hospitals Cleveland Medical Center (UHCMC), Case Western Reserve University, or any location where the specimens are originally collected and subsequently delivered. Participant specimens must be taken directly from the place of collection to the receiving facility and should not be taken to any other location (such as employee's home).

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Individuals responsible for transporting human research participant specimens must take Hazardous Materials Training every two years and maintain a current certificate of DOT/IATA training on file. Registration for this training can be done in the UH GPS Learning Management System.

6. **PROCEDURES:**
   6.1 Training
      6.1.1 DOT/IATA Hazardous Materials/Dangerous Goods Training applies to any individual who:
         6.1.1.1 Prepares hazardous materials for transportation;
         6.1.1.2 Selects packaging or packages for hazardous materials;
         6.1.1.3 Completes a shipper's declaration or other paperwork associated with the transport of hazardous materials;
         6.1.1.4 Loads, unloads, or handles hazardous materials;
         6.1.1.5 Is responsible for safety during the transportation of hazardous materials;
         6.1.1.6 Operates a vehicle used to transport hazardous materials; and/or
         6.1.1.7 Ships or transports materials on dry ice.
      6.1.2 Training must take place within 90 days of initial employment or change in job function. Affected employees shall receive this training every two years. There is a three month "window" that allows recurrent training conducted within the final three months of the two year period to be considered to have been completed on the expiration date of the two-year period.
      6.1.3 Registration for this training can be done in the UH GPS Learning Management System.

   6.2 Classification of Specimens
      6.2.1 To determine appropriate packaging for transport, classify specimens using the guide in Appendix B.

   6.3 Triple Packing
      6.3.1 All infectious material (category A or B) and exempt human specimens packaging must meet the following conditions to comply with DOT and IATA regulation (Triple Packing):
         6.3.1.1 Leak proof primary receptacle;
         6.3.1.2 Leak proof secondary receptacle; and
         6.3.1.3 Outer packaging that is appropriate for the material being transported (capacity, strength, etc.) and at least one surface having minimum external dimensions of 100 mm x 100 mm.
      6.3.2 Primary receptacles must be leak proof and must have positive closures (screw-on, snap-on, or push-on) that are taped. Primary receptacles can be glass, plastic or metal.
         6.3.2.1 Examples of acceptable primary receptacles are: plastic canisters, glass or plastic jars, glass or plastic vials.
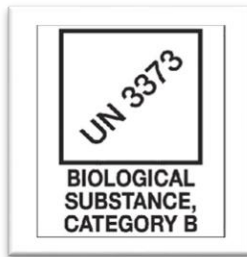   6.3.3 Secondary packaging must be leak proof for liquids and shift proof for solids. There must be a biohazard label on the secondary packaging. Note: It is an

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OSHA regulation, not IATA, that a biohazard label must be placed on the outside of the secondary container. This is done for hazard communication reasons.
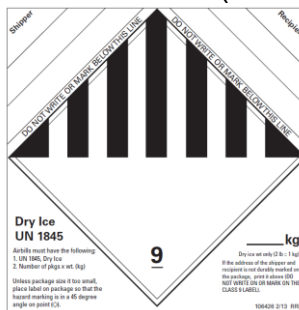
    6.3.3.1 Examples of acceptable secondary receptacles are sealed Styrofoam containers, sealed plastic bags, plastic canisters and screw-cap cans. All must have biohazard labels on them.

6.3.4 If the material being transported is a liquid, there must be absorbent material placed between the primary receptacle and the secondary receptacle. Make sure enough absorbent material is used to absorb all of the liquid if an accident occurs. If several fragile primary packages are used (e.g., glass vials), they must be secured or wrapped in a manner that prevents contact with each other.

    6.3.4.1 Examples of acceptable Absorbent Materials are: paper towels, cotton balls, cellulose wadding, Kimwipes®, and super-absorbent packets.

6.3.5 The material is then placed in an Outer Packaging container. Outer Packaging must be sturdy, rigid and the appropriate size.

    6.3.5.1 Examples of acceptable Outer Packaging are: rigid plastic containers, wood boxes, rigid coolers, corrugated fiberboard or cardboard boxes.

    6.3.5.2 Examples of unacceptable outer packaging are: FedEx® packaging, Styrofoam boxes, plastic bags, paper envelopes.

6.3.6 An external label is placed on the Outer Packaging container as determined by the classification of enclosed specimens and whether dry ice is being utilized. (See Section 6.4, Labeling)

6.3.7 Quantity limitations apply:

    6.3.7.1 Primary receptacle(s) must not contain more than 1 liter of liquid.

    6.3.7.2 For specimens that are packaged with dangerous goods that are necessary for maintaining the viability, stabilizing or preventing degradation or neutralizing the hazards of the infectious substances (e.g., preservatives and fixatives):

        6.3.7.2.1 Each primary container must not contain more than 30 milliliters of liquid dangerous goods that are DOT Class 3 (Flammable), Class 8 (Corrosive), or Class 9 (Miscellaneous); and

        6.3.7.2.2 Each primary container must not contain more than 30 grams of solid dangerous goods that are DOT Class 4 (Flammable), Class 8 (Corrosive), or Class 9 (Miscellaneous).

    6.3.7.3 Outer packaging (the overall package):

        6.3.7.3.1 For liquids, the outer packaging must not contain more than 4 liters (quantity excludes ice, dry ice or liquid nitrogen when used to keep specimens cold); and

        6.3.7.3.2 For solids, except for packages containing body parts, organs or whole bodies, the outer packaging must not contain more than 4 kilograms (quantity excludes ice, dry ice or liquid nitrogen when used to keep specimens cold).

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6.4 <u>Labeling</u>

    6.4.1 Follow the protocol regarding the labeling of participant specimens and the primary receptacle.

    6.4.2 Specimens are then placed in a puncture resistant secondary container. This container is labeled with the international biohazard symbol and closed prior to transport. The biohazard label must be placed on the outside of the secondary container.

    6.4.3 The sturdy outer packaging should include the appropriate labeling as required per the contents.

        6.4.3.1 Proper labeling of Biological Substance, Category B specimens includes:

            6.4.3.1.1 UN Identification Number UN3373

            6.4.3.1.2 Proper shipping name as follows: UN3373 Biological Substance, Category B.

        6.4.3.2 Mark packages containing exempt specimens, "Exempt Human Specimens".

        6.4.3.3 Proper labeling of packages containing dry ice includes:

            6.4.3.3.1 UN Identification Number for dry ice: UN 1845

            6.4.3.3.2 Proper shipping name: Dry Ice or Carbon dioxide (solid)

            6.4.3.3.3 Hazard class 9 (miscellaneous) label.

6.5 <u>Transporting and/or packing samples with dry ice (solid Carbon Dioxide or CO2)</u>

    6.5.1 Dry ice must be placed outside the secondary packaging or in the outer packaging or an overpack.

    6.5.2 Venting: Dry ice must never be packaged in an airtight container. This may lead to a build-up of pressure inside the container, thus causing an explosion. Allow for proper venting of dry ice; do not tape Styrofoam containers containing dry ice closed, tape the outer box only.

    6.5.3 Compatibility: Due to the low temperature of dry ice, many materials such as plastics may be rendered brittle and permeable. Make sure packaging materials

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are not susceptible to damage from exposure to dry ice.

6.5.4 Package Quality: The shipper is responsible for choosing a package which will withstand normal transport activity intact. Packages must be able to withstand multiple handlings and vibrations that occur during normal transportation. Outer and inner packages must be constructed and closed in a manner so that the contents remain within the package.

6.6 Methods of Transportation
6.6.1 If possible, it is recommended that established shipping services are used to transport specimens. This includes courier services between facilities.
6.6.2 Personal modes of transportation can be used to transport materials.
6.6.2.1 Avoid exposing specimens to direct sunlight or leaving them in a vehicle during warm weather conditions.
6.6.2.2 The specimens should be kept in a cool place and taken to the appropriate lab as soon as possible.
6.6.2.3 Specimens are not to be taken back to an individual's home and stored overnight.

6.7 Spill Kits and Sharps Containers
6.7.1 All individuals transporting specimens must have a Spill Kit. (See Appendix C)
6.7.2 If a spill occurs, the UH Safety Office must be notified immediately at 216.844.7745 (select option 2).
6.7.3 If the study personnel are responsible for the collection of samples, any sharps used are to be disposed of in an appropriate location in an appropriate container.
6.7.4 University Hospitals Laboratory Services recommends that the Spill Kit contains the items indicated in Appendix C.

