Institutional Review Board Cooperative Master Agreement Between Virtua Health and The University of Pennsylvania

TERMS OF AGREEMENT

I. Purpose.

The purpose of this Cooperative Agreement (the "Agreement") between Virtua Health System ("Virtua") (FWA # 00002656) and the University of Pennsylvania ("Penn") (FWA #00004028; FWA #00032367) is to allow each party to rely on the other party's Institutional Review Board ("IRB") review. This Agreement also sets forth the respective authorities, roles, and responsibilities of each party when a reliance arrangement is determined to be acceptable.

II. Agreement Scope:

Elective Use. Each institution may independently determine, on a case-by-case basis, whether to rely on the other party's IRB review or whether it will perform its own IRB review.

Research Eligible for Reliance Review ("Research"). Research is eligible for consideration for reliance review if:

a) the research requires IRB approval under applicable law, or either Penn policy or Virtua policy; AND

b) Penn will be engaged in human subjects' research through any of the following: participation of one or more Penn Investigators; or use of Penn funding, Penn data, or Penn facilities; AND

c) Virtua will be engaged in human subjects' research through any of the following: participation of one or more Virtua Investigators; or use of Virtua funding, Virtua data, or Virtua facilities.

- Penn "Investigators" are defined as Penn / Penn Medicine faculty, staff, employees, and personnel; UPHS employees; Penn Medicine / UPHS employees leased to Virtua Health; and Penn Medicine private practice physicians.
- Virtua "Investigators" are defined as Virtua Medical Group employed or leased physicians and/or personnel or Virtua Health medical staff members.

This Agreement does not apply if :

- The research meets one of the eight exempt or limited review human subjects' research categories as set forth in 45 C.F.R. § 46.101(b), which is attached hereto as **Exhibit 1**; OR
- Penn and/or Virtua are not engaged in human subjects' research, as defined in Guidance on Engagement of Institutions in Human Subjects Research from the Office of Human Research Protections ("OHRP") (October 16, 2008), which is

attached hereto as **Exhibit 2.**

In the above non-applicable situations, investigators from each institution separately follow their own institutional research policies.

Non-Exclusivity. This Agreement does not preclude either party from participating in any other IRB authorization agreements with other entities.

III. Period of Agreement.

This Agreement shall commence on May 20, 2022 (the "Effective Date") and continue for five (5) years. This Agreement will automatically renew annually unless a party terminates as provided herein.

IV. Amendments and Termination.

The parties may amend this Agreement in a writing signed by both parties.

Either party within its sole discretion may terminate the Agreement upon sixty (60) days' written notice. In the event of termination, each party will continue its obligations as an IRB of Record for ongoing Research until such responsibility is transferred as agreed in writing by the parties.

V. Responsibility for Financial Conflict of Interest (FCOI) Compliance.

Each party's responsibility for FCOI compliance as required under each party's FCOI policy will be governed in accordance with **Exhibit 3**.

VI. Determination of IRB of Record, Process and Consideration.

Request Process. If an investigator desires or is required to undergo single IRB review (e.g., per NIH mandate), the following steps should be followed. The investigator should identify which institution will serve as the IRB of Record. The investigator must confirm that the proposed IRB of Record is willing to serve in a single IRB capacity.

If the proposed IRB of Record is willing to serve in this capacity, the investigator should submit a request to their institutional IRBs with a request to rely on the other institution's IRB (the "IRB of Record") for oversight of research. The institutional IRB of Penn Medicine employees leased to Virtua Health is the Penn IRB.

The investigator's institutional IRB will review the reliance request, following its written procedures, and determine if reliance is acceptable. If acceptable, the relying IRB will issue a letter indicating willingness to rely on the IRB of Record and this master agreement applies.

Review by IRB of Record. After the institutional IRB (the "Relying Institution") has agreed to rely on the proposed IRB of Record as described above, the investigator seeking review will provide to the IRB of Record a copy of the protocol and applicable supporting documents (e.g., Relying IRB letter(s), Relying institution-specific consent form, etc.). The IRB of Record will conduct its formal review process. Any study described falling under this agreement will be considered "Human Subjects' Research" for purposes of this Agreement.

