Section 6: Informed Consent

6.1 General Policy
Researchers must describe in their research protocol how the informed consent process will be conducted, the setting in which it will occur, a description of the waiting period between informing the prospective participant and obtaining consent and methods in place to prevent undue influence on a potential participant to enroll in a study. The following are points to consider when conducting the consent process.

Researchers should consider obtaining informed consent as a process, not just a consent form, by which the research study is thoroughly explained to the potential subject. The requirement to obtain informed consent should be seen as not only a legal obligation, but also as an ethical obligation. Documentation of informed consent is accomplished through the use of a consent form. Prior to enrolling subjects in a research activity, researchers are required to obtain legally effective informed consent from a potential subject or their LAR and, if the research involves children, a parent's permission or child's consent. (See Section 6.6 Parental Permission/Child Assent).

As part of the informed consent process, researchers are responsible for ensuring subjects (or LARs) are given sufficient opportunity to consider whether or not to participate in the study and must seek to avoid coercion or undue influence. Information given to potential subjects (or LAR) must be in language that is understandable to the subject or representative. Non-English speaking subjects must have information presented in a language they understand (Section 6.4.1 Non-English Language Informed Consent and other Study Documents).
No process or consent form used to obtain and document consent may include exculpatory language through which the subject waives any of their legal rights or releases, or appears to release, the researcher, sponsor, or institution or its agents from liability for negligence. Any consent form used to enroll subjects in a research protocol must be reviewed and approved by an IRB prior to enrollment. In addition, the IRB may request to observe the informed consent process to ensure adequate consent when the research involves particularly vulnerable populations.

Researchers should be aware that the setting in which consent is sought may introduce a feeling of undue influence. For example, students in an educational setting may feel that refusal to participate will affect their grades. Prevention of these sorts of pressures should be addressed in the research design as the process must always preserve the right to refuse participation.

In all cases, consent forms must be consistent with state laws and federal regulations regarding content. The informed consent requirements stated in this manual are not intended to preempt any applicable federal, state, or local laws that require additional information to be disclosed in order for informed consent to be legally effective.

Procedures for requesting a waiver of the requirements for obtaining and/or documenting informed consent are delineated in Section 6.7.

6.2 Elements of Informed Consent
The IRB will determine that the required disclosures will be provided to each subject or a legally authorized representative in accordance with legal and regulatory requirements listed below as required elements of informed consent. The IRB will also consider whether additional disclosures are required for inclusion in the consent process.

It is expected that researchers will use the informed consent form template with required sections and verbiage for preparing consent forms. Other formats may be considered providing that all required elements and applicable additional elements are present. Research-related consent forms must contain all the basic elements of informed consent regardless of the risk level of the study unless a request for waiver or alteration of some or all of the elements is requested by the researcher and the waiver is approved by the IRB. The consent form template contains all the required elements of consent. In addition, the IRB requires that all consent forms be written at a level appropriate to a minimum expected educational level of the target population and in the second person, e.g., “You will be required to ...” The following are the basic required elements (extracted from 45 CFR Part 46.116):

1. A statement that the study involves research.
2. An explanation of the purpose of the proposed research.
3. The expected duration of the subject’s participation.
4. A description of the procedures to be followed.
5. Identification of which procedures are experimental. For studies that are not greater than minimal risk and are not HHS-funded, this element may be omitted.
6. A description of reasonably foreseeable risks or discomforts that the subjects may encounter, and, if appropriate, a statement that some risks are currently unforeseeable.
7. A description of possible benefits, if any, to the subject and others which may be reasonably expected. It should be stated that if it is an experimental treatment or procedure, no benefits can be guaranteed.
8. A disclosure of appropriate alternative procedures or treatments, if any, which are available and might be advantageous to the subject. One alternative might be to choose not to participate in the research. For studies that are not greater than minimal risk and are not HHS-funded, this element may be omitted.
9. A statement describing the manner and extent, if any, to which confidentiality of records identifying the subject will be maintained, a statement that the IRB and other entities may inspect the records, and, if the research is Food and Drug Administration (FDA)-regulated, FDA may inspect the records.