7. **REFERENCES:**
- The regulations for hazardous material transportation are found in the Code of Federal Regulations under 49 CFR parts 100-185.
- UH System Policies
    o SA-6 - Requirement for Hazardous Materials Spill Response Program
    o IC-2 - Standard Precautions
- UH GPS - DOT/IATA Training

8. **FORMS OR ATTACHMENTS:**
- Appendix A: Classification Guide for Transport of Clinical Research Specimens
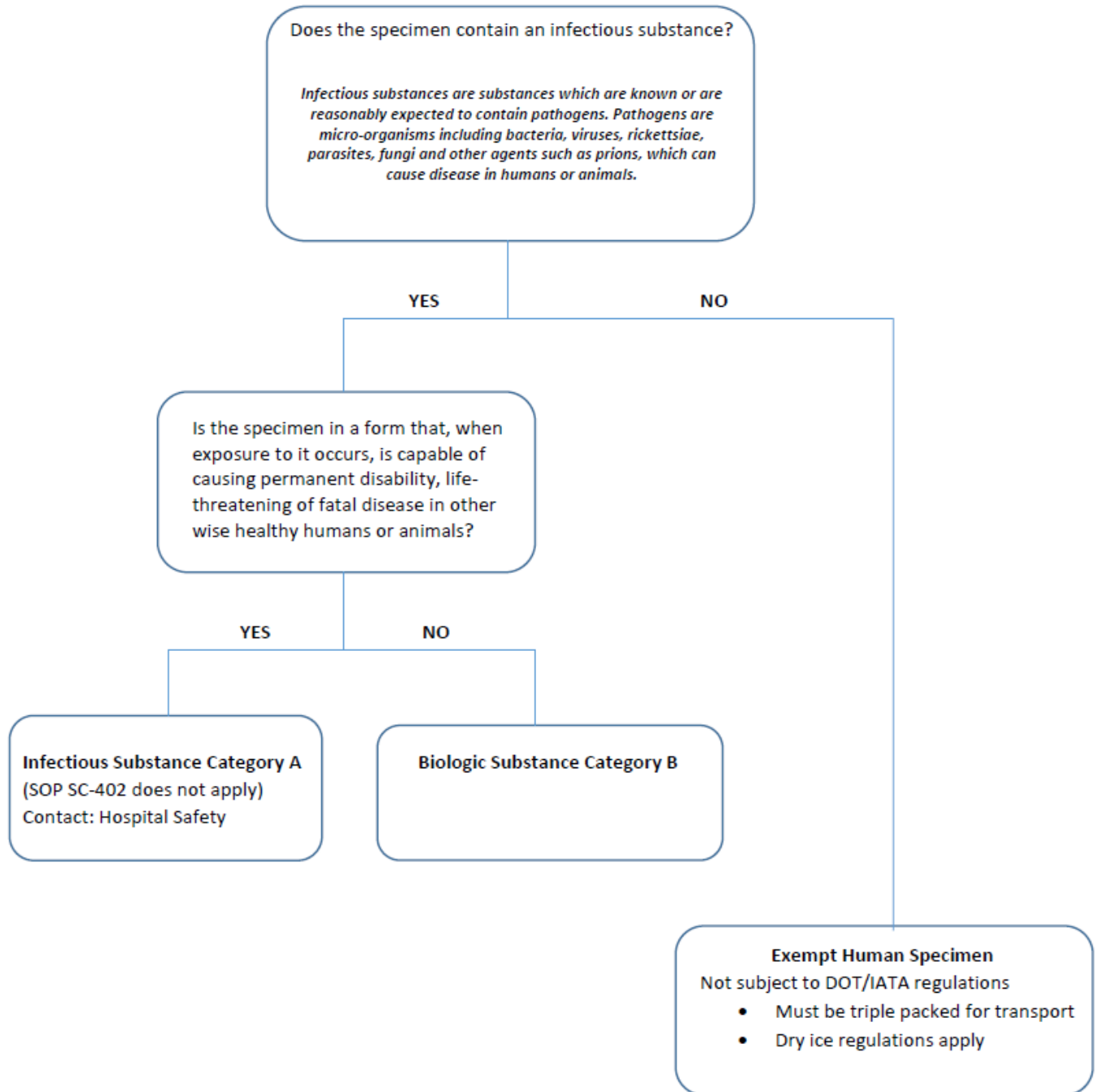- Appendix B: Spill Kit and Instructions

APPROVALS

Signed by Grace A McComsey, MD, FIDSA, Director of the UH Clinical Research Center, University Hospitals Health System –
December 13, 2023

Appendix A

CLASSIFICATION GUIDE FOR TRANSPORT OF CLINICAL RESEARCH SPECIMENS

Clinical Research Specimens: Specimens collected directly from humans including, but not limited to excreta, secreta, blood and its components, tissue and tissue fluid swabs and body parts being transported for the purposes of research and investigational activities.

Does the specimen contain an infectious substance?

Infectious substances are substances which are known or are reasonably expected to contain pathogens. Pathogens are micro-organisms including bacteria, viruses, rickettsiae, parasites, fungi and other agents such as prions, which can cause disease in humans or animals.

YES — **NO**

Is the specimen in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening of fatal disease in other wise healthy humans or animals?

YES — **NO**

Infectious Substance Category A
(SOP SC-402 does not apply)
Contact: Hospital Safety

Biologic Substance Category B

Exempt Human Specimen
Not subject to DOT/IATA regulations
- Must be triple packed for transport
- Dry ice regulations apply

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Appendix B

All individuals transporting specimens must have a Spill Kit.

If a spill occurs, the UH Safety Office must be notified immediately at 216-844-7745 (select option 2)

A. Kit Contents
1. 2 Pairs of Nitrile Gloves
2. Safety glasses/goggles
3. Absorbent Pads
4. Neutralizing agent or solidifier(various ones depending on samples)
5. Scoop/Scraper
6. Hard Surface Disinfectant Wipes
7. Disposal Bags - 2
8. Instructions

Body fluid spill kits can be purchased through I Procurement under oracle # **051780.**
Chemical neutralizer must be purchased separately if needed.
Chemical Spill kits can be purchased under oracle # **017256**.

B. Instructions
1. Contact the UH Safety Office immediately at 216.844.7745 (option 2)
2. Put on gloves and eye protection. Always wear protective gear and exercise caution during clean up.
3. Lay the absorbent pads on top of the spilled material. If applicable, sprinkle neutralizer or solidifier over spill evenly instead of using the absorbent pads. The fluid will quickly set; add more as necessary to insure any liquid is completely contacted.
4. Once absorbent pads are saturated, place them into the disposal bag.
5. Where a neutralizer or solidifier is used, remove solidified material using scoop and scraper and place into the disposal bags.
6. Clean area with a hard surface wipe or disinfectant, if available.
7. After cleanup is completed, remove all personal protection equipment (PPE) and place into disposal bag. Seal disposal bag using the single goose-neck knock to prevent leakage.
8. Dispose of all waste in accordance with local, state and federal regulations. Contact the UH Safety Office for any disposal questions.

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Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

SC-403 – Research Documentation

1. PURPOSE:
To establish documentation standards for clinical research projects to ensure applicable safety, compliance, and billing requirements are met.

2. SCOPE:
All entities conducting clinical research within the University Hospitals Health System (UHHS) must have proper research records for each research project. This SOP outlines the items to be documented and retained throughout the course of the research project.

3. RESPONSIBLE INDIVIDUALS:
Clinical and research personnel who interact with or care for clinical research participants.

4. RELATED TERMS AND DEFINITIONS:
DOS - Date of Service
EMR - Electronic Medical Record
GCP - Good Clinical Practice
HIPAA - Health Insurance Portability and Accountability Act
ICF - Informed Consent Form
ICH - International Conference on Harmonization.
Enrollment / Enrolled – When a participant is consented and deemed eligible by an investigator.

Please reference the [Standard Operating Procedures Glossary of Terms](#) for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
Accurate and complete documentation is the cornerstone of Good Clinical Practice (GCP) and permits an observer to follow a research participant's journey throughout the research project. In addition, source documentation is utilized to account for the use of any investigational products.

Source documentation must be kept in accordance with FDA regulations (21 CFR 11, 21 CFR50.25, 21 CFR 312.62 (b), 21 CFR 812.140 (a) (3) guidelines), Guidance for Industry: Electronic Source Data in Clinical Investigations, and ICH GCP E6.

6. PROCEDURES:
6.1 Medical Record Access
    6.1.1 Access to the medical record is based on job function.
    6.1.2 Orders can only be written by medically qualified and authorized study personnel, in accordance with UH Clinical Research SOP GA-104 - Scope of Practice.

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6.2 Research Registration/Scheduling

6.2.1 All research participants seen onsite at UH facilities must be registered and given a medical record number, if they don't already have one.

6.2.2 "Research insurance" must be placed in the primary insurance position for any clinical study related DOS, in accordance with UH System Policy R-2 Patient Billing under Research Grants.

6.2.3 Research-related appointments must be scheduled in the hospital or entity scheduling system.

6.2.3.1 Scheduling at any wholly-owned University Hospitals location, must occur in UH EPIC for all interventional research studies where patient care is delivered. Non-interventional studies may schedule in EPIC, but is optional.

6.3 HIPAA and Research

In accordance with UH System Policy GM-61 Accessing Medical Records (Section 12.3 research records), PH-3 - Permitted Uses/ Disclosures of PHI (Section 2.11 – for research), PH-4 Authorizations for Use and Disclosure of PHI (Section 7.1 – Research), R-3 Uses & Disclosures of PHI for Research.

6.3.1 Researchers accessing, using, or retaining protected health information (PHI) of UHHS patients must abide by the UHHS's HIPAA-related policies.

6.4 Research Documents

In accordance with UH System Policy GM-1 Records Management, ICH E6 4.9.4.b, 21CFR312.62 Investigator Record Keeping and Record Retention – Case histories, FDA Guidance for Industry - Computerized Systems Used in Clinical Investigations: Source Documentation and Retention, and in alignment with IRB approved protocol:

6.4.1 All original source and essential research documents must be retained throughout the lifecycle of the research project and the appropriate amount of time after the research project closes. Measures should be taken to prevent any premature or accidental destruction.

6.4.2 When original observations are transcribed on paper, the paper document is the source document. This requirement applies to the retention of the original source document, or a copy of the source document.

6.4.3 When original observations are entered directly into a computerized system, the electronic record is the source document. This requirement applies to the retention of the original source document, or a copy of the source document.

