# RESEARCH INVOLVING HUMANS OR THEIR IDENTIFIABLE DATA OR BIOSPECIMENS

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## 1. PURPOSE

The purpose of this policy is to outline authorities and requirements for the review and conduct of research that involves human subjects or their data or biospecimens.

## 2. SCOPE

This policy applies to Human Subject Research or Clinical Investigations to be conducted, even if only in part, at Aurora Health Care, Inc. (AHC) or any entity or facility owned or controlled (wholly or partially) by AHC, or to be conducted by AHC-employed caregivers.

## 3. DEFINITIONS

**Aurora Information -** All information that is owned by Aurora or owned by third parties but provided to Aurora. For clarification purposes only, information remains “Aurora Information” even if it is in the possession and under the control of a third party (e.g., a third party service provider and/or its subcontractors).

**Clinical Investigation** – Any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration, or is not subject to requirements for prior submission to the Food and Drug Administration, but the results of which are intended to be submitted later to, or held for inspection by the Food and Drug Administration as part of an application for a research or marketing permit.

**Common Rule** – The Common Rule is a federal policy regarding Human Subjects protection that applies to federal agencies and offices that have signed on to the Rule (approximately 17). The main elements of the Common Rule include requirements for assuring compliance by research institutions, requirements for researchers' obtaining and documenting informed consent; requirements for Institutional Review Board (IRB) membership, function, operations, review of research, and record keeping.

**Exempt Research** – Human Subject Research that has undergone review by the Research Subject Protection Program (RSPP) Office and/or limited IRB review and determined to meet exemption criteria within the Common Rule.

**Generalizable Knowledge** – To contribute to generalizable knowledge means the results of the activity are expected to: (a) supplement an established body of knowledge or inform a field of study; (b) be distributed in order to influence behavior, practice, theory or future research design; (c) be applied beyond the subject population or site of data collection to other settings; (d) be replicated in other settings; and/or (e) inform public policy.

**Human Subject** – Either:

(a) a living individual about whom an investigator conducting Research: (i) obtains information or biospecimens through Intervention or Interaction with the individual, and uses, studies or analyzes the information or biospecimens; or (ii) obtains, uses, studies, analyzes, or generates Identifiable Private Information or Identifiable Biospecimens; or
(b) an individual who participates in Research as a recipient of the article being tested or as a control.

**Identifiable Biospecimens** and **Identifiable Private Information** - Biospecimens or Private Information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen or information. The identity of a subject is not considered readily ascertainable or associated with the biospecimen or information if the identifiable information being used for the Research or linked to the biospecimen is limited to those elements contained within a Limited Data Set as defined by the HIPAA Privacy Rule. Conversely biospecimens or private information containing or linked to identifiers beyond those contained within a Limited Data Set are considered identifiable.

**Incidental Findings** – Discoveries of individual-level findings that are unrelated to the goals of the study (e.g., finding an indication of lung cancer in an x-ray done to look for tuberculosis for research exclusion criteria or discovery of a genetic marker unrelated to the goals of the study).

**Institutional Official (IO)** – The individual at AHC who is legally authorized to act for and on behalf of AHC in matters related to its human subject protection program.

**Institutional Review Board (IRB) -** A specially constituted review body established or designated by an entity to protect the rights and welfare of Human Subjects: (1) who are recruited to participate in Research or Clinical Investigations; or (2) whose identifiable private data or identifiable biospecimens are proposed to be used in Research or Clinical Investigations.

**Interaction** – Communication or interpersonal contact between investigator and subject.

**Intervention** – Both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulation of the subject or the subject's environment that is performed for research purposes.

**Limited Data Set** – HIPAA Privacy Rule identified Protected Health Information that excludes the following direct identifiers of the individual or of relatives, employers or household members of the individual: (i) names; (ii) postal address information, other than town or city, state and zip code; (iii) telephone numbers; (iv) fax numbers; (v) email addresses; (vi) social security numbers; (vii) medical record numbers; (viii) health plan beneficiary numbers; (ix) account numbers); (x) certificate/license numbers; (xi) vehicle identifiers and serial numbers including license plate numbers; (xii) device identifiers and serial numbers; (xiii) web universal resource locators (URL); (xiv) internet protocol (IP) address numbers; (xv) biometric identifiers, including finger and voice prints; and (xvi) full face photographic images and any comparable images information. A Limited

Data set therefore contains only the following indirect identifiers of the individual or of relatives, employers or household members of the individual: city, state, zip code, dates and other health information that does not contain HIPAA direct identifiers.

**Principal Investigator** - The physician or other individual assuming primary and ultimate responsibility for the conduct of a research project.

**Private Information** – Either:
(a) information that has been provided for a specific purpose by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record); or
(b) information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place.

