Recombinant Human Clinical Trial Guidance

Table of Contents

Work Covered by this Document

This guidance document is intended for researchers who are administering recombinant DNA/RNA materials to humans. This document does not apply to recombinant proteins administered to humans because that type of recombinant material is not covered under section III-C of the NIH Guidelines. If you need help determining NIH Guidelines applicability for your research, please contact the Office of Biological Safety (OBS). Because each research project is unique, the Institutional Biosafety Committee (IBC) may make requests that include more risk mitigation than the information provided in this guidance document.

Key sections of the protocol are outlined here. There are other required questions that will appear in the Bio-ARROW protocol.

Overview:

Layman's Description: The lay abstract should be simplified to briefly describe the study including the study drug, the participant population, the study objectives, and the primary endpoints. You will be able to provide specific details in the Research Description. Briefly mention if portions of the project will be done elsewhere (e.g., drug administration at a different institution).

Personnel:

The following types of personnel should be listed in either the Read/Write Personnel or Read Personnel sections:

- PI for the biosafety protocol
- Individuals who handle study drug and/or patient samples post-drug administration

Sub-investigators do not need to be listed; however, they need to defer any biosafety related questions from staff and/or patients to the PI.

Other Personnel: Please list types of personnel that will be involved in the clinical aspect of the study, such as Clinical RNs, Clinical Pharmacists and other support staff. Specific individuals in these groups do not need to be listed by name.

Point of Contact:

The PI is automatically the Primary Point of Contact (POC) for the Office of Biological Safety communications. You can designate 1-2 individuals on your study team as additional POC to also receive these communications.

Funding:

Please complete this section of the biosafety protocol following the instructions for each question.

Select Agents:

Please complete this section of the biosafety protocol following the instructions for each question.

Description of Locations:

Please list the following types of spaces:

- Location used for study drug preparation (e.g., Pharmacies, Clinical Hematopoietic Cell Processing Laboratory)
- Location used for drug or agent administration
- Locations where blood draws post-drug administration are performed
- Laboratory space used for processing patient samples post-drug administration (e.g., UW Hospital and Clinics (UWHC) Clinical Laboratory (Core Lab), Cancer Pharmacology Lab, and/or Translational Science BioCore (TSB) Translational Research Initiatives in Pathology (TRIP) Lab). If applicable, include autoclave locations.

Materials and Activities:

Please check "Recombinant (transgenic) or synthetic DNA/RNA materials, including human gene therapy" and "Human cells and cell culture, organ or tissues, or biological samples."

Depending on the nature of your work, you may need to check additional boxes. If the study involves a viral vector system or a bacterial based vaccine, you will also need to check "Microbes and disease-causing agents including bacteria, viruses, fungi, prions, protozoa, parasites." If you will not be administering a viral vector or microbe directly to a patient (e.g., CarT products), please do not select "Microbes and disease-causing agents including bacteria, viruses, fungi, prions, protozoa, parasites."

Materials and Activities-Recombinant or Synthetic DNA/RNA Materials:

Please provide the following answers in this section:

Drug Resistance: If a vector is introduced that contains a drug resistance trait, please answer "yes."

Drug Resistance Trait: If you answered "yes" to the previous question, please complete this table.

Genes and DNA/RNA Fragments: Please list the DNA/RNA fragments or genes you are introducing into the patients through drug administration.

Construct Details: If DNA/RNA fragments or genes are carried by a viral vector or a plasmid, please include the information in this question. For CAR-T studies, please add information in the Research Description section and not in this section.

Materials and Activities-Recombinant or Synthetic DNA/RNA Materials-Continued:

Genome Editing: If the study uses any genome editing tools such as CRISPR/Cas9, TALENs or ZFNs, please answer "yes" and complete the corresponding questions.

Research Involving Human Subjects: Please answer "Yes."

Materials Administered to Human Subjects: Briefly describe the recombinant DNA/RNA materials that are administered to humans focusing on the DNA/RNA fragment or gene and construct you are introducing. For CAR-T studies, please add information on how the cells are modified.

Human Subjects Status and Documents:

Site Information: Please identify UW-Madison's role in the trial.

Investigator's Brochure: Please upload the current version of this document.

Clinical Protocol: Please upload the current version of this document.

Pharmacy Manual: Please upload the current version of this document.

UWHC Research Safety Committee: Upload the safety procedures document from the UWHC Research Safety Committee, if available at the time of biosafety protocol submission.

Materials and Activities-NIH Guidelines:

Please check the "III-C" box.

Please check any other appropriate categories that apply to your research.

Materials and Activities-Microbes and Disease-Causing Agents

If the study involves a viral vector system or bacteria (e.g., bacterial based vaccine), this page needs to be completed.

Bacteria: If the study involves a bacterium, please complete this section.

Virus: If the study involves a virus based vaccine, please complete this section.

Viral Vectors: If the study drug includes a viral vector (e.g., lentiviral viral vector, Adeno-Associated Viral Vector) please complete this section. If a collaborator or sponsor is performing the modification (e.g, CarT product) using viral vectors, the viral vector is described in the Research Description and not in this section.

Materials and Activities-Cells, Organs, Tissues or Biological Specimens:

Cell Culture Details: Please answer this question, if applicable. For CAR-T studies, information for cell modification can be added here.

