



How to complete the Application for Protocol Review

This document and all applicable attachments must be submitted for all studies requesting review by COMIRB by the Full Board or via Expedited Review

COMIRB #: COMIRB-assigned protocol number. Please use the protocol manager on the COMIRB website to obtain a COMIRB number.

A. Review Dates

Date of Initial Submission: Enter the date when the study was first submitted to COMIRB for review.

Version Date: Enter a new date for each revision submitted to COMIRB for review. This applies to additional responses to the initial review as well as subsequent amendments or continuing reviews.

B. Project Information

Project Title: List the full title and include any cooperative group or sponsor protocol numbers for ease of protocol identification in the future.

The project title should be the same on all documents submitted to COMIRB for review. The title cannot be changed without first submitting an amendment and / or update form requesting the change and making the change on all approved documents.

Research Area: Select from the drop down menu provided

Initial Continuing Review Amendment

Check the applicable box to reflect the type of review that is being requested with this submission.

C. Contact Information

Principal Investigator: Only a person who is faculty, fellow, resident or student at UCD or one of the Affiliates can be the PI on a study.

Mentor: Fellows, residents and students must have a faculty or staff mentor listed as a co-investigator. This person is responsible for providing support to the mentee and ensuring that the study is conducted according to the protocol as approved and in compliance with all federal, state and local laws.

Co-investigators: List all co-investigators. This includes those listed on the protocol and a representative investigator from each local site where the study



will be performed or subjects recruited. This list should correspond to the main personnel identified on the FDA Form 1572 (if applicable). List only co-investigators who are under the direction of the principle investigator.

Primary Contact: Name of study coordinator, research nurse or other primary contact person with a contact phone number that is not a principal or co-investigator.

Research Coordinators: List all research coordinators that will be part of the study staff.

Note: All members of the study team are required to have the following training:

Course 1 - CITI Basic Course

All investigators and members of their research teams must meet COMIRB continuing education requirements every **three (3) years** after certification of initial education

All affiliated/local principal investigators, co-investigators, and research coordinators listed on human research protocols must also complete:

Course 2 – the HIPAA Research Course

Administrator / Manager: List any person who has responsibility for a research group / compliance group who may need access to protocol manager but is not going to be involved in the daily activities of the study.

Employee ID Number: Use the employee ID # of all persons connected to UCD or their student ID #.

If neither of these is available then a Persons of Interest (POI) # must be obtained.

For those who do not have an employee ID through the UCD, (i.e. **DHMC, DVAMC**, TCH, UCH) and will need a POI number established in order to complete the Research Training course in Blackboard, you will need to contact the Department Administrator of the individual listed on your specific Protocol that is associated with the UCD (i.e.: the Principal Investigator, or Co-PI). Their department administrator will be able to assign POI's, or direct you to someone within their department that has PeopleSoft access and will be able to assist you.

For more specific information on the process for assigning a POI number in PeopleSoft HRMS please see the PBS Step-By-Step Guide called "Add a Person (POI Types including Pre-Employment) - Workforce Administration Module. All



PeopleSoft Step-By-Step guides are available at:
<https://www.cu.edu/pbs/hrms/resources/sbs.html> .

D. Type of Review being Requested

Full Board: All documents detailed on Page 20 of the application form will also need to be submitted

Expedited: See **Attachment F** for definition of Expedited Review Categories. **Attachment F** will also need to be completed. All required Attachments are detailed at the end of the application form

Reciprocity or Secondary Review: COMIRB may act as a secondary review body for research proposed to take place at an outside institution, under the purview of another IRB. In this role, COMIRB holds authority only over investigators from the University of Colorado or its affiliates, though COMIRB may communicate concerns or suggestions to the host university or its IRB.

This does not include studies that for review by WIRB [Western IRB] but would, for example, include NCI-CIRB or National Jewish Hospital.

This type of review is only available if COMIRB has agreed to cede review to another IRB. Permission must first be obtained from the COMIRB director. Attachment A will need to be completed and submitted with the application. **[Only sections A - G need to be completed]**

E. Funding

Please describe in this section any sources of funding you have for your study, including the university, a corporation, foundation, federal grant, or other contributor.

Funding Sponsor: List the funding sponsor and sponsor project number.

Institution receiving Funding:

Check the box describing the institution receiving the grant or write ‘not applicable’ in the ‘other’ space if there is no grant or sponsoring agency or if the grant is not awarded to UCD or one of the affiliates. If the study is funded by a federal grant, check “yes” and provide 3 copies of the grant (unless it is an umbrella grant or previously on file in the COMIRB office). Provide appropriate COMIRB protocol # for the grant.

Initial full board and initial expedited protocols that receive certain types of outside funding are charged a review fee. Possible types of outside funding include, but are not limited to, industry-sponsored studies, federal grants



awarded to an affiliated institution other than UCD, foundation funded studies, etc. Protocols that are supported by a federal grant that is awarded to UCD are not charged a review fee.

Most full board continuing reviews that receive outside funding are charged an annual review fee. At this time, protocols that qualify for expedited continuing review do not require a fee.

F. Performance Sites

Check each institution where the protocol data will be collected and/or where subjects will be recruited.

Affiliate institutions are:

- University of Colorado Hospital (UCH)
- Denver Health Medical Center (DHMC)
- Denver Veterans' Affairs Medical Center (DVAMC)
- The Children's Hospital (TCH)
- Colorado Prevention Center (CPC)

Any of the clinics that are legally part of the above named affiliated institutions are also included as affiliated.

If the institution is not affiliated, please submit a letter of permission from that site to conduct research and complete Attachment A.

Other: Use this to designate if a specific site / center within UCD and Affiliates will be used, e.g. GCRC, CIC, Denver Cares.

[Complete Attachment A if this site will be part of a multi-site study or if more than one clinical site will be used locally.]

[Complete Attachment B if part of the research is being conducted at a non-USA site]

University of Colorado Hospital, Denver Health Medical Center and the Denver VAMC have a separate internal review process that must be completed in addition to this application if either of these sites will be used to recruit or see subjects or if any of the investigators are employees of that institution.

For: [Denver Health Medical Center](#)
[Denver VAMC](#)
[UCH HRRC](#)



G. Description of Study

1. Type of Research Protocol Attached:

Provide a clear description of the study using one of the following

- **COMIRB-Format Protocol.** This is a recommended format. If you are not sure what this format looks like, you can view a template of it on the [COMIRB web site](#)
- **Industry protocol.** This is typically the format used by the particular sponsor of the study. COMIRB will accept this format as long as the design is clear and readable.
- **NIH Grant/Master Protocol.** COMIRB will accept protocols that use the NIH format, which is required if you are the recipient of an NIH grant as long as the study for review is [clearly delineated and readable](#). It must only describe the study being submitted for review.
- **Other formatted version of protocol (from or for external review).** If your study site will be working in conjunction with another site that is under the purview of a different IRB, COMIRB will accept the scientific protocol in the format required by that IRB. If you are writing a protocol for funding purposes and it needs to be more detailed than the COMIRB-format protocol, it can be submitted for review. The protocol must be in a [format that is clear and readable](#).

2. Abstract in lay terms:

The *Purpose of the Study* should be a basic description of your study that people with various educational backgrounds can read and understand. To be effective in this role, your description must be free of barriers to comprehension, such as highly-specialized terms that only a select few are familiar with. The process of simplifying these terms is essentially the process of breaking them down into their constituent parts—using single-word synonyms, explanatory phrases, and even entire supporting sentences. Please keep in mind that people must be able to quickly acquire a basic understanding of your study—without consulting a reference—in order to make the proper decisions about it.