VII. IRB of Record Responsibilities.

The IRB of Record agrees that it will, at all times while this Agreement is in effect:

1. Maintain a Federalwide Assurance ("FWA") with OHRP and the registration of its IRB with OHRP and the Food and Drug Administration ("FDA").

2. Maintain IRB membership that satisfies the requirements of 45 C.F.R. Part 46 and 21 C.F.R. Part 56.

3. Make available to the Relying Institution, upon request, the IRB of Record's Standard Operating Procedures or Policies.

4. Perform initial reviews, continuing reviews, reviews of unanticipated problems involving risks to subjects or others, amendments, incidents of serious or continuing noncompliance, and reviews of any other documents as needed in accordance with applicable regulations.

5. Maintain and make accessible to the Relying Institution, the IRB of Record's application, protocol reviews, letters to Principal Investigators ("PIs"), approvals and disapprovals, approved consents, and portions of the minutes of the IRB of Record's meetings relevant to the research and the Relying Institution.

6. Provide the Relying Institution with approved consent form(s) incorporating the Relying Institution's requirements (e.g., HIPAA, payment for research related injury, and local contacts). Any additional modifications will be subject to approval by the IRB of Record, which will then provide a final approved consent form to the Relying Institution.

7. Perform those deliberations required by HIPAA including, but not limited to:

    a. Issuing a waiver or alteration of HIPAA requirements;

    b. Incorporating HIPAA authorization language provided by the Relying Institution into the site-specific approved consent form;

    c. In cases when Relying Institution's IRB has previously approved standard HIPAA authorization language, inserting that language into the applicable consent form.

    d. If a HIPAA authorization that satisfies the requirements of 45 CFR § 164.508 will be used by the study investigators, the IRB of Record would not need to further review and approve that document. The Relying Institution would be able to implement that authorization per their local policy.

As an alternative, a Relying Institution, may retain responsibility for reviewing and approving waivers of or alterations of authorization for Research ceded under this agreement in accordance with the HIPAA Privacy Rule.

8. Consider any applicable FCOI determinations and associated management plans provided by Relying Institution with respect to any Investigator, defined as the PI and any other person, regardless of title or position, who is responsible for the design,

conduct or reporting of the Research. The IRB of Record will ensure that any management plan is incorporated into its initial or continuing review or other deliberations, as applicable. Likewise, without limiting the foregoing, the IRB of Record will ensure that any financial disclosures to subjects mandated by the Relying Institution's IRB and approved by the IRB of Record are included in the approved informed consent form(s) for the relevant Relying Institution. The IRB of Record retains the authority to determine the manner, format, and language of any financial disclosure in the informed consent, and may also impose additional prohibitions or FCOI management requirements more stringent or restrictive than proposed by a Relying Institution if necessary to approve the Research, provided, however, the IRB of Record will not modify or change any management plan or mandated disclosure to subjects by the Relying Institution's IRB without discussion with and acceptance by the Relying Institution.

In the extraordinary circumstance that the IRB of Record is unable to implement/approve a Relying Institution's prohibitions or management plans, the IRB of Record will so inform such Relying Institution or, if the Relying Institution fails to accept any additional prohibitions or requirements, the Relying Institution will so inform the IRB of Record. If the institutions are not able to identify a mutually agreeable approach, the Research will not be eligible for review under this Agreement.

9. Notify the Relying Institution promptly if the IRB of Record's authorization to review studies is suspended or restricted, including but not limited to a suspension or restriction of the IRB of Record's FWA or Association for the Accreditation of Human Research Protection Programs ("AAHRPP") accreditation, as applicable to each institution.

10. Notify the Relying Institution promptly of any IRB of Record policy decisions or regulatory matters that might affect the institution's reliance on the IRB of Record's reviews or performance of the Research at the Relying Institution.

11. Notify the Relying Institution promptly of any injuries or unanticipated problems involving injury or risks to subjects or others in the Research discovered by the IRB of Record.

