**604 – Guidelines for Developing a Clinical Research Protocol**

The following are guidelines for writing a clinical research protocol for submission to the University of Hawai’i (UH) Biomedical Institutional Review Board (IRB).

The purpose of the IRB is to protect the rights and welfare of people who volunteer to participate in research. The IRB conducts a comprehensive review of proposed research and, once approved, oversees the study until it is complete. To ensure an effective IRB review, a complete description of the planned research must be submitted, along with the Human Studies Program application, for initial review of a study. For some clinical research projects, the sponsor will provide a written protocol. If the sponsor does not provide a protocol, the Principal Investigator (P.I.) must write one.

To facilitate timely IRB review, investigators should pay close attention to the organization and clarity of the information presented in the protocol. The information in the protocol must be consistent with the information provided in the consent form and other study documents. Please format your protocol using a 12‐point font and one‐inch margins, and limit the document to 12 pages in length. Do not submit your dissertation proposal or grant application in lieu of a completed IRB application.

The protocol should include all of the elements numbered below. A discussion of each element follows. The discussions do not address all issues that may be required to adequately describe a clinical study to the IRB. P.I.s should use their own judgment about what information to include.

1. Protocol Title, Version Number and Date
2. Investigator, Sponsor and Product Information
3. Performance Sites
4. Aims and Objectives
5. Background, Significance and Literature Review
6. Research Design, Methods and Procedures
7. Statistical Methods and Analysis
8. Human Subjects Protection
9. References
10. Appendices

## 1. Protocol Title, Version Number and Date

Provide the formal title that you will use throughout the study. The date should correspond with the version number.

## 2. Investigator, Sponsor and Product Information

Provide:

* P.I. name and complete mailing address, email address and phone number;
* Names and affiliations of sub‐investigators and/or co‐investigators;
* Sponsor name and complete mailing address and phone number; and
* As applicable, study product (e.g., drug, device) name, sponsor protocol number, and IND/IDE number.

## 3. Performance Sites

Provide the name and address of the locations(s) where the study will be performed, including the locations of clinical labs and other ancillary facilities involved in carrying out the research.

**4. Aims and Objectives**

Briefly describe the broad objectives and specific aims of this study, including the hypotheses.

## 5. Background, Significance and Literature Review

Review the condition or disease under study (referencing epidemiologic data, etiology and symptoms), as applicable, and discuss available treatments. To ensure there is adequate preliminary data to justify your research, place your hypothesis in the context of previous research. A complete literature review is not necessary. Rather, summarize the findings of prior research to justify your proposed study.

Critically evaluate existing knowledge, and identify gaps that your study is intended to fill. Discuss the potential significance of your study (e.g., how the knowledge you develop may impact future clinical practice, the cost of delivering health care, etc.).

As applicable, discuss the status of the drug(s) or device(s) to be used in the study. If they are FDA‐approved, is their use in the study consistent with product labeling? If not, provide a justification for their use in this study. If a FDA Investigational New Drug (IND) is to be used in the study, summarize prior data from animal and human studies, focusing on safety and efficacy of the drug. If a current Investigator’s Brochure (IB) is available, summarize relevant information in this section of your protocol, and provide a copy of the IB with your IRB application. If an investigational device will be used, state this and identify whether it is a significant risk or non‐significant risk device.

Discuss prior work that you and other investigators on this study have done in this area, including pilot studies. Provide any other information that may help to establish the experience and competence of you and your study team to pursue the proposed project. Provide complete references to relevant publications as well as information on manuscripts submitted or accepted for publication.

## 6. Research Design, Methods and Procedures (limit 3 pages)

Your research design, methods and procedures must specifically support your study objectives and aims and be adequate to answer your research question(s). If the study is not designed to produce valid results, no risks to research participants can be justified.

Design: Describe the kind of study you are proposing (e.g., pilot study, observational study, experimental study, quasi‐experimental study, placebo controlled study, double‐blind study, phase I, II, III, etc.). Describe all arms of the study (experimental and control). Identify primary and secondary endpoints. It may be helpful to provide a schematic diagram of the study design, procedures and phases. Justify why you chose this design to test your hypothesis.