Of course there are some common medical and research terms that the reader will need to be familiar with—terms like “bid,” “randomization,” “placebo,” and “double-blind,” just to name a few. You may safely use these in your study description (more on this below). COMIRB also understands that experts in a given field must be able to recognize an anatomic region or a procedure by



its established name—say, “supratentorial” or “quantitative fluorescence imaging.” But the place for these is in the *study title* or the *study design*. Remember: the goal here is to communicate the study to as broad an audience as possible. Below are some guidelines to help you write your statement.

- A. **Start your statement with standard text.** For most studies, start the sentence with “*The purpose of this study is...*”, or, if you are stating aims, “*The primary aim of this study is...*”. Some studies will require that you use the first sentence to set up or introduce the main sentence. Some studies may even require a couple of introduction sentences and a couple of follow-up sentences. Regardless of the structure, this should not be a detailed discussion: provide only enough background to support the main ideas of your *Study Purpose*. But also make sure that the main ideas are clearly supported.
- B. **Itemize study aims.** If you are stating the aims of your study, itemize them using numbers or letters followed by parentheses, for example:

“The secondary aims of this study are the comparison between treatment arms of 1) the proportion of patients who have experienced a bone related event (BRE), including spinal cord compression, surgery to bone, local radiation therapy to bone, or skeletal fracture; 2) the proportion of patients who have experienced progression of bone metastases; and 3) the time to onset of bone pain.”
- C. **A hypothesis is usually optional.** For many studies, the hypothesis will already be implied in the study’s purpose. Of course, you may state it for clarity’s sake, and you *should* if you have more than one hypothesis.
- D. **Place drug/device names up front.** Place the name of the study drug or device near the beginning of the sentence.
- E. **Keep comparison items together.** If you are comparing two drugs or two procedures, place their names near each other (usually near the front), rather than separated by a long interval. Separating items in a comparison by long stretches of description can be confusing. In the example below, the sentence seems to say that subjects have not responded to vorinostat, when what the author meant was that patients had not responded to D2R44 in combination with retrovin.

e.g. #1:

Not: The purpose of this study is to compare **placebo** in patients with refractory melanoma who have received multiple cycles of D2R44 in combination with retrovin and shown no response to **vorinostat**.

But: The purpose of this study is to compare **vorinostat** to **placebo** in patients with refractory melanoma who have received multiple cycles of D2R44 in combination with retrovin and shown no response.

F. Replace specialized terms. Replace specialized terms with synonyms or word phrases that are more easily understood by laymen whenever this is practical. There will be many times, of course, when there is no suitable substitute for a particular term. Other times, a replacement phrase may be so long that the added complexity outweighs any gain in descriptiveness. Use your best judgment here. The basic rule should be, if you can make the reading easier, do so. Here are some examples.

- a. Percutaneous..... "through the skin"
- b. Symptomatic "show symptoms"
- c. Idiopathic "self-arising" or "arising alone"
- d. Cryptogenic..... "of unknown origin" or "of unknown cause"
- e. Glioma "cancer of the glia cells (non-neuronal cells of the brain)."
- f. Supratentorial..... "located in the upper structures of the brain"

G. Rearrange sentences. Many times, simplifying the language will not be as easy as merely re-phrasing a few words but will instead require recasting the whole sentence. Still, the basic idea is the same: substitute explanatory phrases for compound words.

e.g. #1

The purpose of this study is to determine the highest **hypofractionated stereotactic radiotherapy** dose patients can tolerate without unacceptable (\geq grade 3) acute or delayed central nerve system (CNS) **toxicity**.

The purpose of this study is to examine a multi-session radiation therapy and determine the highest fraction of the total dose that can be given in a single session without the patient experiencing unacceptable (\geq grade 3) acute or delayed radiation sickness of the central nervous system. This therapy will make use of a targeted-beam.

Here, the term "hypofractionated" is explained in a phrase at the beginning, while the term "stereotactic" is explained using an

additional sentence at the end. Also, the specialized use of “toxicity” is more clearly defined as “radiation sickness.”

e.g. #2

Our primary long-term goal is to improve the completeness of surgical resection of malignant brain tumor with **image guided fluorescence imaging**. We hypothesize that the use of **quantitative fluorescence imaging** will enable more complete tumor resection than normal direct visualization, and thereby improve patient survival. As a first step, we will here determine the **ALA** dose and administration time that most accurately detects residual tumor.

Our primary long-term goal is to improve the completeness of surgical resection of malignant brain tumor by using the tumor’s light-reflecting properties to distinguish it from the surrounding tissue under special lighting and after a fluorescence enhancer has been injected into the body. We will use aminolevulinic acid (ALA) as the fluorescence enhancer. We hypothesize that by determining the optimal dose of ALA and the pre-surgery injection time, and by illuminating the surgical cavity with special lighting, we can better detect the margins of the tumor and thereby achieve more complete resection than would be possible with regular visualization under normal lighting.

Here, the highly specialized terms are replaced with explanatory phrases. The change results in 3 additional lines of text, but the reader is much more likely to understand what is actually being done, rather than passing off the unfamiliar terms as indecipherable. Remember, not all of your readers will have the time to consult a reference or peruse the full protocol summary for an explanation.

- H. **Some research terms are acceptable.** Some technical terms are common to medical research in general, and most people reading your study will be familiar with these. You can therefore safely leave these in. These include such terms as “acute,” “chronic,” “monotherapy,” “pharmacokinetic,” “adjuvant,” “randomized,” “trial,” “dose escalation,” and many others. But once you go beyond the realm of common research terms and begin to describe specific procedures or illnesses, you should check to see if you can simplify the language.
- I. **Define acronyms.** Define acronyms that are not well-known. Well-known acronyms include such terms as AIDS, HIV, and DNA. You may use these freely in your statement. You may also use acronyms for drug names if writing out them would make the sentence more difficult to read. However, processes should generally not be written as acronyms,



unless they are defined (though it generally serves no purpose to use and define an acronym in a stand-alone statement).

e.g. #1

The primary objective of this study is to demonstrate non-inferiority in virologic response, defined as a confirmed plasma viral load of less than 400 copies/mL, with **TMC114/RTV** 600/100 mg bid versus **LPR/RTV** 400/100 mg bid at 48 weeks, when administered in combination with an individually optimized background regimen (OBR)

The primary objective of this study is to demonstrate that a combination of **TMC114/RTV** 600/100 mg bid is not inferior to a combination of **LPR/RTV** 400/100 mg bid when taken by HIV patients, as defined by a confirmed plasma HIV viral load of less than 400 copies/mL measured at week 48 of this study, and when administered in combination with an individually optimized background regimen of other antiretroviral drugs.

The acronyms in the drug names are left in, since these allow for a more concise comparison, and since it is evident that 2 drugs are being compared. In situations where a drug is being compared to placebo and there is nothing gained by using the acronym, it is better to spell it out. Note here that the word “combination” is inserted to make it clear that 2 drugs are being given together. The acronym “OBR” is not used, since it will not appear again in the statement.

e.g. #2

The specific aim of this study is to isolate HIV-1-specific **CTL** from **CM** in subjects and compare their **TCR** repertoires with those in **PBMC** and **CM** before and after **HAART**.

The specific aim of this study is to isolate HIV-1-specific cytotoxic T cells present in the colonic mucosa of subjects and compare their T-cell-receptor repertoires with those found in their peripheral blood mononuclear cells and colonic mucosa before and after highly active antiretroviral therapy.

