

## STATEMENT OF AUTHORITY AND PURPOSE

Steering Committee approved 2/2511

In 2001, Aurora Health Care's ("Aurora") President & CEO and Board of Directors established the Research Subject Protection Program ("RSPP") as part of Aurora's ongoing commitment to the protection of human subjects participating in research conducted by the physicians and staff of Aurora.

The RSPP is responsible for the overall coordination and administration of the two duly constituted IRBs that oversee research conducted at all Aurora Facilities: Aurora IRB Behavioral and Aurora IRB Biomedical (collectively referred to as "Aurora IRB"). The RSPP provides guidance and support to investigators and research coordinators in the preparation, pre-review, and ongoing oversight of human subject research conducted at Aurora.

The RSPP also provides the following administrative functions to ensure the ethical and legal conduct of human subject research at Aurora:

- Coordination of IRB meetings;
- Interpretation of regulatory requirements pertaining to human subject research;
- Development of policies and procedures to assure compliance with institutional and federal and state regulations and laws and accreditation standards;
- Maintenance of records pertaining to human subject research activities;
- Education of IRB members; and
- Participation in the ongoing education of investigators and research teams regarding human subject protection issues.

### 1. Governing Principles

The RSPP is guided by the ethical principles applied to all research involving humans as subjects, as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, titled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report"). These principles are defined in the Belmont Report as follows:

- **Beneficence** — The sum of the benefits to the subject and the importance of the knowledge to be gained outweigh the risks to the subjects as to warrant a decision to allow the subject to accept these risks.
- **Respect for Persons** — Legally effective informed consent is obtained, unless the requirements for waiver of informed consent are met by adequate and appropriate methods in accordance with the provisions of applicable regulations.
- **Justice** — The selection of subjects is equitable and is representative of the group that will benefit from the research.

Clinical trials will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with GCP and the applicable regulatory requirements.

### 2. Authority

The RSPP manages the Aurora IRB, which has been established by and empowered under the auspices of Aurora executive authorities, and, by Aurora's Federal Wide Assurance (FWA) with the federal

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Office for Human Research Protections (OHRP). Each of the individual Aurora IRBs subscribes to the same underlying principles and authorities. Aurora requires that **ALL** research projects involving humans as subjects (including involvement of humans in one or more of the categories of research exempted or waived under the federal regulations), or the use of identifiable protected health information be reviewed and approved by the assigned IRB prior to initiation of any research related activities, including recruitment and screening activities. The Aurora IRB is the sole body designated to make human subject research determinations.

Any action taken by one of the Aurora IRBs relating to a research study involving human subjects will be recognized as an action of the Aurora IRB and shall be sufficient to authorize the conduct of the study: 1) at any Aurora Facility (see Glossary for definition), 2) a non-Aurora institution that has entered into an IRB Authorization Agreement or 3) where an independent investigator has agreed to follow Aurora IRB Policies and Procedures as attested by their signature on the *Investigator Assurance for Research Involving Human Subjects* page of Aurora IRB submission form (Form FO 301-A) on file with the RSPP.

The Aurora IRB is established to review biomedical and behavioral research involving human subjects regardless of the source of funding or location of the study to ensure the protection of the rights and welfare of human subjects who participate in such studies. Except for research in which the only involvement of humans is in one or more of the categories exempted or waived under 45 CFR 46 §101(b)(1-6) or 101(i) as determined by the Aurora IRB, all research involving human subjects, and all other activities which even in part involve such research, regardless of sponsorship, are subject to these policies and procedures if one or more of the following apply:

- The research involves an Aurora patient, employee or member of the medical staff as a research subject;
- The research is sponsored by institutional authorities of any Aurora Facility;
- The research is conducted in whole or in part by or under the direction of any employee, faculty, student, member of the medical staff or an allied health professional on the medical staff of a hospital, clinic, or physician group, or any other entity that has entered an affiliation agreement with Aurora or any Aurora Facility, in conjunction with his or her Aurora responsibilities;
- Aurora is considered to be “engaged” in research (OHRP Guidance document entitled *Guidance on Engagement of Institutions in Human Subjects Research*, October 16, 2008); or
- The research involves the use of Aurora’s medical records containing protected health information.
- The Aurora IRB reserves the right to defer the review of the research study to another IRB if the research is conducted at a non-Aurora Facility or under other appropriate circumstances as determined by the RSPP Manager, and in consultation with the Institutional Official when necessary.

The Aurora IRB has the authority to ensure that research is designed and conducted in such a manner that protects the rights and welfare of participating subjects. Specifically:

- The Aurora IRB may disapprove, modify or approve studies based upon consideration of human subject protection aspects;
- The Aurora IRB reviews, and has the authority to approve, require modification in, or disapprove, all research activities that fall within its jurisdiction;

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- The Aurora IRB has the authority to conduct continuing review as it deems necessary to protect the rights and welfare of research subjects, including requiring progress reports from the investigators and auditing the conduct of the study, and observing the informed consent process and the conduct of the research, and observing and auditing the progress of any study under its jurisdiction, as it deems necessary to protect the rights and welfare of human subjects;
- The Aurora IRB may suspend or terminate approval of a study; and
- The Aurora IRB may place restrictions on a study.

