

Submission Form Version Tracking Date:

AURORA IRB Protocol for Research Involving Human Subjects Initial Submission Application
<i>Facilities where research will be conducted:</i> Select a site Select a site Select a site Select a site Select a site AMG/Aurora Clinic (list sites): _____ VLCC (list sites): _____

Removed Regions

For IRB Office Use Only

SECTION I: GENERAL INFORMATION

Protocol Title (include sponsor's protocol number at end of title):			
Principal Investigator (including degrees):		Department/Office:	
PI's Mailing Address:			
PI's Telephone:	PI's Fax:	PI's E-mail:	
List all Co- and Sub-Investigators (including earned degrees):			
If investigators are physician's, indicate types of practice (including sub-investigators):			<input type="checkbox"/> AMG / <input type="checkbox"/> Private Practice
Study sponsor or funding source (Identify all source(s) of funding for the project):			Is this study federally funded? Choose One
Primary contact person who will be responsible for the research files/documents/correspondence with the RSPP office regarding this study:			
Mailing Address:			
Telephone:	Fax:	E-mail:	

SECTION II: SUBMISSION CHECKLIST

Check	Item required	Number of copies
Completed Submission Form with original signatures (can be submitted with signatures pending)	Submit the file electronically to IRB.office@aurora.org (complete protocol title must be referenced in the e-mail)	ORIGINAL + 2 COPIES ELECTRONIC
Informed consent document using Aurora IRB's recommended template language	Submit the file electronically to IRB.office@aurora.org (complete protocol title must be referenced in the e-mail)	ORIGINAL + 2 COPIES ELECTRONIC
Check if you are requesting Waiver of informed consent requirement(s) (justify in Section V)		JUSTIFY
Complete protocol from sponsor / Date including version or revision numbers: _____		3 COPIES
Sponsor's sample informed consent document		3 COPIES
Investigator's Brochure, Package Insert (for approved drugs), or Device Operator's Manual		2 COPIES
Date including tracking numbers: _____		ELECTRONIC, if available
Grant application if HHS-supported and Aurora is awardee institution (http://www.hhs.gov/ohrp/humansubjects/guidance/aplrev.htm)		1 COPY
Pending	NIH Tutorial training certificate for all investigators listed above http://phrp.nihtraining.com/users/login.php	COPY, unless already on file in RSPP office
Pending	Surveys, questionnaires, case report forms	3 COPIES
Pending	Recruitment materials (fliers, posters, etc.) and all materials to be seen by subject (diary/s, information cards)	3 COPIES
Pending	Form SC 502A for Preparatory to Research Activities	ORIGINAL
Pending	PI's current CV or other supporting material evidencing clinical privileges necessary to conduct research study	ORIGINAL
Pending	For IND or IDE studies, Signed FDA Form 1571, 1572, or investigator's agreement (device studies)	1 COPY
Pending	Form GA 104A Conflict of Interest Statement signed by each investigator listed above	ORIGINALS

Please note: The IRB meeting agenda has a limit of 10 protocols per meeting. The RSPP office must receive all of the above items (unless PENDING is listed an option for you to choose) by the submission deadline to be considered a complete submission. Electronic submission of the forms will not be considered a complete submission, nor will it hold a place on the IRB agenda. If there are extenuating circumstances, you may call the RSPP Manager to request a deadline extension; however, extensions are not guaranteed.

SECTION III

A. Expected duration of project (for multicenter studies, give sponsor's expected duration)

From _____ to _____

B. Subject selection

Estimated total number of subjects (at all sites): _____ / Number of control subjects (at all sites): _____

Estimated number to be enrolled by Principal Investigator (and designees) at Aurora sites: _____

C. FDA Determination(s)

Has this study been reviewed by, and determined to require oversight, by the FDA? **Choose One**

Note: The fact that the study may use FDA approved drug(s) or device(s) does not automatically exempt the study from IND or IDE requirements. Contact the study sponsor for guidance.