10. For research involving more than minimal risk, an explanation as to whether any compensation or any medical treatments are available if injury occurs and if so, what they consist of or where further information may be obtained. For studies that are not greater than minimal risk and are not HHS-funded, this element may be omitted.

11. A description of whether or not reimbursement for time, inconvenience, etc. will be given, including the schedule of payments.

12. Information regarding who to contact for answers about the research and in the event there is a research-related injury (this is generally the principal investigator (PI) or another staff member closely associated with the study). A separate contact, typically this is the Office of Research Integrity & Education and the IRB Chair, must be named for questions concerning the subject’s rights to provide input, comments, or complaints.

13. A statement that the subjects’ participation is voluntary, that refusal to participate will not involve penalty or loss of benefits to which the subject is entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is entitled.

Note: for FDA regulated applicable clinical trials (See definition in Section 2) the following statement must be included:
“A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”

The following additional elements of informed consent must be added to the consent form when appropriate:

1. A statement that the particular treatment and/or procedure may involve risks to the subject (or to the embryo or fetus, if the subject becomes pregnant) that are currently unforeseeable. This element should be included when the research involves an investigational drug or device or involves procedures for which the risk profile is not well known.

2. Anticipated circumstances under which the subject’s participation may be terminated by the PI, with or without the subject’s consent. Include when there are known circumstances under which the subject’s participation may be terminated by the PI or sponsor.

3. A description of additional costs for which the subject will be responsible, that may result from participation in the research study. Include when there are additional costs to subjects, over and above standard of care, e.g., additional MRIs, radiographs, DEXA scans, additional visits that may not be covered by insurance/Medicare/Medicaid.

4. A description of the consequences of a subject’s decision to withdraw from the research and procedures for orderly and safe termination of participation by the subject. This element should be included when there is a likelihood that abrupt termination from the research is likely to result in adverse events to the subject.

5. A statement that significant new findings developed during the course of the research that may relate to the subject’s willingness to continue participation will be provided to the subject. Include when there is likelihood that interim findings might indicate increased risk and a reasonable person would wish to reconsider participation.

6. The approximate number of subjects that will be involved with the study, totally and at the University. Include when such information might affect a subject’s willingness to participate.

7. Other additional information may be required by the IRB.
6.3 Other Requirements for Obtaining Informed Consent

1. The IRB must be made aware of the person(s) who will be conducting the informed consent process. These faculty/staff members should be listed in the application and are the only personnel allowed to obtain consent. The IRB requires that the person obtaining consent be appropriately trained in human subjects research (See Section 3.16 Training Requirements) and fully knowledgeable about the project and be able to answer questions that potential subjects may ask regarding the project and/or procedures performed as a part of the project.

2. If potential subjects are deemed as decisionally impaired, informed consent must be obtained from a LAR (See Section 6.5: Third Party/Surrogate Consent). They should be told that their obligation is to try to determine what the subject would do if they were competent, or if the subject's wishes cannot be determined, what they think is in the best interest of the decisionally impaired subject. The IRB must approve the inclusion of decisionally impaired subjects.

3. The consent form is only part of the total consent process in which the researcher conducting the informed consent process, perhaps using the written consent form as an outline, describes all facets of the study and answers the subject's questions. The person obtaining consent is responsible for insuring that research subjects understand the research procedures and risks. Each subject (or LAR) must be provided adequate time to read and review the consent form, in addition to being advised of the procedures, risks, potential benefit, alternatives to participation, etc. Failure of the subjects to ask questions should not be construed as understanding on the part of the subject.

4. The IRB has the authority to observe the consent process at any time. Depending on the perceived risk of the research procedures, the IRB may wish to observe the consent process for that protocol. In these cases, the PI will be contacted and the time and place for observing the process will be scheduled.

5. Obtaining informed consent from subjects must be accomplished prior to performing the research activity and using only an IRB-approved consent form. Written requests for amendments to an existing consent form must be approved prior to implementation, at which time the revised consent form will be stamped with an approval date by the IRB Compliance Administrator and be accompanied by a formal approval notification.