Describe measures you will take to minimize bias (e.g., randomization, blinding). If randomization will be used, describe your randomization procedure. If there will be a control group with no randomization, describe how you will determine who is enrolled into the experimental and control arms of the study. If you will use matched controls, describe matching criteria (gender, age range, etc.). Describe the study blind (e.g., single‐blind, double‐blind). If blinding will not be part of your study design, why not?

Describe your target population and your criteria for selecting and withdrawing study participants. How many participants do you plan to enroll in your study? What are your inclusion and exclusion criteria? Define stop points and criteria for early withdrawal of participants from the study. Discuss when and how participants will be withdrawn as well as your plans for data collection and follow‐up for withdrawn participants.

Estimate the beginning and end of the study in terms of dates or length of time. Also estimate the time it will take to complete each portion of the study, including follow‐up, as applicable.

Methods and Procedures: Describe all study methods and procedures, including interventions, tests, visits, and the sequence of all study activities. If drugs will be administered, describe the dose, frequency, route, and duration. If blood will be drawn, describe the frequency, amount of each draw and the total amount for the study. If a questionnaire will be administered, address its purpose and relevance to study aims, and submit a copy to the IRB for approval.

Describe how the research procedures differ from standard care. Describe any new or experimental methods that you will be using and their advantage over accepted methods.

Discuss potential problems and limitations associated with the proposed procedures, including any hazards to personnel and precautions to be exercised. If procedures are being performed for which the investigators are not specifically credentialed, address the qualifications of those who will be performing them.

Describe data collection procedures, including methods to be used to record data. What data collection instruments will be used?

## 7. Statistical Methods and Analysis (limit 1 page)

Describe the statistical methods you will use for each of your study objectives. Describe and justify the method used to determine your sample size. State the power and the level of significance for the primary objective. Provide information on the required sample size for the secondary objectives. If the sample size is determined by the primary objective alone, what is the power, given this sample size, for the secondary objectives?

What criteria will be used to stop the study, if necessary?

Describe your plans for data and statistical analyses, including the timing of interim and subgroup analyses, as appropriate. Describe which participants will be included in the data analysis for each of your study objectives (e.g., all participants, all participants dosed, all evaluable participants, etc.).

## 8. Human Subjects (Participants) Protection (limit 4 pages)

The Study Population: Describe the composition of the proposed study population (in terms of race, ethnicity, gender, age, socio‐economic factors, diagnoses, substance use, etc.) and your rationale for participant selection. Will any vulnerable populations be included in your study? Vulnerable populations include not only children, pregnant women and prisoners but also people with cognitive, developmental and emotional disabilities, grave illnesses, or other conditions that may render them vulnerable to coercion or undue influence. If it is possible that members of vulnerable populations will participate in the study, describe additional safeguards you have put in place to protect their rights and welfare. If members of vulnerable populations will be specifically included or excluded from participation in the study, justify your decision to include or exclude them.

Recruitment: How will you identify, recruit and contact potential study participants? Describe in detail your recruitment plan. How will your recruitment plan assure the equitable selection of participants and that no group will be arbitrarily under ‐ or over‐enrolled due to convenience factors? Provide copies of all recruitment instruments (flyers, post cards, advertisements, etc.) for approval by the IRB prior to their use. State who (by affiliation and role) will be involved in recruiting study participants?

Procedures: From a research participant perspective, describe all procedures / interventions that may involve them. If participants will be randomized into one of multiple study arms, procedures in all arms should be described. Identify alternative procedures available to participants. Explain the expected duration of participants’ total involvement in the study. If specific findings may affect study participants’ health or welfare, how do you intend to communicate these results to them?

Data Sources and Confidentiality: Describe the research materials to be used or obtained (e.g., specimens, records, data). Will the identities of individual participants be recorded in your research records? Describe who will have access to the data and your procedures for ensuring the confidentiality of research information during and after the research project (e.g., encryption). If codes will be used that can link private information to individual participants, how will they be protected? Under what conditions will research information be placed in participants’ medical records? What will be done with the research data after the study is over?