6.4.4 All source documentation should follow ALCOA+C (**A**ttributable, **L**egible **C**ontemporaneous, **O**riginal, **A**ccurate, and **C**omplete).

6.5 Required Medical Record Documentation

6.5.1 All clinical research-related tasks must be documented on a timely basis by the clinician and/or delegate who performed the task.

6.5.2 Include secondary diagnosis code Z00.6 (research) on billing charge capture

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documents for all care provided as documented below.

6.5.3 Assure that the following elements are documented in the patient medical record, in addition to the research record:

6.5.3.1 <u>Informed Consent</u>
In accordance with FDA 21 CFR 50.27: "Documentation of Informed Consent", and UH Investigator Manual for IRB Submissions, Chapter 9 – General Consent Requirements.

6.5.3.1.1 Original fully executed (signed) Informed Consent forms must be maintained in the research records.
6.5.3.1.1.1 Each signed informed consent must be the most recent, IRB approved document.
6.5.3.1.2 A copy of the fully executed (signed) Informed Consent document must be added to a paper medical record and scanned into an EMR when conducting interventional research studies or studies involving patient care charges.
6.5.3.1.3 The Informed Consent process must be documented in the participant's research record, and when applicable, added to the medical record electronically or scanned into EMR. Refer to the Informed Consent Documentation Checklist.
6.5.3.1.4 During the Informed Consent process, verify the participant's demographics. Update the participant's medical record, if applicable.
6.5.3.1.5 Not all Informed Consent Form changes require re-consent of the participant. If any Informed Consent Form changes **do** require re-consenting, then any subsequent changes to the Informed Consent Form must be discussed with the study participant, and consent must be obtained, prior to completing any new study procedures, as required by the UH IRB. The participant's decision to re-consent or not must also be documented. Continued participation and/or withdrawal should be managed per protocol.
6.5.3.1.6 All original versions of the IRB approved Informed Consent document must be maintained in the research record.

6.5.3.2 <u>Eligibility Assessment:</u>
6.5.3.2.1 Refer to the Eligibility Checklist.
6.5.3.2.2 Final verification of eligibility must be documented and signed off by the PI or PI-delegated, medically qualified member of the study team, before the participant can be enrolled.

6.5.3.3 <u>Enrollment source documentation should include:</u>
6.5.3.3.1 Date enrolled
6.5.3.3.2 Narrative of visit

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6.5.3.3.3 Phraseology must include the following: "participant has been enrolled in the (insert IRB approved short study name) research study" (or "research database" or "research registry" if applicable).

6.5.3.3.4 Signed by an Investigator or designee.

6.5.3.3.5 Update Velos eResearch with the participant's enrollment status.

6.5.3.4 Orders

6.5.3.4.1 Research study related clinical procedures and tests must be ordered by a licensed medical provider and documented as a written order in the study participant's medical record. In accordance with UH System Policies: EMR-2 – Master UHCare Order Management and MM-2 – Medication Orders.

6.5.3.5 Administration or Implant of Investigational Product

6.5.3.5.1 Interventional studies involving investigational drug or biologics are required to have IP administration documented in the EMR by the person administering item, according scope of practice and delegation log.

6.5.3.5.2 Implant of an investigational device must be documented in the procedure note by a physician.

6.5.3.5.2.1 Phraseology must include the following: "Patient met eligibility requirements and has been enrolled in the (insert IRB approved short study name) research study and received (insert investigational device product name).

6.5.3.5.2.2 Must include IDE number

6.5.3.5.3 When applicable, investigational study medications must be managed by Investigational Drug Services (IDS) in accordance with UH System Policy: MM-4 - Investigational Drugs.

6.5.3.5.3.1 If the Investigational Products (IP) are not managed by IDS, the investigator must maintain documentation for IP shipping, storage, preparation, and labeling. Study records must also include, as applicable, randomization records, dispensing, administration, chain of custody procedures, and decoding procedures for blinded protocols (see SP-205 IDS Exception Request).

6.5.3.6 Investigational Medication or Product Reconciliation

6.5.3.6.1 If required by the research protocol, document use, return and destruction of investigational product in accordance with UH System Policy MM-50 Medication Administration

6.5.3.7 Visit Progress Notes (Initial and follow-up visits)

6.5.3.7.1 The Investigator and/or delegate(s) will document progress

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notes for each research visit the participant makes to the clinic or hospital.

6.5.3.7.2 The progress note should include all details of the visit and should reflect information needed for data capture.

6.5.3.7.3 Ensure any adverse events are documented within the note.

6.5.3.7.4 Update Velos eResearch with the visit.

6.5.3.8 Telephone Encounter Note

6.5.3.8.1 The Investigator or delegate will be expected to document telephone contact notes for relevant research study related calls to the participant.

6.5.3.8.2 Update Velos eResearch with the visit, if applicable.

6.5.3.9 Unscheduled Visits

6.5.3.9.1 If a participant has an unscheduled visit, ensure proper documentation of the visit.

6.5.3.9.2 Document any adverse events.

6.5.3.9.3 Update Velos eResearch, if applicable.

6.5.3.10 Long Term Follow-up

6.5.3.10.1 Some research projects require long term follow-up. Documentation similar to a progress visit note should be in the participant's research record.

6.5.3.11 Any other Pertinent Information

6.5.3.11.1 Any information that requires data capture in case report forms, needs to have source documentation to verify accuracy and completeness.

6.5.3.11.2 Documentation of research specific tasks which were not completed, should still be documented.

6.5.3.11.3 In the research records, participant compensation and reimbursement must be documented (*Refer to SOP SS-313 – Research Participant Compensation and Travel Reimbursement, and IRB Investigator Manual for IRB Submissions Chapter 10 – Remuneration*).

6.5.3.12 Withdrawal / Early Termination / Study Completion

6.5.3.12.1 The Investigator or delegate must document in the participant's medical record when a research participant terminates participation in a research study.

6.5.3.12.2 Include all pertinent information for the continuation of care.

6.5.3.12.3 Enter a progress note of study termination, document the date and purpose of the study termination and identify the person completing the note. The EMR must be updated to indicate the research participant is no longer participating in the research.

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6.5.3.12.4 Update Velos eResearch with the participant's status.

7. REFERENCES:
- DHHS 45 CFR 46: Protection of Human Subjects
- [FDA Guidance for Industry: Electronic Source Data in Clinical Investigations](#)
- FDA 21 CFR 11: Electronic Records and Electronic Signatures
- FDA 21 CFR 50.25: Elements of Informed Consent
- FDA 21 CFR 50.27: Documentation of Informed Consent
- FDA 21 CFR 312.62: Investigator Record Keeping and Record Retention
- FDA 21 CFR 812.140: General Responsibilities of Sponsors
- GCP ICH E6 (R2):
  - 1.51: Source Data
  - 1.52: Source Documents
- [Investigator Manual for IRB Submissions](#)
  - Chapter 9 - General Consent Requirements
  - Chapter 10 - Remuneration
  - Chapter 26 - GDPR Requirements
- [UH Clinical Research SOPs](#)
  - GA-104 – Scope of Practice
  - SP-205 – IDS Exception Request
  - SS 314 – Velos eResearch – Access and Data Entry Requirements
  - SS 305 – Investigational Device Billing
  - SS 309 – REDCap Project Access for UH Employees
  - SS-313 – Research Participant Compensation and Travel Reimbursement
- [UH System Policies](#)
  - GM-61 - Accessing Medical Records (See "Access for study and research")
  - MM-2 - Medication order
  - MM-4 - Investigational Products
  - PH-03 - Permitted Uses and Disclosures of PHI
  - PH-04 - Authorizations for Use and Disclosure of PHI R-2 - Research Patient Billing
  - R-3 - Uses and Disclosures of Protected Health Information (PHI) for Research
- Epic Workflows
  - [Research Coordinator Ordering Scope of Practice and Research Ordering](#)
  - [Billing Protocol and Timeline Creation](#)
  - [Patient-Study Association](#)

8. FORMS OR ATTACHMENTS:
- [Informed Consent Documentation Checklist](#)
- [Eligibility Checklist](#) (Word .doc)
- [Recording Demographics in Clinical Research](#)

APPROVALS
Signed by Grace A McComsey, MD, FIDSA, Director of the UH Clinical Research Center,
University Hospitals Health System –
December 13, 2023

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SC-405 – Records Retention, Archive, and Storage

1. **PURPOSE:**
   To properly and effectively manage the retention, archive and storage of UH Research Records.

2. **SCOPE:**
   This SOP applies to all research records, including subject records and regulatory documents.

3. **RESPONSIBLE INDIVIDUALS:**
   The Principal Investigator (PI) and any research personnel designated by the PI to collect, organize, store or archive research records. This includes ancillary services, as applicable (i.e., Investigational Drug Services, etc.).

4. **RELATED TERMS AND DEFINITIONS:**
   - Email Communications
   - PHI (Protected Health Information)
   - Research Records
   - Records

   Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. **POLICY STATEMENT:**
   The Principal Investigator is responsible for determining which guideline(s) apply to their study for the proper storage, retention and archive of research records (Appendix 1: Record Retention Table).

6. **PROCEDURES:**
   The PI should determine which regulatory bodies have oversight of their study (DHHS, FDA, NIH, IRB, GCP, Industry Sponsor, etc.) and follow those guidelines on record retention. Some tools can be referenced below. No specific guidelines overrule any of the others. A best practice is to retain records for the longest period of time required by any of the regulatory bodies that have oversight of the study.

