IRB review and informed consent documents to be used in research conducted in other countries.

OVERALL CONSIDERATIONS:

As a federal agency, all research conducted or supported by the Intramural Research Program must satisfy the requirements of 45 CFR 46 (a.k.a. the HHS Common Rule) and, if applicable, FDA regulations. Furthermore, when NIH investigators are conducting research in other countries, the research is also subject to local law. The NIH IRB will review only for compliance with US law and applicable NIH policy. It will not review for compliance with international laws or policies.

The NIH IRB will review research conducted in other countries only if NIH investigators are engaged in the conduct of the research. NIH investigators are engaged if, for the purposes of the research project, they obtain 1) data about the subjects of the research through intervention or interaction with them; 2) identifiable private information about the subjects of the research or identifiable biospecimens or 3) the informed consent of human subjects for the research. The NIH IRB will not review research in which no NIH investigators are engaged.

For example, if the only activity of NIH investigators is the analysis of coded but unlinked data and specimens in an interventional clinical trial conducted solely in another country, and all interventions or interactions with subjects, such as consenting or administering the investigational drug are conducted by the local investigators, then the NIH is not engaged in the research and the NIH IRB will not review.

When NIH investigators are engaged, the NIH IRB will review the protocol in its entirety to ensure that the protocol meets US regulatory requirements. However, when the research is being conducted collaboratively with local investigators, in the absence of a formal written agreement extending its authority (ie, a reliance agreement), the NIH IRB has no oversight authority over the local investigators, nor their conduct of the research at the international site. The NIH does not intend to seek reliance agreements with institutions located in other countries.

Therefore, the NIH IRB expects that there will be an in-country IRB/EC that will review and approve all research occurring in that country and that that IRB/EC will be responsible for the oversight of any local investigators. Additionally, that IRB must also apply the HHS Common Rule, hold an active Federalwide Assurance (FWA) and be registered with the Office of Human Research Protections (OHRP). The in-country IRB/EC is the body that should be most knowledgeable about local law and custom and can ensure that the protocol is consistent with local requirements. However, it is ultimately the responsibility of the PI leading the research to ensure compliance with all the host nations laws and policies

When the NIH employs contractors to conduct research in another country, the contractor’s activities do not fall under the NIH FWA. Therefore, the NIH Principal

Investigator (PI) is responsible for ensuring that there is proper IRB oversight for the contractor activities. Consult with OHSRP to determine how IRB oversight will be handled.

CONSIDERATIONS FOR INFORMED CONSENT DOCUMENTS TO BE USED IN OTHER COUNTRIES

In developing informed consent documents to be used in other countries, please note that those written on NIH templates or other formats are not appropriate for use in another country. The NIH consent templates are only to be used for research conducted at NIH sites. Similarly, the coordinating center model consent template is appropriate for US-based multi-site research in which the NIH IRB is the Reviewing IRB. Ideally, the consent used in research conducted in other countries should be provided by the sites that are enrolling the subjects. The NIH IRB will review the consent to ensure it meets US regulatory requirements, but beyond what is specified below, it is inappropriate to use template language that was designed for use in the US.

POINTS TO CONSIDER

- Informed consent documents should be written appropriate to the population enrolling in the study. In writing these documents, investigators should carefully consider the overall literacy of the population (including health and medical literacy) and write the document accordingly.
- The informed consent document should **not** be on an NIH consent template. The investigator should use whatever template or format is used by the institution of the local collaborating investigators.
- There is no requirement to include the NIH boilerplate required language, except for the research Privacy Act statement, if identifiable data are being stored in a Privacy Act system of records.
    - If no local consent template is available, the NIH investigator may consider using the shell provided at the end of this document.
- The consent process should be appropriate to the local culture. For example, using a community consent process, or seeking permission from local leaders or heads of households prior to also approaching individual subjects. This process should be described in the protocol.
- The informed consent must comply with the requirements delineated in 45 CFR 46.116 of the 2018 Common Rule and 21 CFR 50 Subpart B, as applicable.
    - When NIH IRB reviews the consent documents, it will only review to determine if the document meets the US regulatory requirements.

REQUIRED ELEMENTS OF INFORMED CONSENT

- Informed consent must begin with the “key information” section. This section is a concise and focused presentation of the information that is most likely to assist a prospective subject, or legally authorized representative (LAR), in understanding the reasons why one might or might not want to participate in the research.

- The informed consent must contain all the required elements of consent specified in 45 CFR 46.116 and, if applicable, 21 CFR 50.25. These elements are listed below:
    - A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;
    - A description of any reasonably foreseeable risks or discomforts to the subject;
    - A description of any benefits to the subject or to others that may reasonably be expected from the research;
    - A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
    - A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
    - For research involving more than minimal risk, an explanation as to whether there is any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
    - An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;
    - A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and
    - One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
        - (i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the LAR, if this might be a possibility; or
        - (ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.
- When appropriate, the additional elements of consent delineated in 45 CFR 46.116(c)(1) through (9) and, as applicable, required elements of Subparts B, C, and D should be included.
- The prospective subject’s agreement to participate in the research must be documented either by signature or other means (e.g., a fingerprint) unless the IRB has waived documentation of informed consent.