12. Notify the Relying Institution if the IRB of Record determines that serious or continuing non-compliance has occurred in the Research at the Relying Institution, and describe the steps the IRB of Record deems necessary for the remediation of the non-compliance, including but not limited to, any suspension, disapproval or termination of the Research, or any sanctions or limitations imposed on researchers at the Relying Institution. The IRB of Record may request that the Relying Institution conduct its own investigation and report back to the IRB of Record or the IRB of Record may conduct its own investigation, in cooperation with the Relying Institution.

13. If the IRB of Record determines that it must report serious or continuing non-

compliance determinations, suspensions or terminations, or the findings of an investigation to OHRP, the FDA and/or other oversight entities, it will notify the Relying Institution in advance. The IRB of Record will give the Relying Institution an opportunity to review and comment on the report before it is sent to OHRP, the FDA or others, provided that the Relying Institution promptly provides such comments. Nothing in this Agreement shall prevent a Relying Institution from making its own report or from taking additional remedial steps at its own institution. In limited situations, the use of a confidentiality agreement may be necessary and will be negotiated by the parties.

14. Notify the Relying Institution promptly if the IRB of Record decides to suspend, disapprove or terminate the Research for any reason, including as a consequence of receiving allegations or findings of serious or continuing non-compliance or unanticipated events involving risks to subjects or others. In limited situations, the use of a confidentiality agreement may be necessary and will be negotiated by the parties.

15. Maintain a human subjects research compliance or audit program that can conduct and report the results of "for cause" or random audits.

16. Notify the Relying Institution about the need for an IRB of Record quality assurance/quality initiative audit at the Relying Institution. The IRB of Record may ask the Relying Institution to conduct its own quality assurance/quality initiative and supply results to the IRB of Record or work cooperatively to conduct such a review audit. If the audit results in a report that will be made available externally (e.g., OHRP, National Institutes of Health, FDA, etc.), the IRB of Record will afford the Relying Institution an opportunity (five (5) business days) to comment on the draft report with appropriate consideration of confidentiality.

17. Accept assurances from the Relying Institutions that all PIs and research personnel for the ceded research have met appropriate training requirements.

VIII. Relying Institution Responsibilities.

The Relying Institution agrees that it will, at all times while this Agreement is in effect:

1. Maintain an FWA with OHRP and the registration of its IRB with OHRP and the FDA.

2. Maintain IRB membership that satisfies the requirements of 45 C.F.R. Part 46 and 21 C.F.R. Part 56.

3. Maintain a human subjects protection program, as required by OHRP.

4. Identify and provide the name and contact information of a Relying Institution official who is responsible for, and has authority for, all communication regarding the research.

5. Provide the Relying Institution PI and/or other research personnel involved in the Research a specific contact at the Relying Institution to address any questions or concerns they may have.

6. Ensure that the PIs and other research personnel at the Relying Institution who are involved in the Research are appropriately qualified and meet the Relying Institution's standards for eligibility to conduct Research. This includes, but is not limited to, having the required professional staff appointments, licensure, credentialing, human subjects training required by the Relying Institution, insurance coverage, and background checks for their assigned role in the Research.

7. Perform local analysis of any specific requirements of state or local laws, regulations, policies, standards (social or cultural) or other factors applicable to the research, and notify the IRB of Record of any relevant requirements or results of the analysis that would affect its conduct of the Research. The Relying Institution will provide applicable information to the IRB of Record as appropriate for consideration.

8. Perform local review by other local ancillary committee reviews (i.e., pharmacy, radiation safety, etc.) as applicable and required by Relying Institution's policies and provide applicable information to the IRB of Record as appropriate for consideration.

9. Ensure, as its sole responsibility, the identification and interpretation of the requirements of its applicable state or local laws, regulations, policies, and ancillary review processes as are relevant to the Research and communicate the requirements to the IRB of Record.

10. Ensure that the provisions of the grant or contract for Research (including federally and non-federally funded) are consistent with the approved research protocol and consent form (i.e., provisions in clinical trial agreements that address research-related injuries).