7. **REFERENCES:**
   - UH System Policy GM-1 - Records Management
   - UH Investigator Manual for IRB Submissions
   - DHHS 45 CFR 46.115, 45 CFR 75.361, and 45 CFR 75.364
   - FDA 21 CFR 56.115, 21 CFR 812.140, and 21CFR 312.62
   - ICH GCP E6R2 3.4, 4.9.0, 4.9.4, 4.9.5, and 8.1
   - NIH Grants Policy Statement 8.4.2

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8. FORMS OR ATTACHMENTS:
- Appendix 1: Records Retention Table
- Appendix 2: Iron Mountain Note to File
- Appendix 3: Iron Mountain Process Checklist
- Appendix 4: Iron Mountain Process Checklist using OnCore

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center
– June 5, 2023

SC-406 – Results Reporting of Clinical Trials in ClinicalTrials.gov

1. **PURPOSE:**
   This Standard Operating Procedure (SOP) describes the process for reporting clinical trials results with ClinicalTrials.gov.
   1.1   Please refer to *SOP SC-401 - Registration of Clinical Trials in ClinicalTrials.gov* regarding the creation of an account and registration of a clinical trial on ClinicalTrials.gov.

   For questions, please email UHResearchCompliance@UHhospitals.org

2. **SCOPE:**
   This SOP will provide instruction and promote consistency among all departments within University Hospitals Cleveland Medical Center regarding the requirement of registering applicable clinical trials with ClinicalTrials.gov. The U.S. Food and Drug Administration (FDA) is the government agency that requires registration of clinical trials. Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA 801 or US Public Law 110-85) passed on September 27, 2007 requires mandatory registration and results reporting for certain clinical trials of drugs, biologics, and devices of all applicable clinical trials initiated on or before September 27, 2007, and is ongoing as of December 27, 2007. This legislation coupled with the Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11) creates the regulatory requirements and procedures for ClinicalTrials.gov.

   The International Committee of Medical Journal Editors (ICMJE) member journals require, as a condition of consideration for publication in their journals, registration in a public trials registry. The ICMJE does not advocate one particular registry, but its member journals require authors to register their trial in a registry that meets several criteria.

   According to the Food and Drug Administration Amendments Act of 2007:
   - Penalties may include civil monetary penalties up to $12,462 fine for failing to submit or for submitting fraudulent information to ClinicalTrials.gov. NOTE: fines increase annually to reflect inflation
   - After notification of noncompliance, the fine may go up to $12,461 per day until resolved. NOTE: fines increase annually to reflect inflation
   - For federally funded grants, penalties may include the withholding or recovery of grant funds.

   2.1   REQUIREMENTS:
         Ultimately the results of all interventional studies need to be submitted in ClinicalTrials.gov.
         2.1.1   FDA Regulated Research Requirements:
                 2.1.1.1   FDAAA requires registration and results reporting of 'Applicable Clinical Trials (ACTs)'. An 'ACT' is defined as:
                           2.1.1.1.1   Interventional studies;

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2.1.1.1.2   Studies where AT LEAST ONE or more of the following applies:

        2.1.1.1.2.1   at least one site in the US or one of its territories, or

        2.1.1.1.2.2   study is conducted under an IND or IDE

        2.1.1.1.2.3   the product is manufactured in and exported from the US or one of its territories.

2.1.1.1.3   Studies that evaluate at least one US FDA regulated drug, biologic, or device product

2.1.1.1.4   Studies that are not Phase 1 (drug and biological products)* or not Device Feasibility (device products)**

2.1.1.1.5   Clinical trials must be submitted for registration with ClinicalTrials.gov within 21 days after the enrollment of the first patient.

*Phase 1 studies of a new drug are usually the first that involve people. Phase 1 studies are done **to find the highest dose of the new treatment that can be given safely without causing severe side effects.**

Device Feasibility are usually **10 or fewer people to test the safety/efficacy of the device, has to meet very specific criteria to fit feasibility.

If you have any question about your study being Phase 1 or Device Feasibility please email UHResearchCompliance@UHhospitals.org and we can help review.

For more information regarding 'Applicable Clinical Trials', see Elaboration of Definitions of Responsible Party and Applicable Clinical Trials. ClinicalTrials.gov also provided the Checklist and Elaboration for Evaluating Whether a Clinical Trial or Study is an Applicable Clinical Trial (https://prsinfo.clinicaltrials.gov/ACT_Checklist.pdf) as a reference.

While Phase I trials or device feasibility studies are not considered 'Applicable Clinical Trials' under the FDAAA regulations, they do need to be registered if the study will be published, use Medicare or receive funding from NIH, as described below.

2.1.2   ICMJE Requirements:

The ICMJE requires, and recommends that all medical journal editors require, registration of clinical trials in a public trials registry before the time of first patient enrollment as a condition of consideration for publication. Editors requesting inclusion of their journal on the ICMJE website list of publications that follow ICMJE guidance should recognize that the listing implies enforcement by the journal of ICMJE's trial registration policy.

2.1.2.1   http://icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html

2.1.3   Medicare Requirements:

Effective January 1, 2015, all Medicare qualifying trials, including some Phase 1 and device feasibility trials, are required to be registered into the ClinicalTrials.gov database. NCT numbers are required on clinical research related claims in order to receive payment. Patients should not be enrolled on a

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trial unless the NCT registration number is in place.

2.1.4 NIH Funding:
The National Institutes of Health (NIH) Policy on Dissemination of NIH-Funded Clinical Trial Information requires registration and results reporting, and applies to all clinical trials funded by NIH, regardless of whether they are subject to the FDAAA 801 and the Final Rule effective January 18, 2017. The Policy is effective for competing applications and contract proposals submitted on or after January 18, 2017, and states that all NIH- funded awardees and investigators conducting clinical trials will register and report the results of their clinical trial in ClinicalTrials.gov. Please refer to the following grants policy information from NIH's Office of Extramural Research to learn more about ensuring compliance with NIH's implementation of FDAAA 801: https://grants.nih.gov/policy/clinical-trials/reporting/index.htm

3. RESPONSIBLE INDIVIDUALS:
3.1 FDA Regulated Research Requirements:
According to federal law, the 'Responsible Party' is responsible for reporting results to ClinicalTrials.gov and is defined as:
3.1.1 The IND/IDE holder of the trial
3.1.2 For studies not conducted under an IND/IDE
3.1.2.1 The study sponsor or the grantee institution,
3.1.2.2 Principal Investigator, if there is no external funding agreement
3.1.3 Situations in which Institution/PI is the Responsible Party
For trials being conducted under a funding agreement, grant (e.g. NIH awards) or department/internal funding, the funding recipient is considered the Responsible Party. Because the PI is in best position to understand the research protocol study results and adverse events, the institution will designate the Principal Investigator to assume the role of the Responsible Party.
3.1.3.1 In situations where UH serves as the primary site for a clinical trial and the institution is determined to be the "Responsible Party," the Institution will designate this responsibility to the Principal Investigator.
3.1.4 Situations in which Institution/PI is NOT the Responsible Party
For most industry sponsored trials, the sponsor will be the Responsible Party, and, as such, the institution and PI will NOT have to manage submissions or results reporting to ClinicalTrials.gov. Similarly, for multi-center trials, or trials sponsored by other academic sites only the lead site (Overall PI) typically bears responsibility for ClinicalTrials.gov reporting; site PIs typically do not have to do additional reporting.
3.1.5 What are the criteria for designating the Principal Investigator as the "Responsible Party" for reporting results?
According to federal law, the Principal Investigator can serve as a Responsible Party if that individual:
3.1.5.1 Is responsible for conducting the trial
3.1.5.2 Has access to and control over the data from the clinical trial
3.1.5.3 Has the right to publish the results of the trial

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3.2 ICMJE Requirements
Anyone involved in the clinical trial could register the trial, in practice this responsibility usually falls with the individual submitting the publication to the ICMJE journal, which is usually the Principal Investigator.

3.3 Medicare Requirements:
In order to ensure proper research billing compliance, it is the responsibility of department research personnel to communicate the NCT number to their Research Finance Specialist (RFS) during administrative study start-up and prior to any patient enrollment on the trial. It is the responsibility of the RFS to associate the appropriate NCT number with study related claims and assure this communication to the appropriate parties in revenue cycle management.

3.4 NIH Requirements:
The trial's "Responsible Party" is responsible for two basic elements of compliance:
3.4.1 The registration of the ACTs in ClinicalTrials.gov, and
3.4.2 The reporting of summary results information (including adverse events)
3.4.3 All NIH grantees, regardless of whether or not they are the "Responsible Party" under FDAAA are responsible for:
3.4.3.1 Certification in the grant application and progress report forms that the Responsible Party has made all required submissions to ClinicalTrials.gov for ACTs funded in whole or in part by the NIH.

4. **RELATED TERMS AND DEFINITIONS:**
Please see "[Section 7. REFERENCES]:" for complete definitions of any additional terms not listed below.

ACT – Applicable Clinical Trial

CCCC – Case Comprehensive Cancer Center

NCT Number – National Clinical Trial (NCT) number, another term for the ClinicalTrials.gov registry number unique to each record. The format for the ClinicalTrials.gov registry number is "NCT" followed by an 8-digit number, (e.g., NCT00000419).

PRS (Protocol Registration and Results System) – A quality control and reviewing body to ensure all aspects of a clinical trial are entered according to federal regulations.

Primary Completion Date (PCD) – The primary completion date is the date when the final subject was examined and/or received an intervention for the purposes of final collection of data for the pre- specified primary outcome (as per protocol), regardless of whether the clinical trial was completed (recruiting and data collection was completed per protocol), or terminated (recruiting or enrolling participants was halted prematurely and will not resume).