INFORMED CONSENT DOCUMENT SHELL

If the local enrolling sites do not have an informed consent template, you may consider using the subheadings below to organize your informed consent document.

The following subsections cover the 9 required elements of informed consent that must be included in all consent documents. The wording of these subheadings is a suggestion, not a requirement. You should tailor them for the research and the subject population being enrolled.

What are the most important things for you to know about this research?

- *Include a concise and focused summary of the most important information a prospective participant should know to decide whether or not to participate. This could include information about the purpose of the study, what will happen during the study, and possible risks and/or benefits. Think of this section as providing information that might "make it or break it" for any given person's decision whether or not they will join.*

It is your choice whether or not to join this research

- *Include a clear statement describing that what you are doing is research, and that it is not designed to specifically benefit the individual person enrolling.*
- *Include a clear statement that participation is voluntary.*
- *Include a clear statement that the subject can withdraw at any time without penalty.*

Why are we doing this research?

- *Describe in lay persons' language, appropriate for the population being enrolled, the purpose of the research study.*
- *Consider the overall health literacy of the intended subjects. Do not use technical terms or language.*
- *Refer to diseases or conditions as they are referred to by the local population.*
- *If you are using an investigational drug or device, you must make a clear statement that the drug/device is investigational.*

What will happen if you join this research?

- *In this section, describe what the research subjects will be required to do if they join the study.*
- *Describe all the research procedures and study visits using terms understandable to the subject.*
- *Inform the subject of the duration of their participation in the research.*

What are the possible risks from this research?

- *Describe the reasonably foreseeable risks associated with the research procedures.*
- *Provide an estimate of the likelihood and severity of the harm occurring in terms understandable to the subject.*

What are the possible benefits of this research?

- *Describe if there are any known direct benefits to the research. If the research involves an investigational drug or device, do not imply certainty of benefit to the investigational agent.*
- *You can include a statement that the research may help others in the future.*

What else might I do if I choose not to join this research?

- *Describe alternatives to participation in the research, if any. For example, if this is a trial testing a drug for a disease, explain what other treatment options are available.*

Will I be paid for being in this research?

- *Describe the plan to provide any form of payment to subjects for their participation in this research; including if subjects will not be compensated for participation.*

Will it cost me anything to be in this research?

- *Describe if subjects will incur any costs related to participating in the research.*

How will the research team protect the information we collect about you?

- *Describe how you will keep information protected from unauthorized access.*
- *NIH Research Privacy Act language is required if personally identifiable information is being stored in a Privacy Act system of records. Contact your IC Privacy Coordinator with questions.*
- *Certificate of Confidentiality language is not required.*

What will happen if I get hurt because of this research?

- *If the research is greater than minimal risk, describe how research related injuries will be handled.*
- *Include information as to whom at the local site/institution the subject should contact in the event of research related injury.*

What will happen with the information and/or specimens after the study is over?

- *If data and/or specimens will be stored for future use, describe that here. Include one of the 2 statements informing subjects whether or not the samples/data may be deidentified for future use as required by 45 CFR 116(b)(9).*

Whom can I contact about this research?

- *Provide contact information for whom the subject can contact to get questions answered about the research or their rights. If not included above, provide contact information as to whom at the local site/institution to contact in the event of a research related injury.*

If applicable to the research, the informed consent document must also include the following additional information. You may also be able to incorporate this information into some of the other sections listed above. Sections may also be combined, if it makes sense to do so. There is no requirement to use these headings, just to include the required information.

Are there risks related to pregnancy and/or breastfeeding?

- *Describe any risks to the pregnant woman or fetus*
- *Describe if there are risks to a breastfeeding child.*

Reasons why participation may be terminated without subjects' consent

- *If it is possible that you may withdraw people without their consent, describe the circumstances in which that might occur.*

What will happen if I withdraw from the research?

- *Describe what steps will need to happen if a subject is withdrawn from the research either by their choice or by the investigator.*
- *For example, if there are safety implications and additional monitoring is required, or an early termination visit, describe that here.*

Will you tell me if you learn anything new that might change my decision to be in the research?

- *Inform the subject that if there is new information that might alter their decision to enroll or remain in the research, you will inform them of this information promptly.*

How many people will be in the research?

- *How many people will be enrolled at the site and in the study overall.*

Will my specimens be used for commercial profit and will I share in the profit?

- *If it is possible that biospecimens may be used now or in the future to develop any products with commercial value, you must describe that possibility here and inform the subject whether or not there is an intent to share the profit with them.*

Will you tell me about any research results that might be important for my health?

- *If you will return any clinically relevant research results to the subject, describe that here.*

Will my specimens be used for whole genome or exome sequencing?

- *If whole genome or exome sequencing is planned, you must inform the subject.*
- *Note, the NIH Genomic Data Sharing policy has additional requirements for informed consent.*