**Research** – Either:
(a) a Systematic Investigation, including research development, testing and evaluation, designed to develop or contribute to Generalizable Knowledge; or
(b) the use of a drug, biologic or device for a purpose or in a manner other than in the course of medical practice; or
(c) the gathering of data that will be submitted to or held for inspection by FDA in support an FDA marketing permit.

**Research Subject Protection Program (RSPP) Office** – The administrative support unit within AHC for the IO and any appointed IRBs.

**Systematic Investigation** – An activity that involves a prospectively identified approach and that incorporates data collection and either quantitative or qualitative data analysis to answer a question or draw conclusions.

## 4. POLICY

### 4.1 Guiding Principles

All Human Subject Research and all Clinical Investigations conducted at Aurora Health Care (AHC) or by researchers employed by AHC will be guided by the ethical principles set forth in the Belmont Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

### 4.2 General Requirements

a) All Human Subject Research and all Clinical Investigations are subject to oversight under AHC's RSPP and must abide by RSPP and Aurora Research Institute (ARI) procedures and guidelines, and AHC system policies, as applicable.

b) All Human Subject Research and all Clinical Investigations must be submitted to the RSPP Office for coordination of review and approval by AHC's IRB, for the ceding of review to an external IRB, or for an exemption determination. When uncertainty exists about whether the activity is Human Subject Research or a Clinical Investigation, the activity must be submitted to the RSPP Office for a determination.

c) IRB review and approval must occur prior to the conduct of the Human Subject Research or Clinical Investigation.

d) Principal Investigators have primary responsibility for ensuring the welfare of subjects involved in Human Subject Research or Clinical Investigations and for protecting their rights. The IRB providing oversight of the research and others engaged in the review and conduct of the research share this responsibility.

e) Attempts to inappropriately influence RSPP caregivers, IRB Chairs, IRB members or the IO in the performance of their duties will not be tolerated and should be reported to the IO or Chief Medical Officer.

f) Neither AHC nor any of its leaders or others may approve the conduct of Human Subject Research or a Clinical Investigation that has been disapproved by Aurora's IRB or an IRB to which review has been ceded. Additional institutional approvals may be required, and AHC research leaders at the Senior VP level and above, in consultation with the IO, may disapprove research approved by an IRB or may impose conditions on the conduct of such research.

g) Regulated Research

i) Human Subject Research and Clinical Investigations subject to federal regulation, including but not limited to the Federal Policy for the Protection of Human Subjects known as the Common Rule, FDA regulations (21 CFR 50, 21 CFR 56, 21 CFR 312 & 21 CFR 812), State law, and privacy and security regulations (45 CFR 160 and 164), will be reviewed and conducted in accordance with applicable regulatory requirements.

ii) When Human Subject Research is funded by the U.S. Department of Health and Human Service (DHHS), requirements of AHC's Federal Wide Assurance with DHHS's Office of Human Research Protection (OHRP) will also be met. This includes, but is not limited to, the application of additional protections found in subparts B, C, and D of 45 CFR 46 for research involving pregnant women, fetuses and neonates, prisoners, and children.

iii) In cases where more than one regulation is applicable and regulatory requirements conflict, the more restrictive regulation shall prevail. Aurora Legal will be consulted as needed.

h) Un-regulated Research Involving Human Subjects

i) Human Subject Research not regulated by federal regulation will be reviewed and approved by AHC's IRB in accordance with the requirements of DHHS regulations, with the following exceptions:

1) Requirements at Subparts B-D of 45 CFR 46 may be incorporated as the IRB determines appropriate on a study-by-study basis.

2) Consent form posting at a public website as mandated by .116(d) is not required.

3) Reporting of suspensions, terminations, unanticipated problems involving risks to subjects and others, and serious and continuing noncompliance to OHRP and federal agencies and departments as mandated by .108.(a)(4)(i-ii) and .113 is not required. These occurrences must still be reported to the IRB and the IO.

4) The requirement for single IRB review for cooperative research at .114(b)(1) is not required. RSPP will, after incorporating stakeholder review, establish and publish criteria for studies other than those mandated by federal regulation or policy that may be ceded to another IRB for review. For any ceded study, an appropriate agreement or equivalent mechanism will outline the responsibilities of the party ceding review and the IRB of Record.