6. Upon receipt of an IRB approved consent form, copies of all old versions should be discarded to prevent inadvertent use of an outdated consent form. Copies of the most recently approved consent form may be made and should be used until superseded by an amended consent form. The consent form must be reviewed at least annually as part of the continuing review process. It is advised the researchers retain a copy of the original, expired consent form(s) for their records.

7. For long-term studies, researchers are reminded that the informed consent process is ongoing and that it does not end with the signing of the consent form. Subjects should be kept apprised of events that might affect their willingness to participate.

8. Researchers are reminded that the informed consent process and form must be in a language understandable to the subject. Therefore, if it is anticipated or known that there will be non-English speaking potential subjects who might be interested in enrolling in a study, the consent form must be translated. It will then have to be reviewed and approved by the IRB. Translation of the consent form should be conducted by a certified translator or if performed by someone who is not a certified translator but is fluent in the translated language the PI must certify that it is an accurate translation by completing Appendix K: Certificate of Translation.

6.4 Documenting Informed Consent
Federal regulations governing the use of human subjects in research activities require written documentation of informed consent (handwritten signature of the subject) unless the research
meets the criteria for waiver of documentation. The subject and research staff member administering the consent interview should sign and date the IRB approved consent form.

1. After completing the consent process and assuring that the subject (or LAR) has no further questions and agrees to participate in the research activity, the person obtaining informed consent should instruct the subject (or LAR) to sign and date the consent form in the appropriate spaces.

2. The researcher or designee conducting the consent interview must then sign and date the consent form in the appropriate space. It is assumed that in most cases, all persons signing the consent form will do so at the conclusion of the consent process.

3. Each subject (or LAR) must be given a copy of the signed consent form. The original consent form should be filed in such a manner as to insure immediate retrieval when required by auditing entities, e.g., OHRP, FDA, IRB.

6.4.1 Non-English Language Informed Consent and other Study Documents
It is neither ethically justifiable to exclude potential subjects in a research study solely on the basis of language spoken nor ethically justifiable to obtain consent of subjects who do not have a clear understanding of the consent document or who do not have the opportunity to freely ask and receive answers to their questions. Without this understanding and opportunity, consent may not be truly informed and may not be legally effective. In order to address these considerations, when enrolling subjects who do not speak English in research, the subject must be provided with:

1. A written consent document in a language understandable to them.
2. An interpreter fluent in both English and the subject's spoken language.

A consent form translated into the appropriate language should be submitted to the IRB. The IRB will accept non-English documents that are:

1. Professionally translated by a certified translator, or
2. Translated by someone who is fluent in the non-English language. The PI must review the document and complete Appendix K: Certificate of Translation verifying the translation is accurate and correct.

A certificate from the certified translator or a description of the proposed translation procedures, including the PI's certifying statement, must be provided to the IRB with the non-English documents.

6.4.2 Use of a Short Form Written Consent Document
A short form is a written document stating that the elements of informed consent required by 45 CFR 46.116 have been presented to and understood by the subject or the subject's legally authorized representative. A short form may be used when the majority of subjects in a study are English speakers, but there are a portion of the subjects who will not be able to understand the consent form written in English.

However, if the majority of the anticipated subjects to be enrolled do not speak English or will be unable to understand the consent form written in English, the consent form must be translated into a language understandable to the subjects.

6.4.2.1 When following DHHS regulations the IRB must determine

1. The consent document states that the elements of disclosure required by regulations have been presented orally to the participant or the participant's legally authorized representative.
2. A written summary embodies the basic and required additional elements of disclosure.
3. There will be a witness to the oral presentation.
4. For participants who do not speak English, the witness is conversant in both English and
6.4.2.2 When following FDA Regulations the IRB must determine

1. The consent document states that the elements of disclosure required by regulations have been presented orally to the participant or the participant’s legally authorized representative.
2. A written summary embodies the basic and required additional elements of disclosure.
3. There will be a witness to the oral presentation.
4. For participants who do not speak English, the witness is conversant in both English and the language of the participant.
5. The participant or the participant’s legally authorized representative will sign the consent document.
6. The witness will sign both the short form and a copy of the summary.
7. The person actually obtaining consent will sign a copy of the summary.
8. A copy of the signed short form will be given to the participant or the legally authorized representative.
9. A copy of the signed summary will be given to the participant or the legally authorized representative.