Please reference the Standard Operating Procedures Glossary of Terms for complete

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definitions of terms in this SOP.

5. **POLICY STATEMENT:**
All applicable clinical trials must have results reported in ClinicalTrials.gov. The primary completion date (PCD) determines the time frame for results reporting.

The Responsible Party has one year (12 months) from the PCD to enter trial results. ALL trial results are required to be entered within 1 year of the Study Completion date (SCD).

5.1 Updating Your Registered Study
Once a trial is registered, both the FDA and ICMJE require that registrations be updated as follows:
5.1.1 FDA updating requirements:
5.1.1.1 Information must be updated at least once every 12 months, to do this make sure to update the Record Verification date to the current month and year.
5.1.1.2 If changes affect human subjects via a protocol amendment, the information must be updated within 30 days of the IRB's approval
5.1.1.3 The record must be updated within 30 days of any changes in recruitment status, completion of the study (PCD and SCD)*
5.1.1.4 Summary results (including adverse event information) need to be submitted not later than 1 year after the trial's primary completion date ALL RESULTS must be submitted no later than 1 year after the study complete date.
5.1.1.5 The record must be updated within 15 days of change in approval or clearance status of drugs and devices not previously approved by FDA

The UH Human Research Protection Program will notify the Responsible Party (or designee) which trials are due for updates.

For the most up-to-date information or to cross reference the requirements for ClinicalTrials.gov please visit: https://clinicaltrials.gov/ct2/manage-recs/faq

*Once all data has been collected for the trial, the Responsible Party or designee will then monitor the patient status (on treatment, off treatment, off study), to determine the PCD. This is the LAST DATE data was collected for your primary outcome measures. This date can be entered in ClinicalTrials.gov as "anticipated" and updated as the study moves forward. Once the date is set as "actual" then the Responsible Party has one year from that date to enter results.

6. **PROCEDURES:**
6.1 Results Reporting in ClinicalTrials.gov
Please be aware that because results are specific to each study, the procedures for results reporting are generic in order to be inclusive of all studies. Results entry can take up to 40 hours to complete, so please do not wait till the last minute. You have

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the ability to save and come back later as needed. Email UHResearchCompliance@UHhospitals.org to obtain a study specific results template to help with entering trial results.

6.1.1 Helpful Tips:

6.1.1.1 Be aware of fields marked with the following:

*	Required by ClinicalTrials.gov
FDAAA	Required to comply with US Public Law 110-85, Section 801

6.1.1.2 The system offers the option to save data if you do not have time to complete the entire process.

6.1.1.3 Verify that all outcome measures in the ClinicalTrials.gov registration are correct before beginning the results reporting. These outcomes will automatically be copied to the results section.

6.1.2 Results Modules: there are nine modules of data to be completed.

6.1.2.1 Participant Flow: Recruitment details, pre-assignment details, arm/group information, type of units assigned, and periods.

6.1.2.2 Baseline Characteristics: Arm/group information, baseline analysis population information, and baseline measure information.

6.1.2.3 Outcome Measures: Outcome measure information, statistical analysis, statistical analysis overview, comparison group selection, type of statistical test, statistical test of hypothesis, method of estimation, and other statistical analysis.

6.1.2.4 Adverse Event Information: The following tables must be completed: (1) All- Cause Mortality, (2) Serious Adverse Events, (3) Other (Not Including Serious) Adverse Events. Additionally, time frame, adverse event reporting description, source vocabulary name for table default, collection approach for table default, arm/group information, adverse events, total number affected by all-cause mortality, total number at risk for all-cause mortality, total number affected by any serious adverse event, total number at risk for serious adverse events, frequency threshold for reporting other (not including serious) adverse events, total number affected by any other (not including serious) adverse event above the frequency threshold, total number at risk for other (not including serious) adverse events, adverse event term, organ system, adverse event term additional description, source vocabulary name, collection approach, and adverse event data.

6.1.2.5 Limits and Caveats: Overall limitations and caveats.

6.1.2.6 Certain Agreements: Are all PIs employees of sponsor, results disclosure restriction on PIs, and PI disclosure restriction type.

6.1.2.7 Results Point of Contact: Name or official title, organization name, phone, extension, and email.

6.1.2.8 Delayed Results (Optional): Delay results type, intervention name(s), FDA application number(s), requested submission date, and explanation. NOTE: this is only due in VERY limited circumstances and you have until one day prior to your due date to submit. Please reach

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out to UHResearchCompliance@UHhospitals.org for help with this.

     6.1.2.9 Document Upload Information: Document type (study protocol, statistical analysis plan (SAP), informed consent form (ICF), or study protocol with SAP or ICF), document date, subtitle, and document. **NOTE:** The study protocol is REQUIRED to be submitted with results submission or all ACTs and NIH Clinical trials.

6.1.3 <u>Submitting Results</u>

     6.1.3.1 The PRS team at ClinicalTrials.gov will review the submission and post comments for corrections/clarifications. Comments are REQUIRED to be addressed within 25 calendar days. For questions regarding comments email UHResearchCompliance@UHhospitals.org. Once the review process is complete, ClinicalTrials.gov will send notification to the Responsible Party or designee that the submission of study results has been approved and will be published on the public ClinicalTrials.gov website within two business days.

     6.1.3.2 Secondary outcome results- must be reported within one year after the final data has been collected for secondary outcome measures. ALL data is required to be posted within 1 year of your Study Completion Date. Anticipated posting dates must be included at the time of the primary outcome results entry.

     6.1.3.3 If corrections or clarifications are requested by the ClinicalTrials.gov team, the Responsible Party [see Section 3 "Responsible Individuals"] must respond within 15 calendar days for any registration related information and within 25 calendar days for any results information.

     6.1.3.4 Cancer studies have their own account, should be registered and have results reported as **Case Comprehensive Cancer Center (CCCC) rather than University Hospitals Cleveland Medical Center**. There is a centralized registration coordinator who acts as the Responsible Party designee. The registration coordinator will work with the Responsible Party and study team to report results on Cancer studies. Contact your Department Administrator for more information on registering Cancer studies.

     6.1.3.5 Once the results of the study are released by the Responsible Party, it will be reviewed by personnel at ClinicalTrials.gov within 30 days, may take longer for review of any voluntary results submission. Any comments are posted on the Responsible Party's account at ClinicalTrials.gov and an email will be sent to the Responsible Party. Corrections to trial results can be made, as needed, and the trial can be re-released. If there are no review comments the results are released to the public website within 2 business days following completion of the review period.

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7. REFERENCES:

- NIH Guidance on Clinical Trials Registration in ClinicalTrials.gov - http://grants.nih.gov/clinicaltrials_fdaaa/
- ClinicalTrials.gov public website - http://clinicaltrials.gov
- ClinicalTrials.gov registration site - https://register.clinicaltrials.gov
- Registration at ClinicalTrials.gov: Fact Sheet - http://prsinfo.clinicaltrials.gov/
- Definitions of Responsible Party and Applicable Clinical Trials - https://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf
- How to Submit Your Results - https://www.clinicaltrials.gov/ct2/manage-recs/how-report
- Protocol Data Element Definitions - http://prsinfo.clinicaltrials.gov/definitions.html
- ClinicalTrials.gov Training Materials - http://clinicaltrials.gov/ct2/manage-recs/present
- Learning Module 1: ClinicalTrials.gov Overview and PL 110-85 Requirements - http://prsinfo.clinicaltrials.gov/WebinarSlidesBasicResults.pdf
- User's Guide for PRS - https://prsinfo.clinicaltrials.gov/prs-users-guide.html#Editingrecord
- UHCMC Research SOP SC-401- Registration of Clinical Trials in ClinicalTrials.gov
- 42 CFR 11 https://www.govinfo.gov/content/pkg/CFR-2019-title42-vol1/xml/CFR-2019-title42-vol1-part11.xml
- https://prsinfo.clinicaltrials.gov/prs-users-guide.html

8. FORMS OR ATTACHMENTS:
None

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – May 11, 2022

SC-410 - Certified Copies of Research Regulatory Documents

1. PURPOSE:
To establish a procedure for the creation of certified copies of research documents at University Hospitals Health System (UHHS).

2. SCOPE:
All research Regulatory Documents for studies conducted at UHHS. This SOP does not apply to patient charts or health records.

3. RESPONSIBLE INDIVIDUALS:
All Principal Investigators (PI) and investigator designees engaging in research at UHHS.

4. RELATED TERMS AND DEFINITIONS:
Certified Copy - A copy of original information that has been verified, as indicated by a dated signature, as an exact copy having all of the same attributes and information as the original.

Regulatory/Essential Document - Those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor, and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements.

Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
For a certified copy of research regulatory documents from a study at UHHS or its affiliates to be considered verified it must have the appropriate attestation (including the signature and date of both the responsible party and witness) attached to document the process. Certified copies include: CDs, DVDs, and zip drives with study information transferred to them, as well as paper copies of original documents or previously certified documents.

6. PROCEDURES:
When creating a certified copy of documents the PI or his designee should have the procedure observed by an impartial witness. After the copies have been made, both the witness and the responsible party should complete the certified copy attestation or electronic certified copy attestation. For physical copies, the attestation should be attached to the end of any copied documents. For electronic documents, please insert the signed document as the last page of the PDF—for copies that involve multiple electronic files insert the signed attestation as its own clearly labeled pdf file for copies that involve multiple electronic files.