Although the acronyms used in this example shorten and simplify the sentence, they also make it necessary for a non-expert to consult a reference in order to decipher the meaning. Again, the statement used in the Application should be as much of a stand-alone statement as possible.

- J. Provide brief background when necessary.** As stated earlier, it may sometimes be necessary to provide some background in order for your readers to understand the main elements of your *Purpose of Study*. You should be able to provide this background in one or two sentences,



and then state the *Purpose* in its own sentence. It may also be necessary to follow up with an explanatory sentence or two after the *Purpose*. But remember, this should not be an in-depth discussion—you should include only enough supporting material to explain the study’s purpose.

e.g. Patent Foramen Ovale (PFO) is a condition in which an opening in the heart that acts to bypass blood flow while a fetus is in the womb fails to shut after the baby is born, remaining open for life. A high percentage of older adults who suffer strokes of unknown cause are found to have a PFO. The purpose of this study is to investigate whether repair of a PFO, made through the skin, is superior to the current standard treatment for a PFO-related stroke in preventing an additional stroke or temporary loss of blood to a localized area. The current standard of care for a PFO-related stroke is prescription of a blood thinner.

3. Study Design:

Will your study utilize a biomedical model?

COMIRB divides research into 2 broad categories: biomedical and behavioral. The items in this section apply only to biomedical studies. If you are conducting behavioral research simply check no and [move to the behavioral section](#).

Is your study potentially therapeutic?

Check yes if there is potential therapeutic benefit to one or more arms of this study. If no, then this is an observational study that may include invasive procedures but it is designed to further knowledge of the field only.

Drug study phase: N/A, I, II, III, IV, Pilot, Other

If you are conducting research with an investigational agent, check **one or more** phase category that best applies to describe the study:

- **Phase I:** Human Pharmacology - A phase I trial is the first stage of testing in human subjects. Normally, a small (20-80) group of volunteers will be selected. This phase includes trials designed to assess the **safety, tolerability, pharmacokinetics** (absorption, distribution, metabolism, and excretion—what the body does to a drug), and **pharmacodynamics** (biochemical and physiological effects on the body—what the drug does to the body). Phase I trials often utilize dose



escalation until the target dose is reached or undesirable side effects are observed.

- **Phase II: Therapeutic Exploratory** - Once initial safety has been confirmed in Phase I trials, Phase II trials are performed on larger groups (up to a few hundred) and are designed to assess **clinical efficacy** of the therapy. Phase II is also used to continue the safety assessments begun in Phase I but with larger groups of volunteers and patients. Phase II studies are sometimes divided into Phase IIA and Phase IIB. **Phase IIA** is specifically designed to assess dosing requirements. **Phase IIB** is specifically designed to assess efficacy. Some trials will combine Phase I and Phase II into a single trial, monitoring both efficacy and toxicity.
- **Phase III: Therapeutic Exploratory** - Phase III trials are normally performed after preliminary evidence of drug efficacy has been obtained in Phase II. A Phase III trial may include several hundred to several thousand research subjects. Phase III is intended to be a definitive assessment of the efficacy of a new treatment in comparison to the current ‘Gold Standard’ treatment. It is also used to assess the overall risk-benefit relationship of the drug and to extrapolate study data to the general population. The results of a Phase III trial may be compiled into a “regulatory submission” and submitted to the FDA or other regulating body. A Phase III trial is sometimes used for “label expansion,” to prove additional efficacy for uses beyond the original use for which the drug was designed, or to obtain additional safety data, or to support a marketing claim. When used for these purposes, the study is sometimes labeled “Phase IIIB.”
- **Phase IV: Therapeutic Use** - Phase IV trials involve the post-approval surveillance and ongoing technical support for a drug. Phase IV studies may be mandated by a regulatory authority or may be undertaken by the sponsoring company for competitive reasons—for example, the drug may not have been tested for interactions with other drugs, or on certain populations, such as pregnant women. Post-approval safety surveillance is designed to detect any rare or long-term adverse effects over a much larger patient population and timescale than was possible during the initial clinical trials.
- **Pilot Study:** A pilot study is a model of a full-sized research study but on a smaller scale. The pilot may involve most or all of the intended procedures for the full study but may run for a briefer time and/or utilize fewer subjects. Pilot studies typically focus on novel and untested aspects of the proposed full-sized project. They are used to identify treatment effect size and identify possible flaws in overall study design.
- **Other:** Any other standard terms used to describe the design phase of the study.



Will your study use randomization?

Randomization is the process of assigning research subjects to treatment groups by using a random method that is free from both selection bias and accidental bias. By using **randomization**, researchers hope to exclude irrelevant factors that might influence the outcome of their research.

An example of a simple randomization scheme would be one in which a computer is used to generate a random number between 0 and 1 for each subject of a study. In this example, all subjects whose numbers fall at .499 or below would be placed in Group 1, while those whose numbers fall at .500 or above would be placed in Group 2. Group 1 would then receive the study drug, while Group 2 would receive placebo.

If yes, define randomization ratio:

The **randomization ratio** is a simple proportion that compares the number of subjects who are randomly placed in one group of a study to the number who are randomly placed in another group of the study. The first number in the ratio normally applies to the main group of subjects—that is, to the group who is receiving the intervention being tested. The second number (and all numbers after that, for studies with more than 2 groups) applies to the secondary group, usually the control group.

For example, if a study uses a random method to place 50 subjects in the group who will receive the active intervention, and 25 subjects in the group who will receive placebo, the randomization ratio could be said to be 50:25, which is simplified to 2:1. In a study where 100 subjects receive intervention 'A', 100 intervention drug 'B', and 50 receive placebo, the randomization ratio would be said to be 2:2:1.

Comparative trial:

A comparative trial is one in which an intervention is compared to one or more other interventions, or to a placebo, or to a policy of no intervention at all.

Control:

Placebo is a substance that has no pharmacological effect but is administered as a control during experimental testing of a biologically active preparation.



Usual Care is the normal care that the subject would receive locally if they were not on the study.

Active Treatment is a defined comparative treatment which is often one of a number of potential standard of care treatments. One treatment is specified to limit variability which may confound statistical analysis of the data.

A **Crossover** study is one in which the members of one treatment group “cross over” into another treatment group and receive the treatment of that group. For example, say that Group A receives active intervention for 6 weeks, while Group B receives only placebo. In a crossover study, Group B might crossover into the active treatment group and receive active intervention for 6 weeks. Group A might crossover into the placebo group and receive only placebo for 6 weeks. Of course, a crossover need not occur in pairs; it can be used within one or more arms of a study.

Historical is the comparison of prospectively collected data to pre-existing data.

Environment of study:

Provide a description of the various locations that will be used in the study. You can check more than one box or if none of the options are applicable provide a concise description after checking the box - **Other:**

Does the composition of the drug involve human gene transfer or recombinant DNA?

Research involving recombinant genetic materials, infectious materials and/ or biological toxins must also be submitted to the Institutional Biosafety Committee (IBC) for their review and approval. A protocol can be submitted to IBC and COMIRB concurrently but a copy of the IBC approval must be submitted to COMIRB before the study can be approved by COMIRB. For further information on how to submit to IBC see:

<http://www.uchsc.edu/safety/BioSafety/InstBioSafCommittee.htm>

Does the protocol involve the use of **radioactive drugs or materials not under an IND (including procedures such as PET scans, VQ scans, etc. for research purposes)?**

If yes, then this protocol must be submitted to the Radioactive Drug Research Committee (RDRC) for their review and approval. The protocol can be submitted to



RDRC and COMIRB concurrently but a copy of the RDRC approval must be submitted to COMIRB before the study can be approved by COMIRB.

