Section 11 Special Research Topics 11.2 Human Biological Specimens	Effective Date: **08/15/2008** Revised: **8/13/2010, 1/9/15**

When NDSU research use of human biological specimens, tissues, or bodily fluid samples constitutes the engagement of the institution in **human subjects** research, policies for protecting the rights, safety and welfare of research participants apply.

1.0 Research subject to IRB oversight.

Human biological specimens are obtained for research in various ways. When the collection and/or use of biological specimens constitutes the engagement of NDSU in human subjects research, IRB review is required. Refer to *2.2 NDSU Engagement in Human Subjects Research* for more information.

1.1 NDSU-directed projects.

NDSU is engaged in human subjects research when the institution receives funding for, or an NDSU **investigator** directs or supervises a project that involves human subjects. This would include projects in which the human subjects activities are carried out by NDSU investigators, or by other entities under the direction of an NDSU investigator.

Examples may include, but are not limited to:

- direct interaction with participants to collect specimens specifically for the research,
- use of excess, or left-over clinical specimens for the research,
- collection of additional material for research use beyond that which is necessary for clinical care,
- obtaining **individually identifiable** existing specimens for research use.

1.2 NDSU interaction with participants.

NDSU is engaged in human subjects research when an NDSU investigator interacts with participants by obtaining their informed consent, or collecting a specimen for research purposes.

1.3 Use of identifiable specimens.

NDSU is engaged in human subjects research when an NDSU investigator obtains (receives or accesses) specimens for which the identity of the donor is readily ascertainable.

1.4 Use of coded specimens.

NDSU is engaged in human subjects research when an NDSU investigator obtains coded specimens from any source and the investigator:

- is able to access the key with linkage to individual identities,
- attempts to contact individuals, or
- unexpectedly learns the identity of one or more individuals.

1.5 FDA-regulated research.

NDSU is engaged in human subjects research when an investigator conducts a clinical investigation to evaluate the safety and efficacy of FDA-regulated test articles (drugs, devices, biologics, etc.). This may include use of existing, **de-identified** specimens to evaluate an in-vitro diagnostic assay or instrument. Examples include, but are not limited to:

- prospective collection of specimens ,
- use of excess clinical specimens,
- collection of additional material beyond that normally collected for clinical care,
- use of existing specimens, whether identifiable, **coded**, or de-identified.

Refer to SOP *11.6 FDA-Regulated Research* for more information.

2.0 Research not subject to IRB oversight.

Use of human biological specimens that does not constitute the engagement of NDSU in human subjects research is outside the purview of the IRB. The following examples assume the NDSU investigator's role in the research is limited to that described below, and does not include any other involvement in the project that would constitute engagement in human subjects research as described in 1.0 above.

2.1 De-identified specimens.

When an investigator obtains (receives or accesses) specimens for which no identifiers or codes to identifiers exist, the research is not subject to IRB oversight. De-identified information is that in which an individual can no longer be identified directly or indirectly through a linkage to identifiable information held by any party.

2.2 Coded specimens.

When an investigator obtains coded specimens (existing or prospectively collected), the research is not subject to IRB oversight provided that the investigator cannot readily ascertain the identity of the individual(s) to whom the private specimens pertain because:

- the NDSU investigator(s) and the holder of the key enter into an agreement prohibiting the release of the key to investigators,
- the releasing institution has IRB-approved written policies and operating procedures applicable to the research project that prohibit the release of the key to NDSU investigator(s), or
- there are other legal requirements prohibiting the release of the key to the NDSU investigator(s).

IRB review or certification of exempt status is not required for research meeting these criteria. An investigator may voluntarily request a written determination from the IRB stating that the research does not involve human subject, as described in 8.0 below. Refer to SOP *2.2 NDSU Engagement in Human Subjects Research* for more information.

3.0 IRB review.

IRB oversight is required for those projects that constitute NDSU engagement in human subjects research.

3.1 Exempt determination.
The IRB may determine that research involving human specimens or tissues is eligible for exemption category 4, when the specimens were in existence at the time the research was proposed, and collected for a purpose other than the proposed research. Additionally, if the specimens are not de-identified, the investigator must either have no access to identifiers or codes, or will not record, even temporarily, any identifiers or coded links to identifiers. Refer to SOP *7.1 Exemption Determinations* for more information.