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7. REFERENCES
- [FDA Guidance for Industry Computerized Systems Used in Clinical Investigations](#)
- ICH-GCP E6(R2) 1.63, 8.1

8. FORMS OR ATTACHMENTS
- [CRC Certified Copy Attestation](#)
- [CRC Electronic Certified Copy Attestation](#)

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APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – May 25, 2022

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QA-501 - FDA Inspection of Investigators

1. PURPOSE:
   To outline the process of an inspection by the US Food and Drug Administration (FDA) and describe activities required to facilitate the inspection. The FDA inspection is typically conducted at sites to determine compliance with federal regulations and adherence to guidelines, to verify the validity and integrity of clinical data submitted in applications for market clearance of medical devices, drugs, or biologics and to assure that the rights and welfare of subjects in the research have been protected.

2. SCOPE:
   This policy applies to all site personnel involved in the implementation and coordination of clinical investigation including the Principal Investigator (PI) and when delegated by the PI, Sub-investigators, Research Coordinator(s) and other designated members of the research staff.

3. RESPONSIBLE INDIVIDUALS:
   The responsible personnel include the PI and when delegated by the PI, Sub-investigators, Research Coordinator and other staff involved in the conduct of clinical research.

4. RELATED TERMS AND DEFINITIONS:
   - Clinical Investigation/Clinical Research
   - Food and Drug Administration (FDA)
   - Inspection
   - Inspection Observation (FDA form 483)
   - Investigational Device Exemption
   - Investigational New Drug
   - Investigator Initiated Research
   - Notice of Inspection (FDA form 482)
   - Principal Investigator
   - Sponsor-Investigator

   Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
   PIs and their research study teams will prepare for and respond to all FDA inspections. The University Hospitals Clinical Research Center (UHCRC) will be notified in advance of the inspection and will provide support throughout the inspection process.

6. PROCEDURES:
   6.1 Receiving notification of an inspection
       6.1.1 When the FDA contacts the investigational site to schedule an inspection, begin completing the FDA Inspection Checklist and obtain the following information:

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6.1.1.1 FDA inspector name and contact information;
6.1.1.2 Additional inspector's information, if applicable;
6.1.1.3 The name of the PI being inspected;
6.1.1.4 Which study(s) is being inspected;
6.1.1.5 The specific personnel to be made available;
6.1.1.6 The specific documents to be made available;
6.1.1.7 Duration of the inspection; and
6.1.1.8 Date of the inspection.

6.1.2 Document any telephone conversation(s) that occur between the FDA inspector and the study staff.

6.1.3 The FDA inspector will usually request that the inspection take place within 10 days.

6.2 <u>Notify the appropriate parties of the impending inspection</u>
Include the name(s) of the protocol(s), IRB protocol number(s), and date of the inspection for all protocols to be inspected when notifying the following parties of the impending inspection:

6.2.1 PI and all study staff (refer to FDA form 1572);
6.2.2 Staff in the facility where the inspector's tour will be given;
6.2.3 Staff in areas where the research was conducted;
6.2.4 Sponsor (if applicable) if the PI is not the sponsor-investigator of the investigational new drug application (IND), or investigational device exemption (IDE);
6.2.5 UHCRC – (216)844-5936; and
6.2.6 Health Information Services (medical records) - (216) 844-3555.
6.2.6.1 Remind all staff to limit idle business conversation during the inspection.

6.3 <u>Preparing for the inspection</u>
6.3.1 Request the medical records for all subjects enrolled in the study. Inform the Medical Records Department and Electronic Health Information Services that this is for a FDA inspection and all records need to be available for the first day of the inspection. If the FDA requests that identifiers remain on the records, the HIPAA Privacy Rule at 45 CFR 164.512(b)(1)(iii) permits this. If the FDA does not require identifiers on records, research staff should redact the identifiers with black permanent marker before leaving.

6.3.2 Reserve a room for the proposed number of days in a private area with a computer that has EMR access for inpatient or ambulatory EMR for the inspection. The room should not contain files or records that do not pertain to the inspection. A copy machine should be located close to the room. The UHCRC may facilitate securing an appropriate location. Keep in mind that the FDA inspectors should not be located in/around patient care and research

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staff workspace areas during the inspection.

6.3.3   Identify a person who will serve as an escort and oversee the inspection. The escort will serve as a guide and general study contact person. The escort will need to be readily available to the inspector at all times.

6.3.4   Create a written list of all the PI's clinical trials. The list should include protocol title, start, and stop date.

6.3.5   Prepare a general overview of the study. This should include: a summary of the study, adverse events, deaths, violations, and deviations. This is to be kept as a reference for the PI and study staff.

6.3.6   Ensure that all study documentation, including informed consent forms, source documents, case report forms (CRFs), regulatory documents, and sponsor correspondence are available for review by the inspector.

6.3.7   Review agreements/contracts for specific details regarding FDA inspections.

6.3.8   Review study documentation for:
    6.3.8.1   Comprehensiveness, accuracy, and compliance;
    6.3.8.2   Weakness/gaps (and correct those that can be corrected [i.e. file violations, draft notes-to-file, locate missing documents, etc.]); and
    6.3.8.3   Unresolved or outstanding issues (and develop a corrective plan for any unresolved/outstanding issues).

6.3.9   Keep all study documents and records ready and accessible; however, do not volunteer a list of them to the inspector. Always wait for a specific request to provide information.

6.4   <u>During the inspection</u>
6.4.1   The PI or PI's designee must be available to meet with the inspector and receive and sign the FDA Form 482 "Notice of Inspection", which will be provided by the inspector. Presentation of the "Notice of Inspection" officially begins the inspection. Email a copy of the 482 to UHResearchCompliance@UHhospitals.org.

6.4.2   The FDA inspector should present their credentials upon arrival to the site. If he/she does not, make sure you ask to see identification prior to allowing access to confidential records. Failure to ask for the inspector's credentials and the Form 482 can be noted as a deficiency in the inspector's report.

6.4.3   The FDA inspector will request a tour of the facility areas where the research took place. Notify staff in the study areas so they will be prepared for the visit and possible questions. The FDA inspector must be accompanied by research staff **at all times** during the tour.

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6.4.4 Research study staff will need to be available at all times to the FDA auditors. All staff should answer questions directly and honestly. **<u>Listen carefully to the question and only answer what was asked</u>**. If you are unclear of the question, ask the inspector to repeat or rephrase the question. Respond to queries promptly. It is acceptable to defer to the PI or other study staff if you don't know the answer.

6.4.5 The standard procedure is that the inspector will request files for review. Provide the inspector only with files that have been requested. Keep a "shadow binder" with a copy of every record or document that is provided to the inspector during the inspection.

6.4.6 The inspector will request copies of some documents. Make a separate copy for yourself of any documents that are requested by the inspector. The inspector's copies should be stamped "Confidential" and your copies should be stamped "Copy". Copies are provided without charge to the FDA.

6.4.7 If the inspector insists on taking photographs or other video or audio recordings, take and retain duplicates at the same time. If the inspector requests to take samples, ask for a receipt of the samples, and pull and retain identical samples at the same time.

6.4.8 The PI should designate an individual to take notes of activities and discussions during the inspection. Keep an exhibit log—a list of all questions asked by the inspector.

6.4.9 The PI should set aside time each day to talk with the inspector, either in person or via phone, and be available for any questions that may arise.

6.5 <u>After the inspection</u>

6.5.1 The FDA inspector will hold an exit interview with the PI at the conclusion of the inspection. The escort, PI and any other appropriate staff should attend this interview. The purpose of this interview is to review the FDA's findings and deficiencies, if any. Any deficiencies will be noted on an FDA Form 483 and given to the PI. The inspector will give a copy of this report to the PI.

6.5.2 Do not sign any affidavits provided to you by the inspector. If the inspector presents an affidavit for signature, politely decline to sign and tell the inspector that you are not permitted to sign documents on behalf of the institution, but you will identify the appropriate person and report back. After that contact (1) your manager, and (2) University Hospitals' Legal Counsel.

6.5.3 During the exit interview, the escort or designee will document the conversation, specifically noting observations, comments, and commitments.

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6.5.4 Maintain all research documentation on site until the Establishment Inspection Report (EIR) is received.

6.5.5 If deficiencies are found during the inspection, a written Inspection Observations (FDA Form 483) will be issued that lists the deficiencies. If no deficiencies are found, then no form will be issued.

6.5.6 E-mail the Exit Interview summary to UHResearchCompliance@UHhospitals.org and UHIRB@UHhospitals.org.

6.6 Response to a FDA Form 483, if applicable

6.6.1 Contact the UHCRC Office of Research Compliance and Education for guidance with the response to a FDA Form 483. A response must be submitted for FDA Form 483.

6.6.2 The written response should include the following information:
6.6.2.1 Determine if a finding was an oversight/single occurrence or if it is a systemic problem requiring a change of procedure/process.
6.6.2.2 Describe corrective actions. This should include justification of why the proposed response would correct this problem and prevent it from reoccurring. Include a timeline for the corrective actions.
6.6.2.3 Address each specific finding, point by point.
6.6.2.4 The response should be sent to the FDA within 15 business days.