6.4.3 Informed Consent Process for Online Survey-Based Research

1. Internet consent documents should include all the elements of a regular signed consent form.
2. Researchers should maintain the format of the template consent document, with study specific information added, as much as possible.

6.5 Third Party/Surrogate Consent

1. The regulations are clear that written documentation of informed consent (or permission of the parents if the subject is a child) of the subject (or LAR) is required.
2. When a PI proposes to conduct a research project utilizing adult subjects who by virtue of age, physical impairment, mental impairment, or any other reason may not be able to personally execute legally effective informed consent, the IRB shall review the project on the basis of risk and benefit. This policy is not meant to imply that the requirement for written documentation of consent is waived. Rather, it applies to those studies in which third party/surrogate consent is obtained from a LAR.

6.6 Parental Permission/ Assent

If the research involves minors under the age of 18 years or individuals over the age of 18 who are decisionally impaired the federal regulations require the assent of the child or minor or decisionally impaired adult and the permission of the parent(s) or guardian(s) (45 CFR 46.408). While children and some adults may be legally incapable of giving informed consent, they nevertheless may possess the ability to assent. The assent process should involve taking the time to explain to a child or adult, at whatever age they can begin to understand, what is going on in the proposed study, why the study is being done, what will be done to them, and that if they object, the research will be terminated. Assent means the potential subject’s affirmative
agreement to participate in the research. Mere failure to object should not, in the absence of affirmative agreement, be construed as assent.

To obtain informed consent for children under the age of 18 years or for adults over the age of 18 who may be decisionally impaired, submit the Parental Permission Form for Child Participation and Child Assent form. For more information see Section 12.4 Research Involving Children.

6.7 Waiver of Informed Consent and Waiver of Documentation of Consent

Waivers cannot be granted for FDA-regulated research and the DU IRB does not approve requests for “Planned Emergency Research” or exceptions to the requirement to obtain consent for “Planned Emergency Research.”

6.7.1 Waiver of Informed Consent

Federal regulations include provisions for approval of a waiver or alteration of part or all of the consent process. There are two general instances when an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in 45 CFR 46.116, or waives the requirement to obtain informed consent. In the first general instance (45 CFR 46.116(c)) the IRB must find and document that:

1. The research is to be conducted by or subject to approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and
2. The research could not be practicably carried out without the waiver or alteration.

In the second general instance (45 CFR 46.116(d)) an IRB may approve a consent procedure that does not include, or that alters some or all of the elements of informed consent or that waives the requirement to obtain informed consent provided that the IRB finds and documents that:

1. The research involves no more than minimal risk to the subjects.
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The research could not practicably be carried out without the waiver or alteration (It is impracticable to perform the research if obtaining informed consent is required and not just impracticable to obtain consent); and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

6.7.2 Waiver of Documentation of Consent

Documentation of Consent cannot be waived if the research is FDA regulated.

The IRB has the authority to waive the requirement for written documentation of informed consent. When waiving the requirement for a consent form, the IRB must review a written description of the information that will be provided to subjects and consider whether to require the researcher to provide subjects with a written statement regarding the research. If required, the IRB encourages researchers to use the consent template, or a reformatted version, with the signature sections removed. The IRB may waive the requirement for the researcher to obtain a signed consent form for some or all subjects if it finds that (45 CFR 46.117 (c)):

1. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality and the research is not FDA-regulated. Each subject will be
asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern or;

2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

The IRB will also consider granting a waiver of documentation in special circumstances involving international research if the research meets the other regulatory requirements.

The determination of the applicability for waiver of the consent process must be documented in the IRB minutes as to the specific paragraph and subparagraph(s) under which the waiver was approved.

