Institutional Review Board Cooperative Master Agreement Between Lancaster General Hospital and The University of Pennsylvania

TERMS OF AGREEMENT

I. Purpose.

The purpose of this Cooperative Agreement (the "Agreement") between Lancaster General Hospital ("LGH") (FWA # 00006038) 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 LGH 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) LGH will be engaged in human subjects' research through any of the following: participation of one or more LGH Investigators; or use of LGH funding, LGH data, or LGH facilities.

- LGH "Investigators" are defined as Lancaster General Hospital employed physicians and/or personnel or Lancaster General Hospital staff members.
- Penn "Investigators" are defined as Penn / Penn Medicine faculty, staff, employees, and personnel who are not employed by LGH; UPHS employees not employed by LGH; Penn Medicine / UPHS employees leased to Virtua Health; and Penn Medicine private practice physicians not employed by LGH.

This Agreement does not apply if:

- Penn and/or LGH 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 1, 2023 (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 is responsible for maintaining policies regarding FCOI compliance.

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 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, or similar documentation, 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 its relevant policies. 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).

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:

Lancaster General Hospital:

Penn Medicine Lancaster General Health
131 East Frederick Street
Lancaster, PA 17602
717-544-1777

Human Protections Administrator:	Kia Ultz, MS
IRB Chair:	Doreen Bett, DO
Institutional Official:	Edmond K. Kabagambe, DVM, MS, PhD, MBA, FAHA, FACE

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.

Edmond K Kabagambe, DVM, MS, PhD, MBA, FAHA, FACE
Digitally signed by Edmond K Kabagambe, DVM, MS, PhD, MBA, FAHA, FACE
Date: 2023.04.20 18:37:28 -04'00'

Signed for and on behalf of LGH
Edmond K Kabagambe, DVM, MS, PhD, MBA, FAHA, FACE
Vice President of Research Administration

Date: 4/20/2023

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: 4/21/2023

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

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