5) The concise summary as mandated by .116(a)(5) is not required.

ii) In addition to the exceptions noted above, unregulated Human Subject Research approved by an IRB prior to the compliance date of the revised Common Rule (first published in the January 19, 2017 issue of the Federal Register) and transitioned to the revised Common Rule on or after the revised Rule's compliance date will, as allowed by .101(l)(3), continue to follow the informed consent and informed consent waiver requirements found at .116 & .117 of the Common Rule in effect at the time the revised Rule was published.

i) The Common Rule's option of broad consent will not be available to researchers involving AHC patients or their health information until an AHC-wide system is in

place to address the requirement to track those who decline or fail to respond to a request to provide broad consent. This system and its requirements will be detailed in RSPP operating procedures.

j) If AHC's research subject protection program is accredited, additional requirements as dictated by accreditation standards may apply to all Human Subject Research and/or Clinical Investigations. Any additional requirements as a result of accreditation will be detailed in RSPP operating procedures.

k) Research involving the use and/or disclosure of Protected Health Information (PHI) will be conducted in accordance with system policy *Use and/or Disclosure of Protected Health Information in Research.*

l) Research involving the use of biospecimens will be conducted in accordance with system policy *Biospecimen Use in Research*.

m) Research involving the use of Aurora Information will comply with system policy *Information Classification.*

n) The review of Human Subject Research or Clinical Investigations ceded to an external IRB must meet applicable regulatory requirements or equivalent protections.

**4.3** Additional Requirements

The following additional requirements apply to Human Subject Research and Clinical Investigations as applicable:

a) Annual Reporting Reminder. Unless AHC's IRB has otherwise determined and justified the need for a continuing review of Human Subject Research, Principal Investigators will be reminded by the RSPP Office on an annual basis of the need to report unanticipated problems, changes to the research (including study closure) and noncompliance in accordance with RSPP procedures for the following studies that do not otherwise require continuing review: (1) studies eligible for expedited review under the Common Rule; and (2) studies that have progressed to the point that they involve only data analysis or accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care. This annual reminder does not apply to Clinical Investigations which are required by FDA regulation to undergo at least annual continuing review.

b) Any additional broad requirements (i.e., not study specific) beyond those articulated above may be initiated by the IO and RSPP Office after stakeholder review. This section of the policy shall be amended to reflect any additional requirements.

**4.4** Authorities, Responsibilities and Functions

All Aurora caregivers have an obligation to protect the rights and welfare of Human Subjects involved in Research and Clinical Investigations. Specific authorities and responsibilities of key parties are delineated below:

a) Institutional Official (IO)

AHC's IO shall have overall responsibility for the Human Subject protection program. This includes but is not limited to the following authorities and responsibilities:

i) Promoting an institutional culture of respect and conscience so that the ethical conduct of Human Subject Research and Clinical Investigations is supported at the highest levels of AHC.

ii) Ensuring effective institution-wide communication and guidance on Human Subject Research and Clinical Investigations.

iii) Ensuring that investigators, IRB chairs, IRB members and RSPP caregivers possess adequate knowledge to conduct and review research in accordance with ethical standards, applicable regulations, institutional policy and RSPP procedures.

iv) Obligating AHC to the terms within the Federal Wide Assurance with the OHRP and to the terms within IRB reliance agreements.

v) Being AHC's official point of contact with OHRP and other federal agencies in matters related to human subject protection.

vi) Ensuring the appropriate allocation of resources, space and staff necessary to comply with all human subject protection regulations, policies and requirements, including but not limited to the IRB's review and recordkeeping duties.

vii) Providing guidance and direction to AHC's RSPP Office in fulfillment of its responsibilities and all matters governed by this policy.

viii) Ensuring the recruitment and appointment of qualified IRB chairperson(s) and members to one or more IRBs as deemed necessary and appropriate, and suspending or terminating appointments of these same individuals if they are not fulfilling their responsibilities. The IO shall not chair or be a member of any AHC IRB.

ix) Ensuring that the performance of the IRB chairs and members is periodically evaluated.

x) Reviewing and approving procedures to implement this policy and other applicable regulatory requirements, as well as working with RSPP to enforce compliance as necessary.

xi) Leading decision making regarding accreditation for the human subject protection program, and if accreditation is sought, ensuring cooperation from leaders responsible of all components of the human research protection program (i.e., IRB, investigator, institution).

xii) When there is insufficient time to bring a situation to the overseeing IRB, suspending some or all parts of an approved activity as necessary to protect the safety and welfare of human subjects or delegating this authority to IRB chairperson(s).

xiii) If desired, developing a charter, appointing members, and chairing an advisory committee to provide guidance and recommendations on matters pertaining to the continuance and improvement of AHC's human subject protection program. If established, the advisory committee shall include representation from at least the following areas: (1) RSPP leadership; (2) IRB membership; (3) Aurora Research Institute leadership; (4) Research Compliance; (5) Legal; and (6) Researchers.

xiv) As necessary or if conflicted, seeking advice and/or deferring authorities and responsibilities to AHC's Chief Medical Officer.

b) Research Subject Protection Program (RSPP) Office

Aurora's RSPP Office shall serve as the administrative support unit for the IO and any appointed IRBs. RSPP responsibilities include but are not limited to:

i) Maintaining and ensuring compliance with Federal Wide Assurance (FWA) terms and conditions, as applicable. RSPP's leader will serve as the Human Protections Administrator for purposes of the FWA.