Does this study involve the use of a: [NOTE: you may answer YES to more than one of the following categories.]

1. **DRUG: Choose One**
2. **DEVICE: Choose One**
3. **BIOLOGIC: Choose One**

If you answered **YES** to any of the categories above, you must complete the questions below associated with that category.

If **DRUG** is answered **YES**:

List ALL of the drugs being used in the research study:

You must answer the following questions for **ALL** of the drugs being used in the research study. If you need more space than that provided below (i.e. there is more than one drug being used in the research study), download the **FDA Determination – Drug** form from the IRB web site, and completed for each of the other drugs in the study.

Name of drug (#1): _____

Is there an IND number assigned to the drug? **Choose One**

IF **YES** [to IND number]:

Enter the IND # _____

Who holds the IND? **Choose One**

Will the drug be provided by the sponsor without cost to the institution or subject? **Choose One**

If the IND number(s) is not listed within the sponsor's protocol, attach a copy of one of the following for each drug with an IND number:

- Communication from the sponsor of the protocol verifying the IND number.
- Communication from the FDA verifying the IND number.

IF **NO** [to IND number], you must check ONE of the following:

- This is an approved drug that is lawfully marketed in the United States, and the study is within its approved indications for use. *Please include a copy of the package insert with your protocol submission.*
- The sponsor has received a letter of IND exemption from the FDA. If this is the case, attach a copy of the IND exemption letter to the submission.
- If the drug is not being used within its approved indications for use, or the sponsor has not received a letter of IND exemption, the following questions must be answered so the IRB can make an IND exemption determination:
- Does the sponsor intend for the investigation to be reported to the FDA in support of a new indication for use or any other significant change in labeling of the drug? **Choose One**
 - Does the sponsor intend for the investigation to be reported to the FDA in support of a significant change in the advertising for the drug? **Choose One**
 - Does the investigation involve 1) a route of administration, 2) a dosage level, 3) use in a population, or 4) other factor that significantly increases the risk (or decreases the acceptability of the risks) associated with the use of the drug product? **Choose One**
 - Will the investigation be conducted in compliance with the FDA requirements for promotion and charging for investigational drugs (found in 21 CFR 312.7)? **Choose One**

If **DEVICE** is answered **YES**:

List ALL of the devices being used in the research study:

You must answer the following questions for **ALL** of the devices being used in the research study. If you need more space than that provided below (i.e. there is more than one device being used in the research study), download the **FDA Determination – Device** form from the IRB web site, and completed for each of the other devices in the study.

Name of device (#1): _____

Is there an IDE number associated with the device? **Choose One**

IF **YES** [to IDE question]:

Enter the IDE #:

What is the device category?

- Category A
- Category B. *If the device has an IDE number and is a Category B device, a copy of the letter to the Fiscal Intermediary requesting Medicare benefit coverage will be reviewed by the Aurora Billing Department.*
- Unknown at this time.

Who holds the IDE? **Choose One**Will the investigational device be provided by the sponsor without cost to the institution or subject? **Choose One**

If NO, and the device/services (either hospital or professional) will be billed to Medicare, prior notification to Medicare is required. Contact Aurora's Special Projects Billing Representative in the Central Business Office at clinicalresearchbilling@aurora.org or 414.649.7589 for a copy of Medicare's requirements.

A copy of FDA's IDE letter giving clearance for the study to begin must be forwarded to the Aurora IRB office before subject enrollment may begin. If there are conditions placed on the study by the FDA, a copy of the **unconditional** letter must be forwarded to the Aurora IRB office when available.

If **NO** [to IDE question]:

To determine whether the medical device meets the criteria for an exemption from the requirement for an IDE number, read the statement below, taken from the Frequently Asked Questions About Medical Devices on the FDA web site.