3.2 Expedited review.
The IRB may determine that research involving human specimens is eligible for expedited review, as long as the research will involve no more than minimal risks and meets the criteria specified under the relevant category. Categories 1 – 5, 8 or 9 may be utilized for research involving biological specimens. The expedited review criteria limit the use of these categories for research that is subject to FDA regulations. Refer to SOP *7.3 Expedited Review* for more information.

3.3 Full board review.
The IRB may determine that research involving human specimens is either not eligible for exemption or expedited review, or that review at a convened meeting is warranted to ensure adequate protection of the rights and welfare of participants. Refer to SOP *7.4 Full Board Review* for more information.

3.4 Collaborative research.
When collaborative projects involving use of human specimens are under the purview of multiple IRBs, arrangements for cooperative review are permitted under certain conditions. Refer to SOP *2.3 Collaborative, Multi-site and Off-site Research* for more information regarding collaborative research requirements.

4.0 Risks and discomforts.
The use of specimens for research may expose participant donors to a variety of risks.

4.1 Physical risks.
When research involves collection of a biological specimen, participants are exposed to physical risks of tissue damage, including bruising or bleeding. Physical risks may also be present when a clinical procedure is prolonged to obtain additional samples for research. Personnel performing such procedures must have appropriate qualifications in order to minimize risks for participants.

4.2 Psychological risks.
Participants may experience distress or anxiety when research uncovers serious health problems, especially if the condition has no known treatment. For many studies, however, it may not be possible and/or appropriate to report individual results, particularly when the test has unknown validity or health implications. When reporting results to participants, investigators should also provide referrals or counseling for appropriate treatment to minimize these risks.

4.3 Sociological, economic and legal risks.
When the results of research are disclosed outside the study through a breach of confidentiality or unauthorized release of data, participants may be exposed to additional risks. For example, a participant may risk losing their job or a promotion opportunity should

their employer become aware of significant health problems. Also, their insurability may be impacted if an insurer discovers this same information. Research results revealing illegal activities (e.g., substance abuse, use of alcohol by minors), may place participants at risk of arrest.

Strict adherence to data safeguarding procedures to protect the confidentiality of participants' information minimizes these risks. Also, for some studies, a Certificate of Confidentiality may be obtained from the National Institutes of Health (NIH) to protect against compelled disclosure of results to law enforcement or other authorities.

4.4 Group harms.

Identified groups or communities, especially those subject to discrimination and/or of low socioeconomic status may also be vulnerable to harms as a result of research. When research results are stigmatizing or support harmful stereotypes about a group, the community as a whole suffers, even when individual participants are not identified in results. To minimize these risks, the investigator should consult the community in advance to obtain approval, ensure potential harms are understood by all parties, and ensure the study will be beneficial to the group.

5.0 Informed consent.

Research involving biological specimens requires consent of participant donors, unless the requirement is waived by the IRB. Use of common, lay language and explanations of scientific or technical terms in the consent document help to ensure participant comprehension of research goals and nature of analysis of their specimen(s). Helpful guidance and sample language for consent forms are available from the National Institutes of Health (NIH) (see *Resources*). In addition to requirements as outlined in *Section 9 Requirements for Informed Consent*, several issues are unique with respect to obtaining consent for collection of research specimens.

5.1 Right to withdraw.

Federal regulations give participants the freedom to discontinue participation in research at any time, without penalty or loss of benefits to which they are entitled. Exercising this right may not be practical, however, when participation consists of a one-time donation of blood or tissue for which no records of identifying information exist. Participants must be informed regarding the limitations of, and procedures for withdrawing from the research. For example, several options may be offered:

- declining contact for any future research,
- removal of all identifiers from their specimen, but allowing its future use,
- prohibiting future use of their specimen,
- destruction of their specimen and all data from prior analysis.

5.2 Permission for tissue banking.

Biological specimens may be collected specifically for the purpose of creating a repository for future research projects. When applicable, inform participants that their specimen will be stored in this manner, the conditions under which it will be provided to other researchers, possible types of analysis, and how their privacy and confidentiality will be protected. A tiered consent process may be used to provide participants with a range of choices, such as:

- use of specimen with full access to identifiable information,
- use of specimen with no access to identifiable information,
- use of specimen for stated research only,
- use of specimen for other types of research only after re-consent,
- unrestricted use of specimen for other types of research.