The term **radioactive drug** means any substance defined as a drug in section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any non-radioactive reagent kit or nuclide generator which is intended to be used in the preparation of any such substance but does not include drugs such as carbon-containing compounds or potassium-containing salts which contain trace quantities of naturally occurring radionuclides. The term “radioactive drug” includes a “radioactive biological product.”

RDRC approval is required for tracer studies etc using a compound not being developed as a radiopharmaceutical or routine nuclear medicine procedures being used for research purposes.

For more information re UCD RDRC contact Riad Safadi at 303 724 0234

Does the protocol involve the administration of therapeutic radiation doses using sealed sources that are for research purposes only?

The Committee for Ionizing Radiation (CIR) is required to review all research involving the administration of therapeutic radiation doses using sealed sources that the participant would not otherwise receive as part of his/her medical care.

For more information re UCD CIR contact Riad Safadi at 303 724 0234

Research v Standard of Care

A clear description of what is standard of care is very important.

This can be 2 simple lists of your procedures by name—one list for experimental procedures, one for standard of care.

In order for COMIRB to accurately assess the risks and benefits of your study, it is important that you clearly delineate which procedures are experimental and which ones are standard of care. It sometimes happens that a study involving many procedures is submitted with no such distinction. This can give the impression that *all* of the procedures are experimental and therefore make the study appear much riskier than it is. In reality, the procedures that seem the riskiest might be the standard of care and might have to be performed whether the subject received care from the study or elsewhere. These should not play a part in the risk-benefit analysis.



State which of the procedures are experimental and which ones are standard of care. You can do this in several ways: by header label, by list label, or by stating it outright—“this procedure is an experimental part of the study.”

It is also important to think about whether the procedure used at this time or in this manner will be billable to insurance.

Is there a standard of care for this population?

“**Standard of care**” refers to a nationally recognized standard of care. Standard of care can be based on published treatment guidelines, algorithms, position statements, consensus documents, etc. Provide references to this standard or journal articles that reference this standard.

If there is no agreed upon standard of care then describe what would be the **usual care** at this institution. The care a subject would receive if they were not enrolled in a study.

Will your study use a social and behavioral model:

COMIRB divides research into 2 broad categories: biomedical and behavioral. The items in this section apply only to behavioral studies. To jump back to biomedical studies, [go to biomedical model](#)

If yes, describe the design:

Epidemiologic: The branch of medicine dealing with the incidence and prevalence of disease in large populations and with detection of the source and cause of epidemics.

Observational: Any research question that requires an understanding of the processes, events, and relationships in the context of a social situation.

Ethnographic: The goal of this type of study is to tell the whole story of a defined group’s daily life and identify the meanings, patterns, and passions of a bounded cultural group.

Qualitative: Any type of research that produces findings not arrived at using statistical methods or other means of quantitative analysis.

Phenomenological: Seeks to understand the lived experience of individuals and their intentions within their life experience.



Grounded Theory: In this type of study, a researcher does not begin a project with a preconceived theory in mind, rather the researcher begins with an area of study and allows the theory to emerge from the data.

Other: If your study does not properly fall under any of the above categories, check the 'Other' box and describe the design type.

Environment of study:

Outpatient refers to any healthcare facility where the subjects go for health services but do not stay overnight.

Inpatient refers to any healthcare facility where the subjects receive health services and stay overnight.

Community refers to a district or locality that is not a health facility or educational facility where people live, work and/or socialize.

School District/Educational: Any facility or institution that is governed by a school board or is used for education purposes.

Other: If your study does not properly fall under any of the above categories, check the 'Other' box and describe the study environment.

H. Human Subjects

Age Range of subjects to be enrolled:

Check each defined range that will be part of the study. The precise range may not fit neatly into the options provided but check all that are applicable. For example: the protocol may state 0-45 years as the age range so all boxes except over 65 would need to be checked.

Also specify the intended age range of subjects to be included.

Inclusion of Vulnerable Populations (check all that apply):

a. The following populations cannot be enrolled into a study without prior IRB approval. If you **will, may or might** need to enroll any of these populations, complete the appropriate attachment. If you come across an eligible subject at a later date who fits any of these categories you must submit an amendment. The amendment must be submitted and approved by COMIRB prior to enrollment of the subject.

See separate attachment for definitions of each below:

Children

Neonates

Pregnant women / fetus/ placental or fetal tissue

Prisoners

Note: For pharmaceutical studies where women who may become pregnant are excluded then even if there is a description of possible clinical follow-up for safety (related to the pregnancy and fetus), this study would not be deemed to include pregnant women. If there is a consent form specifically for pregnant women then the study is deemed to include pregnant women even if the possibility is remote. This sub-study would need to be described in the protocol with an appropriate rationale and Attachment J would need to be completed.

Are any of the following populations being targeted for recruitment?

You might think that your study will not recruit vulnerable subjects, but this is not always as straightforward as it seems. Yet the likelihood of recruiting vulnerable subjects from your particular study population might be high enough that you will need to consider the possibility. You only need to check yes, to any of the potential vulnerable populations listed if you need to realistically include that population to meet the aims and endpoints of the study. This may be due to the population being targeted, the recruitment sites being used or the environment within which the study will take place.

If there is only a possibility that you will come across an eligible subject who meets the definition of a vulnerable population as defined by COMIRB, you can enroll that person but should refer to the appropriate policy on the COMIRB web-site to ensure that any risks are minimized for that population. At continuing review, you will be asked to identify any such persons, and should at that stage amend the application form to reflect inclusion of that population if it is likely to happen again.

For example, your study was set up to recruit seniors over the age of 65 who were living with early Alzheimer's, with exclusion criteria designed specifically to prevent recruitment of decisionally challenged patients. Even with the exclusion criteria, assuming your study was recruiting 100 subjects, there would still be a high likelihood that at least a few of your subjects will become decisionally challenged. You would therefore need to consider this possibility and check the box for "Decisionally Challenged" on the Application. Also, you would need to develop and discuss safeguards as detailed in

Attachment L

For populations listed in section H.2.3, please address the following questions specifically for the population targeted.

i. Please provide reasons for including each vulnerable population included:

Justify based on the specific aims and objectives of the study why each vulnerable population should be included. It is not sufficient to state that it is a convenient population to enroll or that you have access to this population due to your clinical role.

ii. For vulnerable populations listed above (when not including an attachment) list safeguards included to protect the rights and welfare of vulnerable subjects:

Poor/uninsured

Consider the amount and method of payment:

- The payment should not be of such a value that it would entice subjects to attempt to join or stay in inappropriate studies.
- The payment should take into account the likely population to be recruited.
- The payment should not entice potential subjects to fabricate or distort symptoms in order to gain entry.

Payment should not be provided when the research is integrated with a patient's medical care and when it makes no special demands on the patient beyond those of usual medical care.

All costs should be clearly detailed as research costs may severely impact this subject population.

What will be the plan for continuity of care post study?

Nursing home residents / institutionalized patients

- Nursing home residents may also include residents in assisted living environments and hospice either as inpatient or outpatient.
- In situations when the researcher works at the institution, it may be difficult to avoid potentially coercive behavior. The very nature of the relationship with the subject can create the appearance of coercion.
- Recruitment through flyers (screened and approved by the **COMIRB**), or recruitment through a third party unassociated in a power relationship with the resident are usually the best strategies.
- There should also be no exchange of payment in exchange for referrals of potential participants.