*In accordance with 21 CFR 812.2(b), sponsors and investigators of certain studies are exempt from the requirements of 21 CFR Part 812, with the exception of §812.119 (disqualification of a clinical investigator). **Examples of exempt studies are consumer preference testing, testing of a device modification, or testing of two or more devices in commercial distribution if the testing does not collect safety or effectiveness data, or put subjects at risk. Studies of an already cleared medical device in which the device is used or investigated in accordance with the indications in the cleared labeling are exempt from Part 812.** Note: Studies of a cleared device for a new use must comply with the human subject protection (informed consent and additional safeguards for children in research), IRB, and IDE regulations. Similarly, studies of a PMA approved device are exempt from the IDE requirements if the device is being studied for the indications in the approved labeling.*

In addition, diagnostic device studies (e.g., in vitro diagnostic studies) are exempt from the requirements of 21 CFR Part 812 under certain circumstances. The study is exempt as long as the sponsor complies with the requirements at 21 CFR 809.10(c) for labeling, and if the testing: (i) is noninvasive; (ii) does not require an invasive sampling procedure that presents significant risk; (iii) does not by design or intention introduce energy into a subject; and (iv) is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure. 21 CFR 812.2(c)(3).

Check one of the following:

- The device meets the criteria for an exemption from the requirement of an IDE number. No further action is required in this section. Indicate why this is an exempted study (for example, this is a previously cleared medical device that is being used for its cleared indication).
- The device does NOT meet the criteria for an exemption from the requirement of an IDE number
You are therefore requesting that the Aurora IRB make a NSR determination. It is the sponsor's responsibility to make the initial risk determination and present this to the IRB. **Provide a risk determination** based on the guidance from the FDA (see the following link <http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf>). The FDA is also available to help the sponsor or the IRB in making a risk determination. Call the Aurora IRB office for assistance.

If **BIOLOGIC** is answered **YES**:

List ALL of the biologics being used in the research study:

You must answer the following questions for **ALL** of the biologics being used in the research study. If you need more space than that provided below (i.e. there is more than one biologic being used in the research study), download the **FDA Determination – Biologic** form from the IRB web site, and completed for each of the other devices in the study.

Name of biologic (#1):

Is there a BB-IND number assigned to the biologic? **Choose One**IF **YES** [to BB-IND question]:

Enter the BB-IND #

Who holds the BB-IND? **Choose One**Will the biologic be provided by the sponsor without cost to the institution or subject? **Choose One**

If the BB-IND number(s) is not listed within the sponsor's protocol, attach a copy of one of the following for each biologic with an BB-IND number:

- (a) Communication from the sponsor of the protocol verifying the BB-IND number; or
- (b) Communication from the FDA verifying the BB-IND number.

IF **NO** [to IND number]:

Has the sponsor received a letter of BB-IND exemption from the FDA? **Choose One**

IF YES, attach a copy of the BB-IND exemption letter.

IF NO, answer the following questions:

- Does the sponsor intend for the investigation to be reported to the FDA in support of a new indication for use or any other significant change in labeling of the biologic? **Choose One**
- Does the sponsor intend for the investigation to be reported to the FDA in support of a significant change in the advertising for the biologic? **Choose One**
- Does the investigation involve 1) a route of administration, 2) a dosage level, 3) use in a population, or 4) other factor that significantly increases the risk (or decreases the acceptability of the risks) associated with the use of the biologic? **Choose One**
- Will the investigation be conducted in compliance with the FDA requirements for promotion and charging for investigational drugs (found in 21 CFR 312.7)? **Choose One**

D. For investigator-initiated research, does this research study meet the criteria for registration with ClinicalTrials.gov by the International Committee of Medical Journal Editors (<http://www.icmje.org/faq.pdf>) and/or the Food and Drug Administration Amendments Act of 2007 (<http://prsinfo.clinicaltrials.gov/fdaaa.html>)? **Choose One**

E. Product Storage: Discuss in detail how you plan to control (store/disseminate/dispose) test articles?

F. Is this a multi-site study (conducted at sites outside of Aurora) in which the investigator is the lead investigator or Aurora is considered the lead site? **Choose One**