5.3 Waiver of informed consent.
The IRB may waive the requirement to obtain informed consent under certain conditions, typically for research limited to secondary use of existing, de-identified specimens. To approve a waiver or alteration of informed consent, the IRB must make the following determinations:

- the research involves no more than minimal risk,
- the waiver would not adversely affect the rights and welfare of participants,
- the research could not practicably be conducted with the waiver, and
- when appropriate, subjects will be provided with information after participation *(usually does not apply to retrospective collection of specimens.)*

As part of the determination, the IRB may consider terms of any original contract or agreement (if available) under which individuals originally provided their specimens. Refer to SOP *9.3 Waiver or Alteration of Informed Consent Requirements* for more information.

5.4 Commercial product development.
Research involving specimen(s) may lead to development of a medical or genetic test, drug or other product of commercial value. When applicable, participants must be informed of this possibility, including whether or not the institution, sponsor, and/or investigator will profit from the sale of such products.

6.0 Reporting.
When research analysis of specimens reveals findings of clinical significance for individuals or public health, investigators must consider whether these results should be, or are required to be reported to any party.

6.1 Research results.
When research has the potential to reveal information that is clinically significant for an individual, the investigator considers whether or not participants will be notified. If the specimen analysis is clinically valid, has significant implications for an individual's health, and treatment is readily available, investigators may offer, but are not required to inform participants or their physicians of their results. When applicable, the process for notification and/or referral is described in the informed consent document.

6.2 Incidental findings.
Analysis of individual specimens may occasionally reveal a serious health condition that is not the focus of the research. If the possibility exists for incidental findings that are of clinical significance, investigators must consider whether or not to report the findings. If participants and/or their physician will be notified or provided with a referral, the process is described in the consent document.

6.3 Mandated reporting.

Research that has the potential to discover certain contagious, infectious, sexually transmitted or chronic diseases or any illness or injury that may have a significant impact on public health may be required to report findings to the North Dakota Department of Health. Certain entities, including health care providers, medical or diagnostic laboratories, schools and colleges, among others, are mandated to report these diseases; other entities may report voluntarily. When reportable information may be revealed in the research, the informed consent document must describe the nature and extent of disclosure of participants' information to state authorities. Refer to ND Century Code Chapter 23-7 and the ND Department of Health for more information.

7.0 **Genetic research**.

Genetic testing involving analysis of specimens to study linkages to a disease or disorder may involve unique risks for participants.

7.1 Risks.

The identification of genetic conditions or diagnoses, or new information regarding paternity or family relationships may be traumatic or stigmatizing to individuals, as well as family members. When participants will be notified of their results, these risks may be minimized by providing genetic counseling and/or referrals.

Risks related to loss of privacy and breach of confidentiality are also possible, as genetic information is unique to each individual. De-identification by current standards may not fully protect confidentiality, as future technological advances may allow for re-identification of individuals based on genetic information (even in pooled samples), in combination with information from other sources. Stringent data safeguarding procedures to protect the confidentiality of participants' information will minimize these risks. Also, a Certificate of Confidentiality may be obtained from the National Institutes of Health (NIH) to protect against compelled disclosure of results to law enforcement or other authorities. In addition, laws such as the Genetic Information Nondiscrimination Act (GINA) protect against use of genetic information to deny employment or promotion, or limits to health insurance coverage (see References).

7.2 Informed consent.

When applicable, participants are informed of the nature of genetic testing, the type of information it reveals about them, whether or not they will receive their results, and how privacy and confidentiality will be protected. Helpful guidance and sample language for consent forms are available from the National Institutes of Health (NIH) (see *References*).

7.3 Genome-wide association studies.

Some genetic research projects funded by the NIH are considered genome-wide association studies (GWAS). Such research is subject to additional requirements for IRB review and data sharing in an NIH database. Participants must be informed that their information will be shared in a national database, and the IRB must make specific additional determinations to consider the adequacy of the consent process and de-identification procedures, as well as risks for families, groups and populations. See the References for more information.