Note: Nursing home residents and / or institutional patients may also be decisionally challenged. This issue will need to be addressed in section b.

Students of PI or study staff

Though the researcher may be careful to avoid potentially coercive behavior, the very nature of the relationship with the subject can create the appearance of coercion. For this reason, researchers should be aware of the potential for coercion that exists when a research subject is also a student.

Whenever possible, researchers should avoid using their own students if another population of subjects is equally suited to the research question. Recruitment through bulletin board advertisements (screened and approved by the **COMIRB**), or enrollment through a third party unassociated in a power relationship with the student are usually the best strategies.

Even then, it should be made clear that participation is not in any way linked to their evaluation. Where possible other members of the research team should interact with the student.

Students to be recruited in their educational setting

Whenever possible, researchers should avoid using their own students if another population of subjects is equally suited to the research question, e.g., another class section not taught by the researcher, recruitment by another instructor, or blinded/coded data collected by an associate so that subjects are not identified to the instructor.

- Students should be given an opportunity to decline participation without jeopardy.
- Unless the research question is directly related to class material, or the study process is being used as a teaching opportunity, such as in a research methods class, the **COMIRB** discourages the use of class time to recruit subjects or class time used to complete study instruments, etc.
- Use of extra credit points as reward for research participation should be limited to specific circumstances where the research is closely tied to the course subject matter. The number of points awarded should not be sufficient to augment a student's grade by a whole step, e.g., from B to A. Alternatives to research participation must be comparable and described for the **COMIRB**.
- The use of financial rewards should also be limited to dollar amounts which are proportionate to the inconvenience of participation.
- Whenever possible, a teaching opportunity in the form of an "educational debriefing" should be employed. Students should know something about the **COMIRB** review process, the rationale for the study, the process of data collection, and intent of the researcher.



Employees directly under the supervision of PI or sub-investigator

Though the researcher may be careful to avoid potentially coercive behavior, the very nature of the relationship with the subject can create undue influence. For this reason, researchers should be aware of the potential for coercion that exists when a research subject is also a student, employee, colleague, or subordinate of the researcher.

Information about how subordinates and colleagues will be recruited and how coercion will be avoided should be included in the information submitted to the **COMIRB**. Researchers who include colleagues or subordinates as research subjects must be able to provide a rationale other than convenience for selecting them and must show that the recruitment method does not lead colleagues to think they will be impacted by not participating.

The compromised circumstances and fear of retribution, even subtle cues of compromise, can place colleagues or subordinates in a position of involuntary participation in a research project.

Recruitment through bulletin board advertisements (screened and approved by the **COMIRB**), or recruitment through a third party unassociated in a power relationship with the employee are usually the best strategies

People engaged in illegal activities and/or illegal immigrants

Protections of privacy and confidentiality for this population can be extremely important. Particular consideration should be given to the venue of the study and the type of documentation to be maintained.

A certificate of confidentiality may be appropriate.

Others vulnerable to coercion - consider if there are any potentially vulnerable populations based on the study you are seeking to conduct.

iii. If applicable, list steps taken to avoid causing potential subjects to be or feel coerced into participating in the research:

Here are some examples of possible steps depending on the population being considered:

- Ensure payment or other compensation is appropriate for the vulnerable population and or a reasonable amount.
Example: provide a gift card for a grocery store if there is concern cash could be misused. The amount should be reasonable for the requirements of the study (transportation, food, procedures/time required of participants, etc.)



- For physicians in a private nursing home or a physician with a specialty clinic where patients may be enrolled (and the patient already has a treatment relationship with the investigator), ask someone not associated with the study to obtain consent from a potential participant if possible.
For example, provide flyers/brochures in the investigators office (maybe where they check in) that allows subjects to initiate a discussion with a non-treating physician if they are interested in a study.
- For studies that provide equipment for the study (i.e., laptop, PDA, glucose monitor, exercise study equipment, etc.) be clear as to whether the subject will be able to keep the item at the end of the study.
- For someone without insurance, avoid emphasizing the procedures and/or supplies (ie. meter and strips for a diabetes study) they would be provided if they were to enter the study. Be clear up front as to what will occur once the study is completed

iv. If no additional safeguards are needed to protect vulnerable subjects in this study, provide justification here:

It may not be appropriate to exclude one or more of the vulnerable population described above on the grounds of equality / fairness. This is especially true if it is a potentially therapeutic study. Please be aware that if any of the above described populations are included, adaptations may need to be made for individual subjects as discussed above.

Enrollment Numbers:

1. Total Number of Subjects for All Sites:

Provide the number of subjects to be accrued on the study. Depending on the type of study this number may be the same as #2 but if it is a multi-center study it should reflect national accrual numbers.

2. Total Number of Local Subjects Approved by COMIRB

Include the number of subjects to be allocated to experimental and control groups. Consider how many subjects will be needed to sign a consent form in order to reach your study end points. Every person who signs a consent form is counted as a research subject. Please adjust the number to include projected screen failures and withdrawals. This number may reflect enrollment at more than one site if there is more than one affiliate site, or COMIRB has agreed to be the IRB of record for additional non-affiliated sites.

For research that does not involve a consent form, consider the number of records, specimens, or surveys that will be collected.



NOTE:

Studies including mothers and babies need to count each group separately. For example: 10 mothers and 10 babies = 20 subjects.

Four families with approximately 4-5 persons per household = 25 subjects

Duration of Entire Study:

This should be an estimate of how long the study intends to be open including data analysis.

It does **not** refer to the time of each subjects' participation in the study.

Gender and racial/ethnic distribution:

If one gender or one or more minorities will be excluded or underrepresented in this research, particularly in proposed population-based studies, please provide a clear, compelling rationale for the exclusion or under-representation by referencing the objective and specific aims of the study.

Over representation of one race must also be justified. Convenience is not sufficient justification. Example: parent project had all Caucasians enrolled so the sub-study will include only Caucasians.

Inclusion Criteria:

The primary criteria for inclusion of subjects must be included. This list must correlate with the justification and description outlined in the protocol. If locally, the PI intends to deviate from the main protocol, this must be clearly identified and explained.

Exclusion Criteria:

The primary criteria for exclusion of subjects must be included. This list must correlate with the justification and description outlined in the protocol. If locally, the PI intends to deviate from the main protocol, this must be clearly identified and explained.



I. Procedures

Duration of Study Participation for Subjects

Describe the duration of participation for each subject per study visit and the estimated time to accrue and evaluate subjects for the entire project at this site, including follow up. This duration should span the entire period of time for which data and / or specimens will be collected on a subject.

An attachment with a table of procedures is attached to this application?

List your procedures down the left side of your table, and list the days/weeks/visits of your study along the top of the table. In this way, your study will progress from left to right across the table.

NOTE: If you use the same table in the consent form, it should be modified to reflect LAY terminology and may not be appropriate to include technical details such as “concomitant medication”.

See the table below as an example:

TREATMENT CALENDAR

Procedures	Cycle 1			Cycle 2			Follow up
	Day 1	Day 15	Day 35	Day 1	Day 15	Day 35	6 months
History & Physical	X						
Physical Examination	X	X	X				X
QOL Questionnaire	X		X	X		X	X
Blood Draw			X			X	X
MRI	X						X
Urine Sample	X	X	X	X	X	X	
ECT		X			X		
Review of side effects	X	X	X	X	X	X	X
Study drug infusion			X			X	
Toxicity evaluation		X	X		X	X	X

If no, list all study procedures, drugs, surveys etc., you are using in this study:

It is usually best to list procedures in the order they will take place during the study. Inherent in your discussion of procedures should be some discussion of timeline.