6.6.3 Maintain all research documentation on site until the Establishment Inspection Report (EIR) is received.

7. REFERENCES:

- 21CFR 312.68 – Inspection of investigator's records and reports
  https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=312.68
- 21CFR812.45 – Inspections
  https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=812.145
- ICH GCP 1.29 Definition: Inspection;
  https://ichgcp.net/1-glossary/
- ICH GCP 6.10 Direct Access to Source Data/Documents
  https://ichgcp.net/610-direct-access-to-source-datadocuments/
- Inspections, Compliance, Enforcement, and Criminal Investigations, Compliance Program Manual. Updated August 2010
  (http://www.fda.gov/ICECI/ComplianceManuals/ComplianceProgramManual/default.htm)
- Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors FDA Inspections of Clinical Investigators. June 2010
  (http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126553.pdf)
- FDA Form 483 Inspection Observations. Current as of November 2020
  (https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/inspection-observations)

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- FDA Form 483 Frequently Asked Questions. Current as of January 2020 (https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/fda-form-483-frequently-asked-questions)
- CE-22 Reporting to Government and Response to Government Investigations and Accreditation Surveys
- UH System Policies in UH PolicyStat

8. ATTACHMENTS OR FORMS
- FDA Inspection Checklist

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – October 31, 2023

QA-502 – Monitoring Visits

1. **PURPOSE:**
   The purpose of this SOP is to provide guidance to investigators and key study personnel in the preparation before, the conduct during, and after the monitoring of human subjects research projects by a monitor from the study sponsor or Clinical Research Organization (CRO).

2. **SCOPE:**
   All human subjects research protocols conducted and approved by the UH Institutional Review Board, Centralized IRBs, or studies conducted at any UH facility or affiliate facility. This SOP does not override the procedures, policies or processes required by the study sponsor, CRO or other agency.

3. **RESPONSIBLE INDIVIDUALS:**
   Principal Investigators, Sub-Investigators, Research Nurses, Regulatory and Research Coordinators, and other staff listed on the IRB-approved research.

4. **RELATED TERMS AND DEFINITIONS:**

   Corrective and Preventive Action Plan (CAPA) – Actions taken to collect information, analyze information, identify and investigate product and quality problems, and take appropriate and effective corrective and/or preventive action to prevent their recurrence.

   Good Clinical Practice (GCP) – A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected. ICH GCP E6R2 1.24

   Investigational Product (IP) – A pharmaceutical from of an active ingredient, preventative (vaccine), therapeutic (drug or biologic), device, diagnostic, or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

   Monitor – A designee of the sponsor or CRO, who is assigned the task of monitoring the study to ensure the rights and well-being of human subjects are protected. That the reported trial data are accurate, complete, and verifiable from source documents and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s).

   Monitoring – The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), GCP, and the applicable regulatory requirement(s). ICH GCP E6R2

1.38

Monitoring Report – A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor's SOP(s). ICH GCP E6R2 1.39

- Case Report Forms (CRFs)
- Contract Research Organization (CRO)
- Institutional Review Board (IRB)
- Investigator
- Protected Health Information (PHI)
- Research
- Source Data
- Source Documents
- Sponsor
- Sub-Investigator

Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
All Investigators, research, regulatory and key study personnel listed on the protocol should support the preparation and coordination of the monitoring visit as well as reconciliation of findings.

6. PROCEDURES:
6.1 Monitoring Visit
Upon notification of the monitor's visit, inform the Principal Investigator, key study personnel and staff from applicable support services about the visit. e.g., investigational pharmacy, lab services, nutrition lab, etc.
The monitor is only allowed to view study documents in accordance to the protocol.

    6.1.1 Before the Monitoring Visit
        6.1.1.1 Once the monitoring date(s) is confirmed, send a calendar invitation to all study personnel, including any support services with the agenda and schedule of location for meeting.
        6.1.1.2 Reserve a private room, or other quiet area, with internet access and power outlets for the monitor to review the study documents during the visit.
        6.1.1.3 Make sure the PI has time set aside to meet with the monitor and/or to follow-up from the monitoring visit.
        6.1.1.4 Determine the specific documents that will be reviewed during the visit.
        6.1.1.5 Ensure all source documents and medical records are available for review.
        6.1.1.6 Review the Clinical Research Regulatory Binder Files Index (PDF) and verify that the regulatory file is up to date and that all required

regulatory documents are completed, accurate, submitted, up to date and filed. Complete the Internal QA Checklist - Regulatory.

6.1.1.7 Ensure all participant medical records, source documents, case report forms or electronic data entry are complete and accurate. Complete the Internal QA Checklist - Participant.

6.1.1.8 If EMR access for the monitor is required, submit the request several weeks in advance of the monitoring visit.

6.1.2 During the Monitoring Visit
6.1.2.1 Verify the identity of the monitor upon arrival.
6.1.2.2 Escort the monitor to the location of the prepared requested materials.
6.1.2.3 Along with the monitor, sign the monitoring log.
6.1.2.4 Educate the monitor on the use of phones, the access to restrooms, water fountains, any safety and emergency instructions and study staff availability or contact information, as appropriate.
6.1.2.5 Confirm PI interview time and verify that the PI participates in the monitoring visit. This is expected and should be routine.
6.1.2.5.1 If the PI becomes occupied and is unable to meet, establish a phone call immediately post-monitoring visit.
6.1.2.6 Assign research team members to be available to assist the monitor with:
6.1.2.6.1 Access to institutional and department policies and procedures as relevant to the study being monitored.
6.1.2.6.2 Copy and FAX requests (ensure that all records being copied or leaving the site do not have PHI).
6.1.2.6.3 Clarification of queries and corrections.
6.1.2.6.4 Access to medical record per the department's process.
6.1.2.6.5 Travel to support service locations.
6.1.2.6.6 Carrying out the monitoring plan which may consist of serious adverse event review, informed consent review, protocol adherence checks, source document and case report form review, investigational product review and accountability, laboratory sample review, regulatory documents review, any electronic files and data review from the S: drive, REDCap or other approved electronic storage, and equipment and storage records review.
6.1.2.6.7 Keep the Principal Investigator informed of the visit.

6.1.3 After the Monitoring Visit
6.1.3.1 Return all study documents to the secured locations.
6.1.3.2 Return or request a pickup for all hardcopy medical records to their locations.
6.1.3.3 Monitoring findings:
6.1.3.3.1 Ensure that a follow up letter or monitoring report is received from the CRO and/or sponsor representative.
6.1.3.3.2 Review any findings in the monitoring report with the PI and

key study personnel. Develop any necessary process changes and document any corrective and preventative action (CAPA); Refer to *SOP QA-503 - Corrective and Preventative Action*.

       6.1.3.3.3 Prepare complete responses to any findings in the monitoring report, have the PI sign the letter, and send the requested corrections or responses to the monitor in a timely fashion.

   6.1.3.4 Place a copy of the monitoring and site response reports in the Regulatory Binder.

6.2 Closeout Visit

When a study is over it may be officially closed. To be officially closed, a closeout visit must occur and a final report received. The final report documents that the study was officially closed.

6.2.1 Before the Closeout Visit

6.2.1.1 All study documents, including case report forms, informed consent forms, drug accountability and regulatory documents must be complete and filed at the end of the study.

6.2.1.2 All study drugs and other supplies must be returned to the sponsor or disposed of, per policy, at the end of the study.

6.2.1.3 The Principal Investigator must be aware of record retention requirements at the end of the study. These requirements may be found in the study protocol, IRB application, or you may refer to *SOP SC-405 - Record Retention, Storage, and Archiving.*

6.2.1.4 Ensure Note-to-Files are completed to clarify any discrepancies or errors with study procedures and personnel.

6.2.1.5 Request all hardcopy medical records and if needed, ensure access to the electronic medical record or other electronic study files is arranged.

6.2.1.6 Pharmacy records are stored in Investigational Pharmacy and long term Iron Mountain.

6.2.1.7 Refer to *6.1.1 Before the Monitoring Visit*

6.2.2 During the Closeout Visit

6.2.2.1 Along with the monitor, sign the Monitoring Log, as needed.

6.2.2.2 Ensure the monitor has access to all documents required to complete the close out visit.

6.2.2.3 Ensure research staff are available to provide clarification on any study-related issues.

6.2.2.4 During the visit, the PI and key study staff should be available to discuss any issues related to review of the regulatory files, source data verification, IP reconciliation, and data retention and storage.

6.2.2.5 Refer to *6.1.2 During the Monitoring Visit*, as needed.

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6.2.3 <u>After the Closeout Visit</u>

    6.2.3.1 If applicable, ensure that all IP(s) have been destroyed or returned to the sponsor per agreement and documented appropriately.

    6.2.3.2 Store and secure all study records per institution, FDA and or sponsor requirements. Refer to *SOP SC-405 - Records Retention, Archive and Storage*.

    6.2.3.3 Ensure or obtain confirmation that all study-related costs and expenses, including patient care charges, have been charged to the study. Refer to *Policy R-34 - Award Close Out.*

    6.2.3.4 Close the study with the IRB when required.

    6.2.3.5 Refer to *6.1.3 After the Monitoring Visit*, as needed.

7. REFERENCES:

- Food and Drug Administration: 21 CFR 312 & 21 CFR 812
- ICH GCP E6 (R2) Good Clinical Practice: Integrated Addendum to ICH GCP E6(R1) Guidance for Industry, Version: March 2018
- National Institute of Allergy and Infectious Disease
- HIPAA Privacy Rule, Office of Civil Rights (OCR)
- UH Investigator Manual for IRB Submissions, Chapter 19- Compliance and Monitoring
- CRA's Guide to Monitoring Clinical Research, 4th Edition by CenterWatch
- System Policy R-34 – Award Close Out in UH PolicyStat

8. FORMS OR ATTACHMENTS:

- Monitoring Visit Checklist
- Monitoring Closure Visit Checklist
- Internal QA Checklist - Regulatory.
- Internal QA Checklist - Participant.