If YES, describe the plan for managing information obtained in multi-site research that might be relevant to the protection of subjects (e.g. unanticipated problems involving risks to subjects or others; interim results; protocol modifications) and how this information will be disseminated to all involved sites:

G. For research that is not industry-sponsored, list any non-Aurora facilities, clinics, or departments where you will be conducting this research: You are required to make arrangements with the administrators of the non-Aurora facilities to facilitate this research and secure IRB approval from the additional sites. Attach proof of IRB and administrative approval for each site listed. If IRB approval from the additional site(s) has not been obtained, or the site does not have an IRB, final and unconditional Aurora IRB approval will not be granted until all sites have issued IRB approval or entered into an IRB Authorization Agreement deferring oversight to the Aurora IRB.

If you wish to request that the Aurora IRB be the IRB of record for the non-Aurora facility, contact the Aurora IRB Manager at 414.219.7740 to initiate this request.

H. Has this protocol been submitted to and disapproved by another Institutional Review Board? **Choose One** If YES, list by name:

I. Is the research being conducted by a resident investigator? **Choose One**

If YES, the Aurora RSPP office requires that your project undergo pre-review to obtain written administrative acknowledgement. This acknowledgement should be obtained prior to submitting your proposal. Please review the document entitled "STEPS TO CONDUCT A RESIDENT RESEARCH PROPOSAL AT AURORA HEALTH CARE", which can be found at www.aurora.org/irb under "Resident/Fellow Research Projects".

J. Is the research being conducted by a nurse investigator or nursing student investigator, or does the undertaking of this research target Aurora nursing staff as a subject population? **Choose One**

If YES, the Aurora RSPP office requires that your project undergo pre-review to obtain written administrative acknowledgement. This acknowledgement should be obtained prior to submitting your proposal. Please review the document entitled "STEPS TO CONDUCT A NURSING RESEARCH PROPOSAL AT AURORA HEALTH CARE", which can be found at www.aurora.org/irb under "Nursing Research".

K. Does the undertaking of this research involve Aurora staff or employed physicians as research subjects? **Choose One**

If YES, the Aurora RSPP office will forward your submission to obtain clearance to allow the participation of Aurora staff or employed physicians from the Senior Vice President of Human Resources or designee. This clearance is required prior to approval being issued.

L. Do you intend to send data/specimens outside the Aurora system? **Choose One**

If YES, you are required to obtain written acknowledgement from the Vice President of Research and Academic Affairs. This acknowledgement is required prior to approval being issued.

M. Does the undertaking of this research require participation of facilities, clinics, or departments of Aurora Health Care? **Choose One**

If YES, in the table below (attach additional sheets as necessary), provide the name and signature of responsible administrator (a written or e-mailed acknowledgment from the administrator may be attached in lieu of signature):

Facility/Department Name	Arrangements made?	Signature of appropriate administrator
	Pending	
	Pending	
	Pending	
	Pending	
	Pending	
	Pending	

Research involving a radiological procedure at an Aurora facility may also require interpretation services by radiologists in private practice. The acknowledgement of the regional Radiology Department as well as the private practice radiology group must be obtained prior to final IRB approval.

Research at any Aurora Facility involving **histologic evaluation, tissue handling, or archival material** will require the administrative acknowledgement of ACL as well as Great Lakes Pathologists (in addition to IRB approval). Please contact Dr. Anthony Cafaro with Great Lakes Pathologists at 414.328.7950 to determine if their acknowledgement is required. Dr. Cafaro will need access to the research protocol for review.

SECTION IV: SYNOPSIS

The Aurora Health Care Institutional Review Boards (IRBs) are required by federal regulations to ensure that all research involving human subjects is adequately reviewed for specific information and is approved prior to inception of any proposed activity. The IRBs use a "primary reviewer" system to review protocols. As such, one or two IRB members review all materials prior to the convened IRB meeting. Federal regulations require that when a primary reviewer system is used, each committee member receive, at a minimum, a copy of the consent document(s) and **a summary of the protocol in sufficient detail to determine the appropriateness of the study-specific statements in the consent document.** Consequently, it is important that you answer **ALL** questions accurately **USING LAY TERMS** and **it is not appropriate for you to cut and paste sections from the informed consent document and/or the sponsor's protocol to answer questions.** If you need help or have questions about how to complete this application, please call the Aurora IRB office at 414.219.7744 or e-mail us at IRB.office@aurora.org.