Organs, Tissues, or Biological Specimens: Please add blood and any other tissues or specimens removed from the participant post drug/agent administration.

Materials and Activities-Bloodborne Pathogens Personnel:

Exposure Determination: Please list the PI and any research staff handling or working with any human samples (e.g., processing, shipping). Do not include individuals working in core labs (e.g., UWHC Clinical Laboratory (Core Lab), Clinical Hematopoietic Cell Processing Laboratory, Cancer Pharmacology Lab, and/or Translational Science BioCore (TSB) Translational Research Initiatives in Pathology (TRIP).

Materials and Activities-Bloodborne Pathogens Exposure:

Please complete this section of the biosafety protocol following the instructions for each question.

Engineering & Work Practice Controls: At a minimum, please list sharps containers.

Housekeeping: Please complete this section as it relates to activities performed by study team personnel. Please do not include information regarding UWHC Clinical Laboratory (Core Lab), Cancer Pharmacology Lab, and/or Translational Science BioCore (TSB) Translational Research Initiatives in Pathology (TRIP). If the Clinical Hematopoietic Cell Processing Laboratory is used, please include information on their practices.

Biosafety Precautions- Containment:

Aerosol Generating Activities: Please provide the answer appropriate to your study for study drug and sample processing post-drug administration. An answer of "yes" may be appropriate if participant samples are processed by the study team).

Activity List: Please provide a response if previous question was answered "yes." A response for "pipetting" and/or "opening culture plates, ampoules, tubes, bottles and lyophilized cultures" may be appropriate, if participant samples are processed by the study team or a group that doesn't have a biosafety protocol (e.g., Clinical Research Unit (CRU)).

Biological Materials Outside of Containment: Please answer "Yes."

Material Details: Please provide the following response if it is appropriate for your study "Drug/agent administration to patients." If any analyses in the research lab are done outside of containment (i.e., outside of BSC), please include this information.

Centrifuge Containment: Please consider this question for the research and clinical settings (e.g., CRU), if applicable.

Commented [KK1]: Do we want this information if it's hard for IBC to have oversight of clinical core labs?

Commented [SK2R1]: Maybe not, question for Andrea and Ops to consider.

Flow Cytometry Containment: Please answer this question.

Transport procedures: Please upload appropriate transport procedures. If specific transport procedures for the study drug and/or samples are provided by the sponsor, please include these.

Biosafety Precautions-PPE:

Personal Protective Equipment: Please list the PPE for the following activities in separate entries:

- Study drug preparation
- Study drug administration
- Post-drug administration sample handling/processing done by study team

Biosafety Precautions-Disinfection/Inactivation:

Disinfection/Inactivation-General: Please include information for the research (e.g., sample processing) and clinical settings. Please confirm with the hospital including the hospital central lab the methods used for samples post-drug administration, . If the Clinical Hematopoietic Cell Processing Laboratory is used, please include information on their practices. Information provided in the biosafety protocol must be consistent with information found in the UWHC Research Safety Committee document.

Autoclave Testing: If autoclaves are not used for inactivation, please answer "N/A."

Spill and Release Procedures: Please develop a spill protocol using the information for spills found in the UWHC Research Safety Committee document.

Biosafety Precautions-Signage:

Precaution Signage: Please list signage posted in research spaces. If the CRU lab is used, please list their BSL-2 signage. If special signage is used for study drug administration, please describe signage.

Biosafety Precautions-Emergency Response:

Emergency Response-General: Please provide the following, if applicable: "Wash exposed area with soap and water for 15 minutes. For eye splash, flush eyes with eyewash for 15 minutes. Report potential exposures to biohazardous agents or non-pathogenic rDNA organisms to the PI/supervisor, obtain medical attention if necessary and notify the Biological Safety Officer (BSO) and EH&S Occupational Medicine using the online "First Report of Exposure or Release" form within 24 hours (available on the OBS website, www.ehs.wisc.edu/biosafety). Medical follow-up should be sought as needed. Information regarding the materials you are working with (i.e., strain, drug resistance, etc.) will be provided to the medical professional in order for them to make an informed decision on proper treatment." Information in this section should be consistent with information in the UWHC Research Safety Committee document.

Emergency Response-Special: Please provide any special emergency responses, if applicable.

Occupational Health Considerations: Please add a statement (e.g., UW Health offers the Hepatitis B vaccine series to all employees handling human derived material) about offering the Hepatitis B vaccine series to all employees handling human derived material. Please provide an additional response if the study has additional health considerations for employees.

Lab Specific Training: Please provide information regarding training that occurs in the research setting. Please also provide clinical staff specific training that pertains to this study such as that provided by the sponsor and/or Pharmaceutical Research Center (e.g., Education Forum).

Research Description:

Describe the Research: Please provide the following information, if applicable:

- Information about the drug/agent being administered
- How the drug/agent is administered
- Brief synopsis of study procedures
- What is done with blood draws or other patient samples post-drug administration
- Safety considerations including shedding information, if available
- Information about how CAR-T cells are modified (e.g., vector used, who performs modification, modifications made, construct information if known)

Additional Documents: Please provide any supplemental documents that are helpful, if applicable.

BSL3/ABSL3 manual: N/A

Assurances:

Please agree to the assurances. Must be completed by the PI.

PI Signature:

Please sign the protocol. Must be completed by the PI.