8.0 IRB determination of applicability.
An investigator may voluntarily request a written determination from the IRB regarding applicability of a particular project to IRB oversight. Although not required, it may be beneficial when uncertainty exists regarding the involvement of human subjects.

To obtain a written determination from the IRB, submit a written description of the project including descriptions of:

- intended purpose and goals of the project,
- source of specimens, including date(s) of collection and purpose of collection,
- existence of, and access of investigator to any identifiers or codes,
- role of NDSU faculty, staff, or student, as well as another entity,
- any applicable agreement, contract, privacy or confidentiality policy or usage restrictions.

In accordance with guidance from the Health and Human Services Office of Human Research Protections (OHRP), the IRB has final authority to determine whether or not a research project constitutes the involvement of human subjects. Human subjects research conducted without IRB review or determination of exempt status is considered noncompliant and subject to procedures as outlined in SOP *12.3 Complaints and Noncompliance*.

DEFINITIONS:

De-identified: identifiers were originally collected, but have been irreversibly removed from previously identified samples; individual can no longer be identified or linked with their information.

Anonymous: no identifiable information exists; individual identity cannot be known or deduced, no possibility of linkage with additional information or future data collection.

Biospecimen (human): samples of any cellular constituents or liquid secretions of the human body. The molecular makeup of biospecimens reflects the physiologic or pathologic condition of the person from whom they derive; and provide sensitive and specific insight into the biologic state of the donor.

Coded: 1) identifiable information has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and 2) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Genetic research: non-exempt human subjects research involving genetic testing or the collection of genetic information.

Genetic test: an analysis of human DNA, RNA, chromosomes, proteins, or metabolites that detects genotypes, mutations, or chromosomal changes. The following are not considered genetic tests: routine tests (e.g., blood counts, cholesterol test, liver enzyme tests) that do not detect genotypes, mutations or chromosomal changes, analysis of proteins or metabolites related to a disease or disorder.

Genome-wide association study: any study of genetic variation across the entire human genome designed to identify genetic association with observable traits or the presence or absence of a disease or condition (e.g., asthma, cancer, diabetes, heart disease, mental illness).

Human Subject: (HHS) a living individual, about whom, an investigator (whether professional or student) conducting research obtains:

- Data through intervention or interaction with the individual, or
- Identifiable private information.

Human Subject: (FDA) an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. This would include individuals whose private information is used to test the safety or efficacy of a diagnostic device, even if the information is not individually identifiable, and was obtained in a retrospective fashion.

Individually identifiable: the identity of the subject is or may be readily ascertained or associated with the information; data can be linked to specific individuals either directly or indirectly through coding systems. Would also include some demographic information, or other unique information or key details that would allow individual identification to be deduced (i.e., using internet search engines or other means).

Investigator: anyone involved in conducting the research; i.e., study design or supervision, data collection, obtaining informed consent, performing research procedures, obtaining coded private information or specimens, analyzing data (note that this would *not* include someone whose sole role is providing coded private information or specimens to an investigator).

Private information: information that has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). 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. *The IRB has the sole authority to determine whether or not a research project constitutes the involvement of human subjects.*

REFERENCES:

45CFR46.102(f) Definition of human subject
21CFR50.3(g) Definitions (FDA)
OHRP Guidance on Research involving Coded Private Information or Biological Specimens
OHRP Guidance on Tissue Repositories
FDA Guidance on In Vitro Diagnostic Device Studies using Left-over Human Specimens
Genetic Information Nondiscrimination Act (GINA)
OHRP Guidance on GINA
NIH Genome-Wide Association Studies (GWAS)
NIH Consent Form Examples and Model Consent Language for genetic studies
Certificates of Confidentiality, National Institutes of Health
ND Century Code Chapter 23-07 Reportable Diseases
ND State Department of Health maintains list of reportable conditions

RELATED FORMS:
Additional Materials Attachment
Informed Consent Waiver or Alteration Request

RELATED HRPP SECTIONS AND STANDARD OPERATING PROCEDURES:
2.1 Human Subjects Research
2.2 NDSU Engagement in Human Subjects Research
2.3 Collaborative, Multi-site and Off-site Research
Section 7 – IRB Review Process
9.3 Waiver or Alteration of Informed Consent Requirements
11.1 Use of Confidential Records
11.5 FDA-Regulated Research