11. Promptly (generally, within two (2) business days) notify the IRB of Record after receiving notice that a Relying Institution's PI(s) or other research personnel involved in the research has been suspended or restricted, and/or after discovering serious or continuing non-compliance or an unanticipated problem that involves risks to subjects or others within the Research. In limited situations, the use of a confidentiality agreement may be necessary and will be negotiated by the parties.

12. Maintain a human subjects' research compliance program that will conduct and report the results of audits. If an audit is performed at the request of the IRB of Record, the Relying Institution will provide a copy of the report of its findings to the IRB of Record. Nothing in this Agreement shall prevent the Relying Institution from conducting its own investigation or "for cause" or random audit. However, any findings of fact made by a Relying Institution will be shared promptly with the IRB of Record to ensure the safe and appropriate performance of the Research at the Relying Institution. In limited situations, the use of a confidentiality agreement may be necessary and will be negotiated by the parties.

13. Ensure an institutional mechanism exists by which complaints about the Research can be made by local Research participants or others. The Relying Institution will promptly report such complaints to the IRB of Record if they meet the criteria of a potential unanticipated event that involves risk to subjects or others.

14. Be responsible for FCOI Compliance for any of its Investigators in accordance with **Exhibit 3.** The Relying Institution will;

a) Ensure that its Investigators submit financial disclosures as required under the Relying Institution's FCOI Policy;

b) Review Investigator disclosures;

c) Determine whether an FCOI exists;

d) Determine for any FCOI whether it is amenable to management; and if so, implement a management plan that will be provided to the IRB of Record for its review, or issue a determination that the FCOI is not manageable and provide that communication to the IRB of Record;

e) Will consider modifications recommended by the IRB of Record (as described in A.8 above); and

f) Be responsible for its Investigators' compliance with management plans implemented by Relying Institution related to the Research.

15. Provide the IRB of Record with all language needed to complete the identified site-specific sections of the study-specific template consent forms approved by the IRB of Record (and, when applicable, the Relying Institution's standard injury compensation language for inclusion in the consent form).

a. The current Virtua Consent Form Requirements for which may be updated by Virtua from time to time, is contained in Virtua's IRB Informed Consent Policy.

b. The current Penn Consent Form Requirements for Multicenter Studies, which may be updated by Penn from time to time, is attached hereto as **Exhibit 5**.

16. Ensure that Relying Institution principal investigators maintain all research records and HIPAA authorizations in accordance with federal and state laws and regulations, as well as any institutional policies and obligations communicated in writing by the PI.

17. The Relying Institutions must:

a. Accept the IRB of Record's determinations for waivers or alterations of HIPAA requirements.

b. Provide the Relying Institution's IRB-approved standard HIPAA authorization language for inclusion in the consent document.

c. Work with the IRB of Record to establish whether a separate HIPAA authorization form will be used for Research or whether HIPAA authorization language will be incorporated into the consent form.

If a separate HIPAA authorization form will be used for Research, the Relying Institution will ensure the accuracy of the information within the form, the

compliance of the form with the HIPAA Privacy Rule, and, as stated in such sections, that the form permits PHI to be used by and disclosed to the IRB of Record, the IRB of Record's Institution, and all Relying Institutions (whether listed individually or described as a group) as necessary for conducting, reviewing and overseeing the Research (including investigation and evaluation of events).

If the HIPAA authorization language will be incorporated into the consent document, the Relying Institution will work with the IRB of Record to provide, as requested, any language specific to the Relying Institution.

In the event that the IRB of Record has communicated to the Relying Institution(s) that it does not, as a matter of policy or otherwise, make research-related HIPAA determinations, the Relying Institution(s) will make such determinations for the Research. Without limiting the foregoing, if in such case a Relying Institution determines that authorization for use and disclosure of PHI is required, it will use a separate (freestanding) authorization form.

18. The Relying Institution may, at any time, choose to change its decision to cede review for the research. In such cases the IRB of Record and Relying Institution will work together to facilitate the transfer of IRB oversight with the goal of limiting the potential disruption to the Research. Until the IRB oversight is transferred the IRB of Record will continue to assume oversight responsibility.