6.8 Authorization to Use or Disclose Protected Health Information
Researchers may perform research activities in which they collect or have access to Protected Health Information (PHI). To use or disclose PHI, researchers must obtain an authorization signed by the subjects.

6.8.1 Required Elements

1. A description of the information to be used or disclosed presented in a specific and meaningful fashion.

2. The name or other specific identification of the person(s), or class of persons, to whom the use or disclosure will be made.

3. A description of each purpose of the requested use or disclosure.

4. An expiration date or event that relates to the individual or the purpose of the use or disclosure.

5. A statement of the individual’s right to revoke the authorization in writing and the exceptions to the right to revoke, together with a description of how the individual may revoke the authorization.

6. A statement indicating when the authorization for use and disclosure occurs; e.g., at the end of the research.

7. Signature of the individual and date. If the authorization is signed by a personal representative of the individual, a description of such representative’s authority to act for the individual must also be provided.

In addition to the core elements, the authorization is required to contain statements adequate to place the individual on notice of all of the following:

1. The individual’s right to revoke the authorization in writing, and either:
   a. The exceptions to the right to revoke and a description of how the individual may revoke the authorization; or
   b. To the extent that the information in Section 6.7.1 is included in the notice required by 45 CFR 164.520, a reference to the covered entity’s notice.

2. The ability or inability to condition treatment, payment, enrollment, or eligibility for benefits on the authorization, by stating either:
   a. The covered entity may not condition treatment, payment, enrollment, or eligibility for benefits on whether the individual signs the authorization when the prohibition on conditioning of authorizations applies; or
   b. The consequences to the individual of a refusal to sign the authorization, the covered entity can condition treatment, enrollment in the health plan, or eligibility for benefits on failure to obtain such authorization.

3. The potential for information disclosed pursuant to the authorization to be subject to re-disclosure by the recipient and no longer be protected.
4. The authorization must be written in plain language.
5. The individual must be provided with a copy of the signed authorization.

6.9 Waiver of Authorization for Use and Disclosure of PHI
In order to use or disclose PHI without an authorization signed by the research subject, the researcher must obtain one of the following:

1. Documentation that an amendment or waiver of the research subjects' authorizations, for use/disclosure of PHI has been approved by the IRB. This provision of the rule might be used, for example, to conduct records research when researchers are unable to use de-identified information; or

2. Where researchers represent:
   a. That the research is only for purposes of preparing a research protocol or similar uses preparatory to research.
   b. That he or she will not remove any PHI from the covered entity and
   c. That PHI is necessary for the research purpose; or

3. To disclose PHI of decedents, where the researcher represents that the use or disclosure of PHI is:
   a. Solely for research on the PHI of decedents,
   b. Necessary for the research, and
   c. Documentation of the death of the individuals about whom PHI is sought and provided.

6.10 Re-Consenting Subjects
Researchers have the responsibility to inform subjects of any new information that might affect subjects' willingness to continue participation in the research. In these cases, an amended consent form, delineating the findings and the changes to research risks/benefits, must be reviewed and approved by the IRB. Subjects should then be briefed on the changes, asked if they wish to continue participation and signify their willingness to continue participation by signing the amended consent form. For minor changes to the consent form that will not change risk/benefit, re-consenting is generally not required.

6.11 Record Retention Requirements for Subject Consent Forms
The PI shall maintain, in a designated location, the original copy of all executed subject consent forms. The signed consent forms, along with all research-related files, are to be available for inspection by authorized officials of the University administration, the IRB, regulatory agencies, sponsors and, if applicable, the FDA or HHS. For non-FDA regulated studies, forms should be retained for at least three years after completion of the study. For FDA-regulated studies, all signed subject consent forms shall be retained by the PI for the appropriate period(s) specified below:

1. Drugs: 2 years following the date a marketing application is approved or the study is discontinued.

2. Devices: 2 years after a study is terminated or completed and the records are needed to support FDA approval.

Should a PI or project director depart the University prior to the completion of an activity or less than the time specified above, the PI is responsible for initiating mutually satisfactory arrangements with their department and the University administration as to the disposition of executed subject consent documents.