Please provide the requested information in the shaded text boxes. As you type your answers, the shaded text boxes will expand as needed. If you are unable to prepare this form on the computer, please use it as a guide and complete the requested information as a separate document.

BACKGROUND (provide concise narrative review of the literature or previous studies that support the scientific aims of the research and basis for this study. This should be a relatively detailed overview of past scientific investigations, but the language should be understandable to the non-scientific IRB members. *If the study involves an unapproved device that does not have an IDE, include the rationale for a Non-significant Risk determination.*

OBJECTIVE (briefly state the objective – aims and hypotheses to be tested)

ENDPOINTS (briefly state the study endpoints)

DESIGN AND PROCEDURES *Note: The IRB must understand all activities that are considered part of the protocol and what components are done solely for research purposes (even if not considered experimental).*

- A. Provide a comprehensive synopsis of the protocol. Include, as applicable, specific details about all activities performed (procedures/tests/interventions), study visits (to include standard of care follow-up visits), randomization, study groups, how drugs will be administered (routes and dosages), how devices will be deployed, sub-studies (e.g., genetic or future unspecified research). Indicate if you are not participating in a particular element of the study as described in the protocol.
- B. List the procedures or interventions being performed for research purposes:
- C. Are there procedures or interventions being performed for diagnostic or treatment purposes (meaning these procedures or interventions would be done even if the subject were not enrolled in the research study)? **Choose One** If YES, then list.
- D. Is there a "follow-up" component to this study? **Choose One** If YES, briefly summarize below:
 1. If applicable, describe research related interventions **required per protocol** that occur in the case of relapse/reoccurrence/device failure. This includes treatments, interventions, tissue sample collection or diagnostic tests that the subject **would not** undergo outside of the research study. (The IRB would consider this **active follow-up**):
 2. If applicable, describe follow-up activity that is limited to the review and collection of information from medical records or contacting subjects, and/or review of survival status either by contacting the subjects or querying the National Death Index. (The IRB would consider this **post-intervention follow-up**):
- E. Will subjects be required to discontinue or modify any current medications or be denied any standard of care treatment(s) for any condition in order to be eligible for or participate in this study? **Choose One** If YES, provide a justification for your response.
- F. Describe the resources (medical and/or psychological/social (or psychosocial [ie. genetic counseling, financial assistance]) available to subjects should they need them as a consequence of their participation in the research (if you do not anticipate that there will be any consequences to a subject's participation, please state):
- G. Describe the setting in which the research will be conducted (i.e., physician's private office, hospital, clinic, etc.):
- H. The IRB expects that you have adequate resources to conduct the research. Complete the following:

Check this box **ONLY** (and do not complete questions 1-4 below) if your protocol is being supported by an Aurora-employed Department of Clinical Research Coordinator **AND** these questions have been addressed and will be monitored during the course of the research study.

 1. Describe how you, as the Principal Investigator, have sufficient time to complete the research (e.g. review adverse events or significant new findings, determine subject eligibility, take part in the informed consent process, etc.):
 2. Do you have adequate numbers of qualified staff to conduct this research? **Choose One** Please explain:
 3. Describe the process for ensuring that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions:
 4. Are the facilities adequate to conduct this research study? **Choose One** Provide a justification for your response:
- I. If the investigators listed on page 1 of this submission form have different roles in the conduct of this research, identify each individual and describe his/her specific role in the study (the IRB needs this information in order to verify that each individual holds the appropriate privileges):
- J. Have you formally delegated research procedures to research staff members? **Choose One** If YES, attach the sponsor's Delegation of Authority Log (or complete and attach form RR 402-C).
- K. Research staff conducting any research activities (as delegated by the principal investigator) are required to comply with Aurora IRB policy GA 104.