IX. Contact Information.

Any written submissions required under this Agreement shall be addressed and mailed to the addresses indicated below:

Virtua Health:

The Virtua Health Institutional Review Board
1200 Howard Boulevard, Suite 100
Mt. Laurel, NJ 08054
(856) 761-3844

Human Protections Administrator:	Andrea Racobaldo
IRB Chairs:	Erik Delue, MD, Oncology IRB
	Rashida Shakir, MD General IRB
Institutional Official:	Reginald Blaber, MD, EVP and CCO

Penn:

The University of Pennsylvania Institutional Review Board
3600 Civic Center Blvd., 9th Floor
Philadelphia, PA 19104

(215) 573-2540

Human Protections Administrator:	Jessica L. Yoos, MA, M.Phil.Ed., CIP
IRB Chair:	Anil Vachani, M.D.
Institutional Official:	Dawn Bonnell, Ph.D.

X. Compliance with Laws.

Consistent with the terms of this Agreement, each party shall at all times comply with all federal, state, and local laws, ordinances, and regulations in effect and pertaining to the subject matter of this Agreement during the period of this Agreement including without limitation OHRP's Terms of Assurance.

[Intentionally left blank. Signature page follows.]

In witness whereof, the parties have executed this Agreement as of the Effective Date written above.

Digitally signed by Dr Reginald Blaber
DN: cn=Dr Reginald Blaber, o=Virtua, ou=Executive Offices, email=mragodo@virtua.org, c=US
Date: 2022.05.06 08:27:24 -04'00'

Signature of Virtua

Reginald Blaber, MD
Institutional Official
EVP and CCO

Date: _____

DocuSigned by:
Jessica Yoos
D788AE9A45C54C9...

Signed for and on behalf of Penn
Jessica L. Yoos, MA, M.Phil.Ed., CIP
Director, Human Research Protections Program (HRPP)

Date: 5/5/2022

Exhibit 1 – Exemptions (2018 Requirements) 21 CFR §46.104 Exempt research

Exhibit 2 – OHRP Guidance - Engagement of Institutions in Human Subjects Research (2008)

Exhibit 3 - Responsibility for Financial Conflict of Interest Compliance

[Intentionally left blank. See following pages.]

Exhibit 4 – Virtua Health Policy for Informed Consent Form Requirements

[Intentionally left blank. See following pages.]

Exhibit 5 – Penn Consent Form Requirements for Multicenter Studies

Requirements are outlined on the IRB website (see https://irb.upenn.edu/reliance-agreements, Requirements for external consent templates)

Exhibit 3

Responsibility for Financial Conflict of Interest Compliance for Studies conducted at Virtua with participation of Penn Investigators

Virtua and Penn each shall have a Financial Conflict of Interest Policy (FCOI Policy) that is compliant with *Promoting Objectivity in Research,* 42 CFR 50, Subpart F and *Responsible Prospective and Contractors,* 45 CFR 94.

FCOI Compliance Requirements for Virtua Investigators

Virtua's *Public Health Service (PHS) Research Financial Conflict of Interest Policy* (Virtua FCOI Policy) will apply to any Investigator (defined as any individual, regardless of title or position, who is responsible for the design, conduct or reporting of the research) who is a Virtua Medical Group employed or leased physician and/or personnel or a Virtua Health medical staff member participating in research at Virtua sites (hereafter referred to as "Virtua Investigator").

For each Study involving Virtua Investigators, the Virtua Investigators will submit financial disclosures in accordance with Virtua's FCOI Policy, which shall require that Virtua Investigators submit a financial disclosure in connection with each new research project and on annual basis, and which shall be updated as required under Virtua's FCOI Policy.

Virtua shall in accordance with its FCOI Policy review Virtua Investigator disclosures and determine whether a Financial Conflict of Interest (FCOI) exists and if so, either implement a management plan or determine that the FCOI is not manageable and that the Virtua Investigator may not participate in the research unless the FCOI is eliminated.

Within 10 days, Virtua will report to Penn's Research Integrity Office any FCOI determinations and, if found to be manageable, provide a copy of the management plan which shall include the Investigator's written acceptance.