Are any materials being given to subjects?

Check all the applicable boxes describing material that will be given to subjects and detail the number of different items or if possible distinguish the different documents by title. This is important information for tracking purposes. Provide a copy of each document with this submission unless it is a standard validated tool that is commonly used. Clearly identify questionnaires / tools that are standard.

Special Procedures

Indicate if any of these attachments are relevant to this study:

Attachment G: Use of the internet

This attachment should be completed if the internet is going to be used to recruit subjects or as a tool to obtain data, e.g. housing a survey for subjects to complete or to observe in chat rooms.

Attachment P: Stored data for future use / Recruitment

Do not complete if data is only being stored for this study as the confidentiality issues to be addressed are in the application form. The assumption is that once a study is closed then there will be no further analysis or sharing of **identifiable** data. If that will not be the case then this attachment should be completed.

This attachment is also for studies that want to pool data into a communal data repository or would like to establish a recruitment database.

Attachment Q: Genetic Research is to be completed if blood or other body fluid or tissue samples are examined for biochemical, chromosomal, or genetic markers that indicate the presence or absence of genetic disease.

This type of testing is also known as:

- DNA testing
- Gene testing



- Genetic screening method
- Molecular genetic testing

Attachment R: Tissue and blood storage for this study is to be completed if any blood or other samples are to be collected for this study. This applies for both investigator-initiated studies and multi-site studies.

Attachment S: Tissue/blood banking for future use is to be completed if blood or other body fluid or tissue samples are to be stored either locally or externally for studies other than this research study by this research team or other researchers.

Attachment S1: Tissue/blood banking for future use VA form is required if any samples are being collected from veterans and being stored locally or externally for studies other than this research study by this research team or other researchers.

J. Potential Risks to Subjects:

Do you view this study as minimal risk?

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45 CFR 46.102(h)(i)).

Justify this determination:

Your justification should be based on the interventions involved in the study and the minimization of risk.

If your study is minimal risk, it may be eligible for expedited review. The categories eligible for an [Expedited Review](#) are outlined in **Attachment C**. You will need to complete **Attachment C: Research requesting Expedited Review** if you are requesting expedited review for this study.

Using a format similar to that in your consent form, include the following:

1. **List risks by procedure.** List all of the known risks for each procedure in your study. This is most commonly done by dedicating a paragraph to each procedure.
2. **Within your list of risks for each procedure, separate the risks into “very common”, “common”, and “rare”.**



Include any significant known or potential risks of drugs, radiation exposure, and/or procedures. Avoid long lists of rare and relatively insignificant risks. Describe both the risks of the experimental group and the risks of the control group (if applicable).

Only include pre-clinical animal risk data for phase I studies.

- 3. Describe the plan to mitigate overall risk.** It may also be appropriate to discuss actions you will take to mitigate some specific risks. Describe any safety monitoring procedures, close monitoring, safety blood tests, person performing procedure, where procedure will be done etc.

Note: The risks of a breach of privacy or confidentiality are to be detailed later.

Is it possible that the research team may be made aware of certain incidents/diseases that are reportable to state authorities?

By law, you are required to report new cases of certain infectious diseases to the Colorado State Health Department. The main ones have been listed. Please indicate here on the application whether or not you will be **testing** for these. Do not check if you are obtaining this information as pre-existing data from a medical history or medical records.

If your study involves questions, questionnaires, interviews, observation, or other situations that could reveal child neglect, child abuse, or violence against another person—either threatened or carried out—you must answer “yes” to this question.

Risk/Benefit Analysis:

COMIRB is required to assess whether the potential benefit from conducting the study outweighs known risks.

Describe any benefit(s) to the subject or to others, which may be expected from the research. This section should explain the merit of the study.

Describe the anticipated benefit to the experimental group as well as the anticipated benefits to the control group.

- 1. For participant:** These should be direct benefits to the subject. It cannot include payment but can include education, use of a device, closer monitoring, specific tests but only if they will receive the results of those tests. [These benefits can be listed in the consent form.]



2. **For society:** This can include the potential for generalizable knowledge to be gained. It can also include potential new information that will be of value to a targeted population. [These benefits can **not** be listed in the consent form]

3. **Justify the importance of the knowledge gained:** This should be based on the background and objectives of the study.

NOTE: This is not necessarily the same information that should be added to the consent form.

K. Recruitment Method and Plan

Subjects may only be recruited from an affiliated institution if the project has received prior written approval **for conduct of the study at that institution**. If you wish to add another affiliated institution to your approval all the appropriate documentation must be sent to the contact person of the affiliated institution.

Provide a description of the recruitment methods to be used for each distinct population:

Describe:

How potential subjects will be identified: potential subjects cannot be specifically identified or contacted until IRB approval for the research has been obtained. It is possible to obtain general data relating to the availability of a specific population to ascertain the feasibility of the study.

The setting in which the recruitment will take place: Describe the location or method by which potential subjects will be identified. Below are the common ways to recruit subjects. Use this section to provide specific details of the plan.

Who will make initial contact: Describe, if appropriate, how initial contact will be made. The options outlined in the application form are the most common ways to recruit subjects:

Clinical Relationship is defined at UCD and affiliates as professional contact with a definable patient population. This does not need to be a personal relationship with each subject but can refer to a clinic, family practice, center or service where the PI or one of the research team worked regularly or covered. For example covering cardiology service at UCH does not enable an investigator to contact patients who had orthopedic problems at UCH. As this relationship could have been established at any time up to five years



previously, it is important to ensure that the current site is aware and supports this recruitment.

For investigators at the VA, a HIPAA waiver of authorization will need to be requested even if recruiting from their own clinical population. For VA studies, only veterans can be recruited unless the investigator can justify why there are likely to be insufficient veterans available to complete the study.

Existing research relationship is developed by screening or enrolling subjects into previous studies. These people have voluntarily provided you with their contact information. According to UCD and affiliates policy, it is legitimate to continue to have contact with this population. It is not necessary to have established a research database or use a HIPAA authorization to formalize this relationship. However, the contact information is only available to the original investigators listed in the original study and cannot be shared internally with other colleagues unless they were part of the original research team.

HIPAA A Authorization is used when the research team does not have an existing or previous clinical or research relationship. The form has to be given to potential subjects by a health professional who does have such a relationship. The HIPAA A form lists the information that the health professional is requesting to give to the research team. Only if the potential subject signs and dates the HIPAA A authorization form, does the research team have authority to directly contact that potential subject.

Potential subjects can be identified using a **recruitment database** but access to the contact information is limited by the terms of the protocol that established the recruitment database. It is important to follow the stipulations and restrictions of the original protocol to protect the confidentiality and privacy of the subjects whose data has been collected. If the subject indicates to you that she/he does not wish to be contacted now or in the future, this request must be respected and the information fed back to the managers of the recruitment database so that it can be appropriately addressed.

All **Advertisements** to recruit subjects require prior approval by COMIRB and can only be used in the manner outlined in the recruitment section of the application form. There are specific guidelines that must be followed regarding the content of advertisements described below.

Forms of recruitment to be used

In-person or face-to-face - consider how potential subjects will be identified and who will approach them. For research involving patients, a person with a treatment relationship should initiate contact unless a signed HIPAA A form has been obtained.