Choose One Statement

Research staff employed through the Aurora Department of Clinical Research must follow DCR SOP 002 and disclose the conflict of interest to their research manager, who will manage the conflict according to their policy.

All other research staff (not employed by the Aurora Department of Clinical Research) who have a conflict of interest are required to disclose the conflict of interest by submitting the *Study Specific Investigator Conflict of Interest Statement* (Form GA 104A).

- L. Design aspects (i.e., placebo control, blinding, randomization, number of study arms, etc.). If the study is placebo controlled, provide a justification for the use of placebo in this study.

- M. Who designed the clinical trial? (i.e., drug or device manufacturer, investigator, etc.):
- N. Describe data collection methods. Surveys, instruments, case report forms (if available), etc. must be attached.
- O. Who will be collecting this information? List by title (i.e., study coordinator, principal investigator):
- P. Statistical methods, data analysis, and interpretation (include the factors considered in determining an appropriate sample size) **(NOTE: this information does not need to be included for FDA regulated studies that have an IND/IDE or are Phase IV):**
- Q. List any known or anticipated factors that would lead to early termination of subject participation or early study completion.
- R. Will biological samples be taken as part of the research study? **Choose One** If YES, indicate the plan for disposal once study is completed:
- S. Will biological samples be collected and stored for future unspecified research (banking)? **Choose One**
The Aurora IRB has expectations that the site maintaining the samples will follow all applicable regulations, including oversight by an IRB. Attach documentation from the sponsor/site maintaining the samples regarding plans for IRB oversight. If the Aurora IRB is or will be the IRB of record, state that.

If YES, complete the following questions:

1. Is this collection optional (that is, subjects may participate in the main study without participating in the sample collection)? **Choose One**
2. Describe how biological samples will be identified; if the samples are de-identified (not using a code and no HIPAA identifiers are associated with the samples), state that:
3. Complete a-c for samples that are coded (identified):
 - a. Specify who will have access to the code:
 - b. Is there an expectation the subject's Protected Health Information (PHI) will be accessed in the future? **Choose One** {If **YES**, this must be clearly stated in the informed consent/authorization to collect and store biological samples for future use. Subjects should be given a choice as to whether or not their PHI can be accessed for future unspecified research.}
 - c. What PHI will be linked to the code: {This should be consistent with the information in the informed consent document.}
4. Indicate when and how unused samples will be disposed of: {this should be consistent with the consent document}.

DOES THE RESEARCH INVOLVE ANY OF THE FOLLOWING?

Choose One	Deception of subjects
Choose One	Sexually explicit materials or questions about sexual orientation, experience, or abuse
Choose One	Questions about any kind of illegal or illicit activity
Choose One	Purposeful creation of anxiety
Choose One	Any procedure that might be viewed as an invasion of privacy
Choose One	Physical exercise or stress
Choose One	Extraction or use of blood, body fluids, or tissues
Choose One	Genetic research (DNA)

If you have chosen YES above, justify: _____

RESEARCH SUBJECTS

This research involves **Choose One**

Does the research specifically require the inclusion of subjects from any of the following categories?

a.	Choose One	Aurora staff/physicians (Aurora RSPP will obtain administrative clearance from Lorelle Mahoney, Senior Vice President)
b.	Choose One	Children {if YES indicate age range and see SOP SC 501 to determine if an assent document is necessary}
c.	Choose One	Children who are wards of the State (e.g., a child in the legal custody or guardianship of the state of Wisconsin, a child in foster care, etc.) –{NOTE: If an enrolled child becomes a ward of the State, you must notify the RSPP office immediately.}
d.	Choose One	Over 65 years of age
e.	Choose One	Physically disabled
f.	Choose One	Mentally ill or developmentally disabled
g.	Choose One	Economically or educationally disadvantaged
h.	Choose One	Pregnant females as target population
i.	Choose One	Fetuses or abortuses or neonates
j.	Choose One	Subjects in emergent care setting
k.	Choose One	Subjects in institutions (e.g., halfway houses, nursing homes, etc.)
l.	Choose One	Prisoners {NOTE: The Aurora IRBs are not duly constituted to review research involving prisoners. If you intend to enroll prisoners, or if an enrolled subject becomes a prisoner, you must notify the RSPP office immediately.}
m.	Choose One	Non-English speaking subjects (Please see the Informed Consent guidance document on the Aurora IRB web site for more information or call the RSPP Office.) {If YES indicate language understood by the prospective subject or the legally authorized representative. }