Upon request by Penn's Research Integrity Office, Virtua shall provide to that office documentation related to Virtua Investigators' FCOI compliance (including but not limited to copies of disclosures, review documents, correspondence, and research protocols). This information will be provided with the understanding that its review shall be conducted in confidence by appropriate Penn officials and may only be released by Penn in statistical or aggregate form that protects the Investigator's privacy, or to comply with the requirements of research sponsors, or as may be required to comply with Penn policies and procedures or any applicable legal requirements.

FCOI Compliance Requirements for Penn Investigators

The *University of Pennsylvania Policy on Conflicts of Interest Related to Research* (Penn FCOI Policy) will apply to Penn Medicine / UPHS employees leased to Virtua Health, Penn / Penn Medicine faculty, staff, employees, and personnel, UPHS employees, and Penn Medicine private practice physicians participating in research at Virtua sites (hereafter referred to as "Penn Investigator").

In order to participate in research, Penn Investigators must comply with Penn's FCOI Policy requirements, including but not limited to disclosure requirements and completion of FCOI Training.

Penn shall in accordance with its FCOI Policy review Penn Investigator disclosures and determine whether an FCOI exists and if so, either implement a management plan or determine that the FCOI is not manageable and that the Penn Investigator may not participate in the research unless the FCOI is eliminated.

Within 10 days, Penn will report to Virtua's Research Integrity Office any FCOI determinations and, if found to be manageable, provide a copy of the management plan which shall include the Investigator's written acceptance.

Upon request by Virtua, Penn shall provide to Virtua documentation related to Penn Investigators FCOI compliance (including but not limited to copies of disclosures, review documents, correspondence, and research protocols). This information will be provided with the understanding that its review shall be conducted in confidence by appropriate Virtua officials and may only be released by Virtua in statistical or aggregate form that protects the Investigator's privacy, or to comply with the requirements of research sponsors, or as may be required to comply with Virtua policies and procedures or any applicable legal requirements.

VIRTUA

MANUAL TITLE **INSTITUTIONAL REVIEW BOARD**			**POLICY NAME** **INFORMED CONSENT, BROAD CONSENT; WAIVER/ ALTERATION OF CONSENT**	
MANUAL OWNER **IRB** **POLICY OWNER:** **IRB**	**DATE OF ISSUE** **2002**	**DATE OF LAST REVIEW** **9-18-20**	**DATE OF REVISION** **9-18-20**	**EFFECTIVE DATE** **9-18-20**
REVIEW INTERVAL **36 Months**	**REVIEWED/APPROVED BY: (Committees)** **IRB Chairs, IRB Administrator** IRB MEMBERS,			

THIS POLICY IS APPLICABLE TO: Virtua Health Memorial Hospital Burlington County, Inc; Virtua West Jersey Health System, Inc. ; Virtua Memorial Burlington – Psych; Virtua Health and Rehabilitation at Mt. Holly; Virtua Health and Rehabilitation Center at Berlin; Virtua Home Care – Community Nursing Services; Virtua Home Care at West Jersey; Virtua Health Foundation, Inc; Virtua Our Lady of Lourdes Hospital, Inc.; Virtua Willingboro Hospital, Inc.

1. **Documentation of Consent.** Subject to certain limited exceptions, no investigator may involve a human being in research involving a new drug, biological product or medical device without first obtaining the informed consent of the subject or that subject's legally authorized representative. The informed consent must be documented by the written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy of the written consent that is identical to the form signed by or on behalf of the subject must be given to the person signing the form prior to the commencement of that person's participation in the study.

2. **Minimizing Coercion.** The consent must be sought only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.

3. **Consent Process.** The consent process is as important to the protection of human subjects as is the consent form. Potential subjects should be provided with an explanation of the study and be given an opportunity to ask questions and seek additional information during the consent process.

4. **Plain Language.** The language used in the consent procedure (including printed consent forms) must be understandable to the subject or the legally authorized representative and minimize the use of scientific language. When possible, the target grade level should be written in the subject's native language at a 6th to 8th grade reading level.

5. **Non-English Speaking Persons.** In the event a non-English speaking person wishes to participate in a research study, a certified translation of the approved consent form will be given to the participant. A translator will be provided to orally explain the protocol and to answer any questions the participant may have. The translated consent form should be reviewed by another individual who speaks and reads the language it is written in to validate the content.