Regarding federally funded research, if the study is part of an application to a federal sponsoring agency, the research protocol must be reviewed by the Aurora IRB before or when the application is processed and prior to expenditure of any grant funds.

The Aurora IRB also has a relationship to other Aurora institutional review committees (e.g., regional review committees, Radiation Safety, etc.). The Aurora IRB functions independently of, but in coordination with those other committees. Research that has been reviewed and approved by the Aurora IRB may be subject to review and disapproval by the Institutional Official, applicable Site Administrator of the Facility, or other committees. However, those officials or committees may not approve research if it has not been approved by the Aurora IRB.

### 3. Accountability and Administrative Oversight

A. In the fulfillment of its functions the Aurora IRB shall be accountable to the Institutional Official and, by virtue of his or her reporting duties, ultimately to the Aurora Board of Directors. The Institutional Official, or his or her designee, shall be directly responsible for overseeing the operations of each Aurora IRB and for reporting to the Aurora Board of Directors with respect to the operations of each IRB as he or she deems necessary or appropriate.

B. Even if a research study has been approved by the Aurora IRB, the Institutional Official, in consultation with a respective IRB Chair, or the Site Administrator(s) of the Facility, Facilities or other entity where the research study will be conducted, or the Vice President of Research and Academic Relations, may disapprove or impose any condition to the conduct of such research study at such Facility or entity. However, neither the Institutional Official nor any Site Administrator nor the Vice President of Research and Academic Relations shall have the authority to approve the conduct of a research study or any use of an investigational drug or investigational device at a facility when the Aurora IRB has not approved the research study.

C. Any Aurora IRB Chair may consult with another IRB Chair, the Institutional Official, RSPP Manager, or a member of a facility's medical staff leadership regarding a research study.

### 4. Definitions of Human Subject Research

Under the Organization's policies and procedures an activity is human research if it is described in any one of the following:

- FDA regulations
- DHHS regulations or other Common Rule Regulations

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### A. Human Subject Research Under FDA Regulation

Activities are human research under FDA regulations when they meet the FDA definition of “research” (21 CFR §50.3(c), 21 CFR §56.103(c), 21 CFR §312.3(b), or 21 CFR §812.3(h)) and involve a “subject” as defined in FDA regulations (21 CFR §50.3(g), 21 CFR §56.103(e), 21 CFR §312.3(b), or 21 CFR §812.3(p)).

Under FDA regulations activities are “research” when they involve:

- a. Use of a drug other than the use of an approved drug in the course of medical practice (21 CFR §312.3(b));
- b. Use of a medical device other than the use of an approved medical device in the course of medical practice (Food, Drug and Cosmetic Act §530(g)(3)(a)(i)) to evaluate the safety or effectiveness of that device (21 CFR 812.2(a)); or
- c. Gathering data that will be submitted to or held for inspection by FDA in support of a FDA marketing permit for a food, including a dietary supplement that bears a nutrient content claim or a health claim, an infant formula, a food or color additive, a drug for human use, a medical device for human use, a biological product for human use, or an electronic product- (21 CFR §50.1(a), or 21 CFR §56.101(a)).

In the above criteria “approved” means “approved by the FDA for marketing.”

Under FDA regulations, individuals are considered “subjects” when they become participants in research, either as a recipient of the test article or as a control (21 CFR §50.3(g), 21 CFR §56.103(e), 21 CFR §312.3(b)). If the research involves a medical device, individuals are considered “subjects” when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control (21 CFR §812.3(p)).

The following activities are not human subject research but also require IRB review under FDA Regulations 21 CFR 56 (but do not require IRB review under 21 CFR 50): humanitarian device use under 21 CFR 814.3(n) and 814.124.

### B. Human Subject Research Under DHHS or Other Common Rule Regulations

Activities are human subject research under DHHS regulations when they meet the DHHS definition of “research” (45 CFR §46.102(d)) and involve a “subject” as defined in DHHS regulations (45 CFR §46.102(f)).

Under DHHS regulations activities are “research” when they are a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge (45 CFR §46.102(d)).

Under DHHS regulations “subjects” means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information (45 CFR §46.102(f)).

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes (§46.102(f)).

Interaction includes communication or interpersonal contact between investigator and subject (45 CFR §46.102(f)).

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect

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will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects (45 CFR §46.102(f)).

Human subject research that is approved by the Aurora IRB and involves children as subjects may not be conducted outside the state of Wisconsin.