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – October 31, 2023

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QA-503 – Corrective and Preventative Action (CAPA) Plan

1. **PURPOSE:**
    The purpose of this SOP is to provide guidance to investigators and study personnel in writing a Corrective and Preventative Action (CAPA) plan in order to develop plans for addressing existing or potential problems identified during the conduct of research, and to prevent reoccurrence.

2. **SCOPE:**
    All research protocols under the purview of the UH Institutional Review Board (IRB). This SOP will serve as a guide to research personnel with the steps to writing a CAPA plan.

3. **RESPONSIBLE INDIVIDUALS:**
    All Investigators, research, regulatory, and study personnel who engage in research.

4. **RELATED TERMS AND DEFINITIONS:**
    Corrective and Preventative Action (CAPA) Plan - A quality process used to address an existing noncompliance issue and the steps taken to prevent further recurrence. Actions taken to collect information, analyze information, identify and investigate product and quality problems, and take appropriate and effective corrective and preventive action to prevent their recurrence.

    Root Cause - Factor that caused an issue or problem.

    Root Cause Analysis - a class of problem solving methods used to identify the initial causes of problems or events.

    Corrective Action - Action taken to rectify a problem.

    Preventative Action - Action taken to eliminate the root cause of a problem or potential problem including the detection/identification of issues.

    Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. **POLICY STATEMENT:**
    A CAPA is written to identify a discrepancy or problem in the conduct of the research study, note the root cause of the identified problem, identify the corrective action taken to prevent recurrence of the problem, and document that the corrective action has resolved the problem. Please note that IRB approval is necessary prior to modifying procedures laid out in the IRB-approved protocol unless the change is necessary to prevent immediate harm to participants.

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6. PROCEDURES:

6.1 Form a team
    6.1.1 Identify the individual(s) responsible for:
        6.1.1.1 Developing the CAPA plan
        6.1.1.2 Implementing the CAPA plan
        6.1.1.3 Training staff on the CAPA plan
        6.1.1.4 Evaluating of the results of the CAPA plan

6.2 Identify the issue or potential issue
    6.2.1 Document a brief description of the issue
    6.2.2 Evaluate the magnitude of the problem and potential impact
        6.2.2.1 Investigate the impact of the issue on the overall research

6.3 Identify the root cause
    6.3.1 Describe the reason the issue arose
        6.3.1.1 Investigate how or why the incident occurred

6.4 Describe the corrective actions taken or planned
    6.4.1 Indicate who will perform the corrective actions and when
    6.4.2 If items are incomplete or unavailable, include a statement regarding attempts made to complete the action
        6.4.2.1 Consider sponsor, regulatory (Food and Drug Administration, Office Human Research Protection, Office of Civil Rights) or local institutional requirements when creating the corrective action plan

6.5 Implementation
    6.5.1 Describe the procedures implemented to resolve the problem and indicate who's responsible for the procedure

6.6 Effective Date of Resolution
    6.6.1 Indicate an effective date for the corrective action

6.7 Preventative Action
    6.7.1 Describe the preventative actions taken or planned and who's responsible
    6.7.2 Create a listing of all tasks that must be completed to correct or prevent the problem.
    6.7.3 Send copy of the final CAPA to the appropriate authority if required

6.8 Evaluation and Follow-up
    6.8.1 Describe the procedure to evaluate the implementation and completion
    6.8.2 Indicate the study staff who are responsible for the evaluations
    6.8.3 Include the timeframe for evaluation
    6.8.4 Send evaluation follow-up report to appropriate authority if requested

6.9 Comments-Optional
    6.9.1 Document observations

6.10 If the CAPA Plan is related to an internal process, maintain documentation separate from the original study files

6.11 If the CAPA Plan is in response to an FDA audit, maintain documentation as part of your study files

6.12 As applicable, follow any of the reporting requirements listed in Chapter 20 of the UH Investigator Manual for IRB Manual (Reportable New Information)

7. REFERENCES:
- Feinstein Institute for Medical Research
- FDA 21 CFR 820.100
- FDA.gov- Corrective and Preventive-Actions
- Preventive/Corrective Actions (CAPA) Guidelines. R.M. Baldwin, Inc.
- UH Clinical Research Center Investigator Manual for IRB Submissions

8. FORMS OR ATTACHMENTS:
- CAPA Template

APPROVALS

Signed by Dr. Grace McComsey, Vice President of Research, Associate Chief Scientific Officer, University Hospitals Health System, Director, UH Clinical Research Center – August 26, 2022

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Clinical Research
Standard Operating Procedure

University Hospitals
Clinical Research Center

QA-504 – Requesting Remote EMR Access for Monitors and Auditors

1. PURPOSE:
To provide instruction on how to obtain EMR access for Unaffiliated Entities.

2. SCOPE:
This SOP applies to all individuals participating in the conduct of clinical research at University Hospitals ("UH") (e.g., Regulatory Specialists, Study Coordinators, Research Nurses, etc.) to whom an Investigator assigns a study task of requesting EMR access for monitors and auditors.

3. RESPONSIBLE INDIVIDUALS:
The Principal Investigator (PI) is responsible for ensuring that all persons requesting remote EMR access for monitors and auditors are given:

3.1   Limited version of Epic Hyperspace via EpicCare Link
3.2   REDCap User Access Form, if applicable.

4. RELATED TERMS AND DEFINITIONS:

Unaffiliated entity – An individual neither employed nor contracted by UH, such as a monitor or auditor. In this SOP this will be referenced as a "Monitor."

EpicCare Link – Epic's tool for granting community access to UH's patient database through a web browser.

Epic Hyperspace – the front-end software that is presented to healthcare providers and administrative staff in healthcare organizations when launching their Epic system. Within this software, providers and staff are able to see patient PHI, procedures, and other items associated with the patient's electronic medical record.

EMR – Electronic Medical Record

Please reference the Standard Operating Procedures Glossary of Terms for complete definitions of terms in this SOP.

5. POLICY STATEMENT:
All Investigators, Research, Regulatory, and Key Study Personnel listed on the protocol shall support the preparation and coordination of granting Monitors EMR access.

6. PROCEDURES:
6.1   Requesting UH Epic Access
    6.1.1   Study Team will send the Monitor the UH EpicCare Link via email (epiccarelink.uhhospitals.org)
        6.1.1.1   The email must include the following information, which the Monitor will

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need to complete his or her request for an Epic account:

    6.1.1.1.1   Research Study ID

        6.1.1.1.1.1 This is the protocol short title in Oncore/Velos

    6.1.1.1.2   Principal Investigator

    6.1.1.1.3   Study Contact/Coordinator Name

    6.1.1.1.4   Study Contact/Coordinator Email and Phone Number

6.1.2 From the EpicCare Link in the email, the Monitor will select "Request New Account"

    6.1.2.1 Even if the Monitor has access to Epic at another Institution, the Monitor will need to create a new account at UH.

    6.1.2.2 The Monitor must create his or her own account and shall not share an account with anyone else.

    6.1.2.3 The Monitor only needs one UH account for all research projects.

6.1.3 Upon Monitor's submission of the New Account request, Research IT will create an account and send temporary credentials to the Monitor within 3-5 days.

    6.1.3.1 Research IT will copy the Study Coordinator on the email to the Monitor.

6.1.4 The Monitor shall use the temporary credentials to finalize the creation of an Epic account at UH.

    6.1.4.1 If there are issues with the account, contact ResearchIT@UHhospitals.org.

6.2 <u>Preparing for the External Visit</u>

6.2.1 The Study Coordinator will release the Research Participants' information to the monitor utilizing the "Reports" function in Epic.

    6.2.1.1 The amount of time the monitor should have access to the selected Research Participants is required.

    6.2.1.2 Five (5) consecutive days is the maximum amount of time a monitor can have access without re-associating the Research Participant(s) and updating the access dates.

    6.2.1.3 A custom report will need to be made if the Monitor needs to access inactive Research Participants.

    6.2.1.4 A Monitor can review Participants across multiple studies, if the Study Coordinator includes them in the report.

6.2.2 The Study Coordinator will review Clinical Research SOPs referenced in this SOP.

6.3 <u>During the External Visit</u>

6.3.1 The Study Coordinator will instruct the Monitor to access the Research Participants' medical records via the EpicCare link.

    6.3.1.1 The Monitor only has access to the Research Participants the Study Coordinator assigned to the monitor.

    6.3.1.2 The Monitor will be able to view all records for the Research Participant(s) across all healthcare organizations utilizing Epic.

7. REFERENCES:

- UH System Policies in UH PolicyStat

- o IS-7 – Remote Computer Access
- o IS-12 – Access to Electronic Records and Computers for Inquiries and Investigations
- o IS-14 – Acceptable Use of UH Electronic Assets
- o IS-15 – UH Network and Systems Access
- o IS-19 – User Identified (ID), Creation and Modification
- o IS-22 – Sharing of UH Clinical or Business Data with Third Parties
- o R-3 – Uses & Disclosures of PHI for Research
- Clinical Research SOPs
  - o SS-311 – REDCap Project Access for External, Non-Research Credentialed Users
  - o QA-501 FDA Inspection of Investigators
  - o QA-502 Monitoring Visits
- Epic Workflows
  - o Research Reporting
  - o External Study Monitor
  - o Research Coordinator Email template
- REDCap User Access Form

8. FORMS OR ATTACHMENTS:
None.

APPROVALS

Signed by Grace A McComsey, MD, FIDSA, Director of the UH Clinical Research Center,
University Hospitals Health System –
December 13, 2023