6. **Key Information.** The informed consent, as a whole, must present information in sufficient detail organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding the reasons why one might or might not want to participate in the research. The informed consent must begin with a concise and focused presentation of the key information relating to the research that will facilitate comprehension.

   The first page of the consent should contain a "key information" section. This key information should state the following: (1) that the consent is for research; (2) purpose of the research, expected duration of participation and procedures to be followed; (3) reasonably foreseeable risks/discomforts; (4) benefits that may reasonably be expected; (5) appropriate alternatives and procedures. As a whole, the consent must present information in sufficient detail organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the subject's understanding the reasons why one might or might not want to participate in the research.

7. **Exculpatory Language.** No informed consent may include exculpatory language through which the subject or the legally authorized 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.

8. **Required Elements of Informed Consent**: The following information shall be provided to each subject or the legally authorized representative:

   a) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of subject's participation, a description of the procedures to be followed and identification of any procedures that are experimental or investigative.

   b) A description of any reasonably foreseeable risks or discomforts to the subject.

   c) A description of any potential benefits to the subject or to others which may reasonably be expected from the research. The consent must also be clear if no direct benefit is expected.

   d) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject or affect the subject's willingness to participate in the research.

   e) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained, including the possibility that representatives of the institution (such as the IRB) or the FDA may inspect the records for auditing purposes.

   f) 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.

   g) An explanation of whom to contact for answers to pertinent questions about the research and subject's rights and whom to contact in the event of a research-related injury to the subjects.

   h) A statement that participation is voluntary and that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled; and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

   i) For research involving the collection of identifiable private information or identifiable biospecimens, one of the following statements must be included:

      - that the identifiers might be removed 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 legally authorized representative, if this might be a possibility;

- 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

9. **Additional Elements of Informed Consent**.

a) A statement that the particular treatment or procedure may involve unforeseeable risks to the subject (or the embryo/fetus, if the subject is or may become pregnant).

b) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or legally authorized representative's consent.

c) Any additional cost to the subject that may result from participation in the research study.

d)The consequences of the subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

e) A statement that significant new findings developed during the course of the research, which may affect the subject's willingness to continue to participate will be provided to the subject.

f) The approximate number of subjects involved in the study.

g) A statement that the subject's biospecimens (even if the identifiers are removed) may be used for commercial profit and whether the subject will or will not share in the commercial profit.

h) A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.

i) A statement as to whether the biospecimens collected include whole genome sequencing.

10. **Broad consent** for the storage, maintenance and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or for non-research purposes) is permitted as an alternative to the informed consent requirements in paragraph 8 above. If a broad consent is used, the following shall be provided to each subject or the legally authorized representative:

a) A description of any reasonably foreseeable risks or discomforts to the subject;

b) A description of any benefits to the subject or to others that may reasonably be expected from the research.

c) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.

d) 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.

e) a general description of the types of research that may be conducted with the identifiable private information/biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted

f) a description of the identifiable private information/biospecimens that might be used in research, whether sharing of identifiable private information/biospecimens might occur and the types of institutions or researchers that might conduct research with the identifiable private information/biospecimens

g) a description of the period of time that the identifiable private information/biospecimens may be stored and maintained as well as the period of time which it may be used for research purposes (both of which could be indefinite)

h) unless they will be provided details about specific research studies, a statement that the subject/legally authorized representative will not be informed of the details about specific research that might use the subject's identifiable private information/biospecimens, including the purpose of the research and that they might have chosen not to consent to some of those specific research studies.

i) a statement that clinically relevant research results, including individual results, may not be disclosed to the subject

j) contact information for who will answer questions about the subject's rights and about storage and use of the subject's identifiable private information/biospecimens and whom to contact in the event of research-related harm

The following statements should be added, if appropriate:

a) a statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.

b) For research involving biospecimens, whether the research will or might include whole genome sequencing

If the subject refuses to give Broad Consent, the IRB cannot waive consent for the storage, maintenance or secondary research use of the identifiable private information or identifiable biospecimens. Nor can the IRB alter any of the elements of the Broad Consent.