Written correspondence (letters/postcards, etc) - for protection of the privacy and in respect of the confidentiality of subjects, it is best practice to seal all correspondence with potential subjects in an envelope. For studies conducted at Denver VAMC or with veterans, this is a requirement. All letters and postcards to be sent to subjects must be pre-approved by COMIRB.

For research involving patients, recruitment letters should originate from a person who has already established an existing relationship with the patient. Subjects who are sent recruitment letters should be sent letters inviting them to **Opt-in** not **Opt-out** of the study. Failure to respond to a recruitment letter should not imply consent to contact that person or access their medical records.

To try to avoid complaints and respect the privacy of subjects, COMIRB recommends that no more than 3 attempts are made to contact potential subjects by mail.

Electronic correspondence (emails) - it is important to be careful about the type of information being sent or requested by e-mail. Appropriate protections must be in place. The proposed content of all emails must be submitted to COMIRB for approval before any such contact is initiated. In your recruitment plan, you should explain how you gained access to the e-mail accounts for recruitment purposes.

To try to avoid complaints and to respect the privacy of subjects, COMIRB recommends that no more than 3 emails are sent to contact potential subjects by email.

Prior to **contact by telephone**, all telephone scripts must be approved by COMIRB. For research involving patients, recruitment telephone calls should originate from a person with an existing relationship with the patient (clinical, research, or through a HIPAA A form). To try to avoid complaints and to respect the privacy of subjects, COMIRB recommends that no more than 3 attempts are made to contact potential subjects by phone. Detail how many attempts will be made and how many messages will be left.

Advertisements can be used in a number of different ways but the same requirements apply for each type of advertisement. Additional institutional approvals may also be required.

- Flyers in Participating Institution
- Flyers in Community
- Radio
- Television
- Newspaper
- Internet
- Clinics



All recruitment materials are required to contain the following:

1. The protocol must be specifically approved for conduct or recruitment at an affiliate institution
2. List P.I. and COMIRB #
3. The materials must be approved for posting per individual institutional policy for posting notices and advertisements
4. Name and phone number of person to contact for further information
5. Purpose of the research
6. Primary eligibility criteria for subjects
7. Brief description of benefits (e.g. payment, medication, visits, etc. provided at no cost)
8. Compensation provided (do not put dollar amount)

The COMIRB reviews the submitted material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence to the subject to participate which includes but is not limited to:

1. Statements implying a certainty of favorable outcome or other benefits
2. Claims, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation
3. Claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic or device
4. Using terms like “new treatment,” “new medication,” or “new drug” without explaining that the test article was investigational
5. Promising “free medical treatment” when the intent was only to say participants will not be charged for taking part in the study
6. Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media
7. Does not include exculpatory language.
8. Offers by the sponsor to include a coupon good for a discount on the purchase price for the product once it has been approved for marketing

Any advertisement to recruit subjects should be limited to the information the prospective subject needs to determine their eligibility and interest.

Incentives/Remuneration

Will participants be paid for their time, reimbursed for travel or meal expenses or receive any sort of “gift” for participating in this study?

The use of finder’s fees or similar recruitment mechanisms is strictly forbidden. Finder’s fees are defined as when clinicians or other individuals not



involved in the research study are directly compensated with cash or gifts for locating and/or recruiting individual subjects directly into a study.

Incentives provided by the Sponsor to the PI/Study Staff are not considered “finder’s fees” and do not need to be reported to COMIRB but are subject to UCD or Affiliate policy. A plan should be developed by the department to limit any potential or perceived coercion.

Subjects may be compensated for their time and inconvenience of participating in a study if the investigator or the sponsor wish to do so. If subjects are to be paid several guidelines must be followed:

The payment may not be coercive.

- The payment should **not** be of such a value that it would entice subjects to attempt to join or stay in inappropriate studies.
- The payment should take into account the likely population to be recruited.
- The payment should not entice potential subjects to fabricate or distort symptoms in order to gain entry or maintain eligibility.

Payment must be prorated.

- Payment may not be based solely on the completion of a project. This may entice subjects with significant adverse events or a real desire to quit to stay in a study against their true wishes.
- The exception to this may be research that involves a single encounter.
- Provisions should be made for subjects that have an adverse event during the study that would otherwise have completed or where an adverse event is truly a study endpoint.

For Minors:

- A system should be developed so that the subject, not the parent, will be able to receive the benefit of the payment such as savings bonds, or gift certificates.

NOTE: All payments to subjects are taxable income. COMIRB policy is to add a standard language to the consent form stating this for all studies to be reviewed at full board. This statement is not required for expedited studies.

The PI and research team must follow UCD policy or that of the appropriate affiliate for reporting this payment to the institution.

Are any other materials being given to subjects?

If the answer is “yes”, attach a picture of all material to be given to participants or the object itself.



If a picture is to be submitted, please ensure that any logos or statements on the object can be clearly read.

- The object should not be of such a value that it would entice subjects to attempt to join or stay in inappropriate studies.
- The object should take into account the likely population to be recruited.
- The object should not misrepresent the potential benefits of the study.

L. Informed Consent

Consent Process

It is important to remember that the consent document is only a part of the entire consent process. In addition to providing the written document to the potential subject, it is the investigator's responsibility to assure that the subject receives adequate verbal explanation, and answers all questions as truthfully as possible. It is also the investigator's responsibility to be assured that the subject is able to adequately understand the nature of the research project, any associated risks and can give genuinely informed consent.

The consent document must meet requirements of federal regulations (21 CFR 50.20 and 45 CFR 46.116) which states that "except as provided in 21 CFR 50.23 or elsewhere in the policy (45 CFR 46.116), no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence."

Will completion of the survey indicate consent?

There needs to be a clear statement on the document that indicates that this survey is for research purposes and that by completing the survey and returning it, the individual is agreeing to participate in the study.

Will subjects be screened over the phone?

If yes, provide a copy of the script or screening questions with this submission.



Will subjects provide information about other identifiable individuals, such as relatives or friends?

The federal regulations governing human research subject protections define a “**human subject**” as “a living individual about whom an investigator conducting research obtains:

- (1) Data through intervention or interaction with the individual, or
- (2) Identifiable private information. In accordance with this definition, the collection (e.g., in conjunction with obtaining a medical or pedigree history) of identifiable private information about other individuals associated with the research subject may require that the written informed consent of that person be obtained prior to collecting this information.

The federal regulations define “**private information**” as including “information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, medical record information)”. Private information must be individually “**identifiable**” (i.e., “the identity of the subject is or may readily be ascertained by the investigator or associated with the information”) in order for obtaining the information to constitute research involving human subjects. Written informed consent of the family members is not required if:

- 1) The recorded information about family members is not of a private nature (e.g., readily observable traits such as baldness or obesity)
- 2) The recorded private information is not linked to the specific identity of the family member or to identifiers (e.g., social security number, hospital record number) wherein the identity of the family member could be readily ascertained.

However, family members may be possibly identified through their link to an identified research subject (i.e., one could ascertain who the mother of a research subject is, if identifiable information about the research subject is known). As COMIRB generally views first degree relatives as “**identified**” through their link with a known proband, see the guidelines below to determine if a waiver of consent is needed.

These guidelines are for investigators to determine whether collecting information about a family member would create a “**human subject**” who would need to provide informed consent, and also to provide guidelines for the consideration of a waiver process.

Guidelines:



Obtaining information about the family history of an individual will result in the family members being considered “human research subjects” if:

1. The family members are alive.
2. They are first degree relatives of the individual, and the link between the person and the individual is clear (i.e., mother, father, etc.) or identifiers (such as name, birthdate, etc.) are collected.
3. The information collected would be considered private.