Risks and Benefits: Describe, in detail, all known and potential risks and discomforts (physical, psychological, social, legal, etc.) to study participants. Bullet points may be helpful. Describe what steps will be taken to minimize risk, including risk to privacy and confidentiality. Discuss plans for ensuring that medical or other professional services will be available, as necessary, to address adverse events experienced by participants.

Describe potential benefits to participants and/or society. Address why the risks to participants are reasonable in relation to potential benefits.

Informed Consent: Describe your plan for obtaining and documenting informed consent. Who will obtain informed consent from participants? Will a consent form be used and, if so, will all federally required elements be included? Will potential participants have the opportunity to ask questions and receive answers prior to signing the consent form? Where will this informed consent conversation take place? If children are involved, will your study have an assent form?

How will you determine the autonomy of participants and whether they are capable of freely giving informed consent? What steps have you taken to minimize the possibility of coercion or undue influence? Are you asking the IRB to approve a waiver of informed consent or alteration of required consent form elements? Attach to your CHS application drafts of all consent and assent forms to be used in your study.

How will you ensure that informed consent is continued throughout the study? What are your plans for providing participants with any new information that may affect their willingness to continue participation in the study?

Monitoring: Describe your plan for monitoring the safety of participants and the quality of the data collected. Who is responsible for data and safety monitoring, what information will be monitored, and what is the frequency of review? Will your study have a data and safety monitoring board (DSMB)?

Compensation and Cost: Will participants be compensated for their time and expenses? If so, what will be the level and timing of the compensation? What compensation will be available to participants if they are injured as a result of their participation in the study? Will there be uncompensated costs for such participation? If so, what are they expected to be, and how do you justify asking participants to bear this expense?

Biological Specimens: Does the study involve the collection or analysis of biological specimens? Which specimens and how are they being collected? If they are existing at the time this research is being proposed, did participants provide consent for use in future studies under a prior research project? If so, please provide a copy of that consent form to the IRB.

Will you be asking participants in this study for consent to use their specimens for future research? If a specific research use is planned, this use must be described, and prospective participants should be given the opportunity to state whether they will permit their specimen(s) to be stored for this purpose.

If specimen storage is requested for unspecified research uses, include the following IRB-approved language in the consent form, just prior to the signature section of the consent form:

**"Consent for future research uses of your biological specimens**

The following questions ask whether biological specimens [specify… urine, blood, tissue, etc.] collected from you during this research project may be stored and used to support future research.

* My specimens may only be stored and used for future research that relates to the clinical area [describe clinical area] being investigated under this study.

Initial one: Yes \_\_\_\_\_\_\_\_ No \_\_\_\_\_\_\_\_

* My specimens may be stored and used to support any future research.

Initial one: Yes \_\_\_\_\_\_\_\_ No \_\_\_\_\_\_\_\_

* I will consider providing consent to use my specimens to support future research. Prior to any future research use, please provide me with a consent form that describes the protocol.

Initial one: Yes \_\_\_\_\_\_\_\_ No \_\_\_\_\_\_\_\_

* My specimens may be stored and used for the development of commercial products without any financial compensation to me.

Initial one: Yes \_\_\_\_\_\_\_\_ No \_\_\_\_\_\_\_\_ "

HIPAA Privacy Rule: If the research will be performed in collaboration with a hospital or other “covered entity,” is privacy authorization language included in the consent form? Will the study use protected health information (PHI) to identify, contact and/or screen potential participants? Is a privacy authorization waiver, partial waiver or alteration being requested?

## 9. References

Provide complete references for all points that can be attributed to a specific source. They should be sequentially numbered throughout the protocol.

## 10. Appendices

List all documents (e.g., questionnaires, consent forms, recruitment materials, screening tools, participant instructions and diaries, investigator’s brochure, diagrams, etc.) that are being provided with the protocol for IRB review.

If you have questions, contact the UH Human Studies Program at 808.956.5007