11. **Short Form Consent**. A "short form" written consent document stating that the required elements of informed consent have been presented orally to the subject or the subject's legally authorized representative. When this method is used,

there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary. The person obtaining "short form" consent must be the PI or a co-investigator for the study, who shall sign a copy of the summary. A copy of the summary shall be given to the participant or the representative, in addition to a copy of the "short form."

For non-FDA regulated research studies, the short form written informed consent form must state that the key information required by 45 CFR 46.116(a)(5)(i) (described above) was presented first to the subject, before any other information was provided.

12. **Waiver of Documentation of Consent**: The IRB may waive the requirement for the investigator to obtain a signed informed consent for some or all subjects if it finds any of the following:

a) that the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research and the subject's wishes will govern;

b) that 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; or

c) if the subject or legally authorized representative is a member of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research.

13. **Waiver/Alteration of Consent.** The IRB may waive the requirement to obtain informed consent or alter some or all of the elements of informed consent provided the following requirements are satisfied and documented:

a) the research involves no more than minimal risk to the subjects;

b) the research could not practicably be carried out without the requested waiver or alteration;

c) if the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format

d) the waiver or alteration will not adversely affect the rights and welfare of the subjects; and

e) whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

14. **Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials.** In order to waive or alter these consents, the IRB must find and document that the research or demonstration project could not practicably be carried out without the waiver or alteration. Additionally, that the research is designed to study public benefit or service programs; procedures for obtaining benefits or services under those programs; changes or alternatives to those programs; or possible changes in methods or levels of payment for benefits or services under those programs.

15. **Screening, recruiting, or determining eligibility.** The IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting or determining the eligibility of prospective subjects without informed consent if either of the following conditions are met:

    a) the investigator will obtain through oral or written communication with the subject or legally authorized representative; or
    b) the investigator will obtain identifiable private information/biospecimens by accessing records or stored identifiable biospecimens.

16. **Frequency of Review.** The consent form will be reviewed for appropriateness by the IRB at initial submission and annually, for continuing review; and more frequently, if indicated.

17. **Approved Consents.** A consent form, bearing the IRB approval stamp evidencing the date of approval, must be signed and dated at the time of consent (including in an electronic format) and a copy provided to the person signing the form; the original will be maintained by the investigator. The case history (source document) for each individual shall document that informed consent was obtained prior to participation in the study.

18. **Standard Language.** The IRB has adopted standard language and format to be used in portions of all consent documents unless special circumstances make it inappropriate. It is the investigator's responsibility to ensure that his/her consent conforms to the standard language and format, where appropriate, prior to submitting for the IRB review.

19. **Amendments to Consent.** The following conditions may prompt an amendment of the original consent: (a) the discovery of new information which could affect the subject's willingness to continue participation, or (b) any change in the contact personnel. Any amendments to consent forms must undergo the same IRB review and approval process prior to being given to the subject. Existing subjects should sign new consent forms to assure their understanding of the new information and to provide them an opportunity to reconsider their participation.

20. **ClinicalTrials.gov.** Pursuant to 21 CFR 50.25(c), the following statement must be reproduced word-for-word in informed consents documents for applicable clinical trials. Applicable clinical trials generally include controlled interventional studies (with one or more arms) of drugs, biological products, or devices that are subject to FDA regulation, meaning that the trial

has one or more sites in the United States, involves a drug, biologic or device that is manufactured in the United States (or its territories), or is conducted under an investigational new drug application (IND) or investigational device exemption (IDE). Trial sponsors and investigators have the responsibility of determining whether or not a trial is an "applicable clinical trial." Definitions vary for applicable device and drug trials including biologics.

"A description of this clinical trial will be available on *http://www.ClinicalTrials.gov* as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time."

21. **Posting of clinical trial consent form.** For federally funded clinical trials, one IRB-approved consent form must be posted on a publicly available web site, e.g. ClinicalTrials.gov. The informed consent must be posted after the clinical trial is closed to enrollment but no later than 60 days after the last study visit by any subject.