If these three criteria are met, the family member would be considered a human subject and consent from such individuals must be obtained unless the investigators petition COMIRB for a waiver of consent. In order to obtain IRB approval of a waiver of the requirement to obtain informed consent of the family members for this research activity, the principal investigator must submit a request for such a waiver to the IRB. In this waiver request the principal investigator must address and justify each of the regulatory criteria (45 CFR 46.116 (d)) for granting such a waiver. [**Attachment M - Waiver of Consent and Attachment O - Waiver of Authorization** will need to be completed.]

Exceptions:

- a. An exception to this policy exists where other requirements associated with the conduct of the research study result in the disclosure, to the investigators, of the specific identity of the related family member about whom the private information was obtained, e.g., questioning a child about private information concerning his/her parents wherein the required parental signatures on the child consent form would disclose the parents’ identities.
- b. If family members of the research subject (i.e., the proband) will be contacted to obtain consent for the collection of their identifiable private information (i.e., the private information is recorded to include linkage with the family member’s name, social security number, or hospital record number) or for their participation in other research activities, the research study should be first introduced to the family members by the research subject (i.e., the proband). With notification of the family member’s written permission obtained either from the proband or directly from the family member (in the form of HIPAA authorization A or by returning a signed postcard to the researcher), the family member may be subsequently contacted by the study investigators.



Consent Waiver

Is a waiver of consent or consent documentation being requested?

In accordance with 45 CFR 46.116(d), COMIRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or may waive entirely the requirement to obtain informed consent, if **ALL** of the following apply:

1. The research involves no more than minimal risk to subjects; and
2. The waiver or alteration of the consent process will not adversely affect the rights and welfare of the subjects; and
3. The research could not practicably be performed without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

A request for a waiver to document (i.e., to obtain a signed consent form) is different from waiver of consent because the consent process still occurs, albeit verbally (e.g. in a telephone survey).

If you are requesting a waiver of consent or consent documentation, be sure to complete **Attachment M**.

Are you using any level of deception?

Researchers using deception should disclose all study risks that exceed the minimal risk threshold. Deception should only be employed when there are no feasible alternatives and are essential to accomplish the goals of the research.

You should include a plan to debrief in a sensitive and timely manner.

Definitions of Deception:

Major: mislead subjects about their health status, the researchers, or research purpose

Minor: incomplete disclosure of some purpose of the study to avoid biasing the results

Use of deception requires that the researcher complete Attachment N and also get approval of a waiver of informed consent, due to the initial consent being incomplete.



[Complete Attachment M - Waiver of Consent].

Consent Documentation

Will a copy of the consent form be provided to the subject?

Subjects should be given an approved copy of the consent to review and ask questions. A consent form is only valid for enrollment if consent is obtained between the approval date and expiration date detailed on the front page of the consent form document.

The consent form should be signed and dated by the subject providing consent or the appropriate authority who has been approved to sign on his/her behalf. Each page of the consent form should also be initialed by the subject. The consent should also be signed and dated by the person who obtained the consent. A witness to the participant's signature or the participant's legally authorized representative's signature will sign and date the consent document. **If the sponsor or IRB requires a witness to the consenting process in addition to the witness to the participant's signature and if the same person needs to serve both capacities, a note to that effect is placed under the witness's signature line.** It is also good practice for the PI to sign the consent form to indicate that they are aware that the subject is enrolled but this is not a requirement of the IRB. [It may be a requirement of the sponsor].

A signed copy of the consent form should be given to the subject for their records. A copy should be kept in the Case Report Form or study records and, if applicable, a copy should also be put in the medical records for the study.

COMIRB policy is not to re-consent subjects with each new version of the consent. The panel reviewing the study and/or any changes made to the consent document will determine if the changes are substantive enough to require re-consenting. This stipulation will be detailed in the minutes.

Will a signed and dated copy of the HIPAA B form be provided to the subject?

Consent Process

A signed and dated copy of the HIPAA B form should be given to the subject. The original should be kept in the Case Report Form or with the study records and if applicable a copy should also be put in the medical records for the study.



Note: There may be occasions, such as change of PI or new sponsor, when it may be necessary to re-authorize subjects otherwise identifiable health information cannot be used by entities that are not listed on the HIPAA B form.

If a signed and dated HIPAA B form is not going to be obtained then a Waiver of Authorization must be requested by completing **Attachment O**.

Will consent be obtained prior to any research procedures being done?

While it may be possible to do some general screening by phone prior to a subject signing a consent form, it is not possible to conduct any research procedures prior to consent being obtained.

Will the PI or member of study team be solely responsible for obtaining consent?

The PI is responsible for ensuring that appropriate informed consent is obtained on all subjects, even if he or she does not actually obtain the signature on the consent form. Obtaining and verifying consent is an on-going process. COMIRB requires all members of the research team listed on the application form to undergo mandatory education. This is not, however, intended to replace the practical training and oversight provided by the PI to ensure that all involved parties understand and facilitate the informed consent process.

Will all persons obtaining consent be appropriately trained?

It is the PI's responsibility to ensure that all persons who obtain consent are appropriately trained. COMIRB requires all members of the research team listed on the application form to undergo mandatory education. The PI is responsible for ensuring that all other research personnel who have contact with subjects are appropriately trained to obtain and document informed consent.

Will consent be obtained in a quiet and private setting?

COMIRB requires that whenever practicable, a discussion of the study based on the informed consent document is conducted in a quiet and private setting with minimal distractions and pressures. Depending on the type of study being conducted, COMIRB recognizes that this is not always possible e.g. if subjects are being recruited in the emergency room or in the street.

If consent is not going to be obtained in a quiet and private setting, then a description is needed of the setting to be used, a justification provided as to why this is necessary as well as a plan to minimize the risk to privacy and to minimize distractions.



NOTE: Attachment L will also need to be completed if the study is seeking to obtain consent in a stressful environment e.g. the emergency room.

Will potential participants be given time to...?

It is important to give potential participants the opportunity to read the consent document, have their questions answered and have time to consider whether or not to be involved in the study. By doing so, participants have time to better understand the commitment and risks of the study. Participation in research is voluntary, and so it is important for potential participants to have time to ask questions and have any concerns addressed.

Will a signed and dated copy of the consent form be given to the subject?

It is important that the subject is given a signed and dated copy of the consent form to take home. By doing so, the subject has a document to reference as the study progresses and the consent form has important contact information in case of questions or injury.

If the plan is not to have the subject sign and retain a copy of the consent then this requires COMIRB to approve a waiver of documentation of consent as outlined in **Attachment M**.

Will comprehension and autonomy be assessed by asking questions and assessing their response?

The most common way to assess the ability of potential subjects to consent for themselves is to ask questions and use their response to assess whether or not they may be decisionally challenged. Depending on the population being assessed, there may also be objective, standardized tools to facilitate this assessment. Such tools include the mini-mental exam.

OTHER CONSENT CONSIDERATIONS

Are non-English speaking subjects likely to be consented?

If a research study is targeting subjects who do not speak English, the investigator should have COMIRB approve the English version of the consent form and the consent process first. After the English version is approved, a translated consent form should be obtained by the investigator and submitted to COMIRB. The credentials of the translator must be provided to COMIRB. The credentials for interpreters/translators will need to be submitted only once. These credentials will be kept on file like investigators' CVs. The translator must have expertise (native language or evidence of fluency) in the language including medical and legal terminology, in order to translate consent forms.