### 5. Responsibility

#### A. Aurora IRB Review of Research

Unless otherwise provided herein, all research involving human subjects, and all other activities, which even in part involve such research, in which an Aurora Facility is engaged in research, must be reviewed and approved by the Aurora IRB regardless of sponsorship. Other IRBs formally designated by Aurora also have the authority to review and approve human subject research conducted at an Aurora Facility.

No intervention or interaction with human subjects in research, including recruitment, may begin until the Aurora IRB (or other designated IRB) has reviewed and approved the research protocol. Specific determinations as to the definition of “research” or “human subjects,” and their implications for the jurisdiction of the Aurora IRB under institutional policy, are determined by the Aurora IRB.

All individuals involved in human subject research have an obligation to protect the rights and welfare of human subjects. This obligation is the Aurora IRB’s primary purpose and responsibility. The Aurora IRB reviews and oversees such research to ensure that it meets well established ethical principles and that it complies with federal regulations at 45 CFR 46 and 21 CFR 50 and 56, that pertain to human subject protection, as well as any other pertinent regulations and guidelines, such as the Good Clinical Practice (GCP) Guideline (E6) of the International Conference on Harmonisation, and the Privacy Standards under HIPAA. The Aurora RSPP helps to ensure that Aurora Facilities are aware of research being conducted within their facility.

Investigators must contact the RSPP office for guidance before engaging in the following activities:

- Any clinical investigation that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration (FDA) under relevant investigational drug or medical device provisions of the Food, Drug, and Cosmetic Act, or clinical investigations that need not meet the requirements for prior submission to the FDA, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.
- Collection of data about a series of standard procedures or treatments for dissemination or generalization.
- A patient’s care or assignment to intervention is altered for research purposes in any way.
- A diagnostic procedure for research purposes that is added to a standard treatment.
- Systematic investigation involving innovative procedures or treatments, for example, if a physician plans to collect information about the innovation for scientific purposes or will repeat the innovation

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in other patients in order to compare it to standard treatment and his/her intent is to contribute to generalizable knowledge.

- Emergency use of an investigational drug or medical device or humanitarian use device (HUD). Note that when emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research subject, and data generated from such care *cannot be included in any report of a research activity*. Nonetheless, consent should be obtained from the subject or his/her Legally Authorized Representative whenever possible.
- Human cell or tissue (genetic tissue) research that typically involves repositories that collect, store, and distribute human tissue materials for research purposes. However, human cell or tissue repository activities *do not require* Aurora IRB review if material submitted to the repository satisfies *both* of the following conditions: (i) The material, in its entirety, was collected for purposes other than submission to the repository (e.g., the material was collected solely for clinical purposes, or for legitimate but unrelated research purposes, with no “extra” material collected for submission to the repository); and (ii) The material is submitted to the repository without private identifiable information as defined under DHHS regulations. No codes or links of any sort may be maintained, either by the submitter or by the repository, that would permit access to identifiable private data about the living individual from whom the material was obtained.
  - Investigator-initiated research, where an investigator both initiates and conducts, alone or with others, a clinical trial. In the case of investigator-initiated studies, it is the investigator’s responsibility to keep the Aurora IRB informed of events and information that requires reporting in accordance with Policy RR 403.
- Case studies in which a series of subject observations are compiled in such a way as to allow possible extrapolation or generalization of the results from the reported cases.
- Failure to Submit a Project for Aurora IRB Review

The implications of engaging in research without obtaining appropriate approval are significant. Results from such studies may not be published unless Aurora IRB approval had been obtained prior to collecting the data. To do so is in violation of Aurora policy. It is also against the policy of Aurora to use those data to satisfy thesis or dissertation requirements. The Aurora IRB will not retrospectively approve data already collected for human subject research purposes. Questions regarding data collection and whether they constitute research as defined by the federal regulations (e.g. quality assurance projects, patient databases, etc.), should be discussed with the RSPP office prior to implementation.

Results of human subject research conducted without appropriate Aurora IRB approval cannot be published. Furthermore, FDA may reject such data if it is submitted in support of a marketing application. Finally, if an investigator conducts research at any Aurora Facility that requires Aurora IRB approval, such conduct should be reported to the RSPP office. The RSPP Manager will then begin the noncompliance process (see SOP CO 601).

## MISSION STATEMENT

### of the Aurora Research Subject Protection Program (RSPP) and Aurora IRBs

The Aurora RSPP and the Aurora IRBs, working together with employees and staff of Aurora Health Care, will

- **R**eview and approve research proposals according to the ethical principles and guidelines of the Belmont Report, the applicable sections of the Code of Federal Regulations, and the International Conference of Harmonisation Good Clinical Practice guidelines;
- **S**afeguard the rights, welfare, and dignity of the humans subjects who participate in the research process;
- **P**romote the highest ethical standards for conducting research; and
- **P**rovide a strong foundation of knowledge and cooperative education to facilitate the conduct of biomedical and behavioral research.