n.	Choose One	Decisionally Incapacitated (You must address specific questions about the use of a surrogate decision maker for decisionally incapacitate subjects in section VI of the submission form.)
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Any of the categories above (a-n) may be considered by the IRB to be vulnerable populations, depending on the research being conducted. If your research specifically requires the inclusion of subjects from any of those categories, please address the following questions.

1. Provide a justification for the inclusion of the above vulnerable subjects in this study:
2. Provide a description of additional safeguards included in the protocol to protect these vulnerable subject's rights and welfare or to eliminate their vulnerability. Examples include: use of an interpreter throughout research participation; translated research documents; handicapped accessibility to clinic; need for transportation from nursing home, etc.
3. If you intend to exclude an otherwise eligible class of persons who might benefit from the research (e.g., pregnant women, minors, educationally or economically disadvantaged, etc.), provide an ethical and scientific justification for this exclusion:

SUBJECT RECRUITMENT {Please note: The RSPP office will be requesting information regarding the ethnicity/race and gender of subjects accrued at the time of continuing review.}

- A. List subject inclusion and exclusion criteria, as well as any unique qualifiers required for participation (if the list is longer than one page, you may attach a copy of the inclusion and exclusion criteria to the end of the submission form):
- B. Indicate how you will identify potential research subjects. The IRB must know if you anticipate enrolling subjects from the investigators private practice, referrals from other physician groups, from a database of prior research participants, or from advertisements. If you are identifying potential research subjects by reviewing patient medical records without obtaining prior consent/authorization from the patient to access such information, you are required to complete and attach Form SC 502-A (which can be obtained from the RSPP office). ***Under federal and Wisconsin state law, you may not directly contact a potential research subject if you do not have a treating relationship with that patient.***
- C. Describe your access to patient populations that will allow you to recruit the necessary number of subjects for this study.
- D. Describe recruitment procedures (include fliers, posters, radio or TV scripts, recruitment letters, etc.). There may be Aurora logo requirements that must be met. If recruitment is by referral, detail procedure and submit letters to be sent to referring physicians. *Please note that IRB approval of an advertisement does not constitute administrative approval to post the advertisement within Aurora. Please contact Aurora Creative Services for more information.*
- E. If the first contact that the prospective research subject has is with a receptionist who follows a script to determine basic eligibility for the specific study, describe the procedures that will be followed and how the receptionist is qualified and trained. Additional questions to address are: How is the personal information collected and stored? What happens to personal information if the caller ends the interview or simply hangs up? Does a marketing company gather the data? If so, are names, etc. sold to others? Are names of non-eligible subjects maintained in case they would qualify for another study? Are paper copies of records shredded or are readable copies put out as trash? Include a copy of any scripts.
- F. Indicate whether the research subject will be paid for participation or given other recruitment incentives for participating. The amount of all payments or other compensation for participation (e.g., gift certificates) and the proposed method and timing of disbursement must be described here, and set forth in the informed consent document:
- G. If a potential subject is eligible to participate in more than one research study being conducted by this investigator(s), give selection criteria that will be used to determine the most appropriate study for the subject to enroll (if there are no competing studies, that is an appropriate answer).