ii) With assistance from AHC Legal, Compliance and the IO, interpreting and conveying regulatory requirements pertaining to Human Subject Research and Clinical Investigations.

iii) Assisting the IO in the maintenance of Institutional Review Board(s) that meets applicable regulatory requirements in regard to its membership and/or, in consultation with Aurora Legal, ceding review only to qualified

external IRBs as deemed appropriate and as delineated in RSPP operating procedures.

iv) Serving as the administrative unit for any AHC IRB.

v) Ensuring that any AHC's IRB functions independently, but in coordination with other required committee (e.g., biosafety, radiation safety) or administrative (e.g., Aurora Research Institute pre-authorization) approvals.

vi) Guiding any AHC IRB in the timely and effective performance of its responsibilities and authorities, and ensuring all regulatory requirements are met in the review and approval of Human Subject Research or Clinical Investigations.

vii) In consultation with appropriate stakeholders, establishing, revising as necessary, and implementing written operating procedures and guidelines as required by regulation, AHC's FWA, AHC policy, and any applicable accreditation standards.

viii) Educating and providing guidance to IRB members, researchers and others reviewing, engaged in or contemplating the conduct of Human Subject Research or Clinical Investigations.

ix) Grant and document exemption determinations.

x) Making determinations as to whether or not an activity is Research that involves Human Subjects, whether or not the Research is a Clinical Investigation, and whether or not AHC is engaged in the activity.

xi) Coordinating and ensuring that effective and timely communication and reporting occurs between the IRB, investigators, IO and federal agencies as required by regulation and this policy.

xii) Reminding investigators of IRB reporting requirements.

xiii) Require actions or changes in connection with researcher or study team noncompliance that is not serious or not continuing noncompliance.

xiv) Taking other actions as necessary to ensure compliance with federal, state and local law, relevant AHC policies and RSPP procedures.

xv) Maintaining records related to responsibilities noted above as required by regulation and as detailed in AHC's policy *#223-Record Retention, Storage and Destruction*.

c) Institutional Review Board (IRB)

Any AHC IRB(s) shall have all the authorities granted to an IRB by federal, state and local regulation and AHC policy. Additional authorities may be granted to any AHC IRB by the IO after communication of the rationale for those additional authorities to stakeholders and consideration of stakeholder input. Stakeholder input is not required when additional authorities impact only IRB operations. This section of this policy shall be amended to reflect any additional authorities granted. The process in which AHC IRB's fulfill their responsibilities will be documented in operating procedures.

Authorities and responsibilities granted to AHC's IRB(s) include:

i) reviewing and approving, requiring modification or additional information to secure approval, or disapproving Clinical Investigations, non-exempt Human Subject Research, Humanitarian Use Device uses, and exempt Human Subject Research for which limited IRB review is a condition of exemption;

ii) conducting continuing review in accordance with regulatory requirements and providing justification when exceeding those requirements;

iii) requiring verification of information from sources other than the investigator;

iv) as deemed necessary for the protection of subjects, suspending or terminating IRB approval of Research not being conducted in accordance with IRB or regulatory requirements or that has been associated with unexpected serious harm to subjects or others;

v) observing or having a third party observe the consent process and conduct of the research;

vi) waiving or altering written authorization required by the HIPAA Privacy Rule for research uses or disclosures of protected health information;

vii) determining whether research can move forward under proposed management plans or whether additions to the management plan are necessary (see AHC system policies *#269-Conflicts of Interest in Research-Individual* and *#270-Conflicts of Interest in Research-Institutional*);

viii) being available for consult if questions arise regarding actionable Incidental Findings. The IRB shall not dictate action to be taken since Incidental Findings are generally clinical issues.

## 5. PROCEDURE

Procedures implementing this policy and applicable Human Subject Research and Clinic Investigation regulation will be developed by RSPP, with stakeholder input, and maintained on the RSPP website.

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| **CROSS REFERENCES:** | AHC system policy #269 - Conflicts of Interest in Research-Individual<br>AHC system policy #270 - Conflicts of Interest in Research-Institutional<br>AHC system policy #140 - Use and/or Disclosure of PHI for Research<br>AHC system policy #223 - Record Retention, Storage and Destruction<br>AHC system policy #263- Biospecimen Use in Research<br>AHC system policy #288 – Information Classification |
| **OWNER:** | Institutional Official |
| **REFERENCES:** | Federal Wide Assurance (FWA) for the Protection of Human Subjects<br>Federal Policy for the Protection of Human Subjects (Common Rule)<br>21 CFR 50 – Protection of Human Subjects (Food and Drug Administration)<br>21 CFR 56 – Institutional Review Board (Food and Drug Administration<br>August 2, 2017 Letter to the HHS Secretary, Attachment F – Recommendations on Reporting Incidental Findings |
| **PRIOR REVIEW / REVISION DATES:** | |