RISK – PROTECTION – BENEFITS Answers for the questions below are central to research involving human subjects and is a major consideration for the IRB. You must demonstrate a reasonable balance between anticipated risks to research subjects, protection strategies, and anticipated benefits to participants and/or others.

- A. **Risks for Subjects.** Identify any reasonably foreseeable physical, psychological, economic, or social risks for subjects, and if possible, provide an estimated frequency of occurrence (i.e., "common", "less common", "rare"), distinguishing research risks from therapeutic risks. State that there are "no known risks" if appropriate.
- B. **Minimizing Risk.** Describe *specific* measures used to minimize or protect subjects from anticipated risks related to research procedures or investigational articles (e.g., additional lab tests, more frequent physical assessments or exams, pregnancy tests, birth control, etc.).
- C. **Privacy.** Describe the provisions to protect the privacy interests of subjects (i.e. the interests of individuals in being left alone, limiting access to themselves, and limiting access to their information).
- D. **Risk of Breach of Confidentiality.** Identify any reasonably foreseeable risks for subjects that would result from a breach of confidentiality (e.g., loss of insurability or employability, invasion of privacy, loss of social or financial standing).
- E. **Minimizing Risks of Breach of Confidentiality.** Describe how you intend to store protected health information related to the subject. For example, will the information be stored in hard copy in a locked filing cabinet or a secured computer or computer file? Indicate whether there will be restricted access to the maintained file. Indicate whether the investigator will remove the subject's name and other identifiers, and whether a code is assigned to the subject's information before the research data is sent to the sponsor or governmental agency and indicate who will have access to this code (reminder: only medical records related to the research study should be given to the sponsor or others). Finally, state your plan for destroying the subject identifiers and documents once the study is closed, include how such destruction will take place and indicate how long you plan to keep these documents before destroying. Indicate whether a Certificate of Confidentiality has been or will be obtained, if applicable.

If this study involves collection and storage of biological samples for future unspecified research (banking) and the samples contain subject identifiers or are coded (meaning there is a link to identifiable health information), state the plan for destroying subject identifiers or link to the subject's identifiable health information, once samples have been used up, destroyed or the study is completed and closed at the Aurora IRB.

- F. **Data and Safety Monitoring Plan** If this research involves more than minimal risk* to subjects, describe in detail the provisions for monitoring the collected data to ensure the safety of subjects. Include whether there will be interim analyses; stopping rules, if any; and any other pertinent information. * *NOTE: if you have questions regarding whether the study meets the requirements for a "minimal risk" study, please contact the Aurora IRB office.*

Indicate whether a DSMB/DMC has been/ will be created, its composition and the frequency of meetings.

- G. **Benefits.** Describe any reasonably expected benefits for research subjects, a class of subjects, or society as a whole. If no benefits are expected for the individual subject, this should be stated. Provide more detailed information than what is provided in the informed consent document. Payment for research participation is not considered a "benefit".
- H. **Alternatives.** The Aurora IRBs are ICH GCP compliant. If your sponsor does not require ICH GCP compliance, check here and you **MUST** additionally provide a written statement to that effect from the sponsor (e-mail is appropriate). You would then not be required to include the Alternatives matrix in the consent document; however, the standard Alternatives section is still required.

List the alternative procedures or courses of treatment that may be available for subjects in this study. If palliative treatment is the only option, state that. Remember that the choice to not participate is always an option. If this is not a treatment study, you may indicate N/A below.

In your opinion, does the research involve more than **minimal risk (defined in federal regulations to mean that "the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests")** to subjects? **Choose One**

SECTION V: INFORMED CONSENT PROCESS

The Process of Consent: Since the central requirement for human subject research is that people participate voluntarily, the consent process is one of the most important parts of planning a research proposal. The process must assure that the potential subject understands the study and its risks and benefits and can certify his or her willingness to participate. The informed consent process should occur throughout the subject's participation in the research study. Prepare a copy of the informed consent document, using the Sample Informed Consent Template as a guide.

The Aurora IRB policy states that the Investigator must conduct the consent interview unless he or she delegates his or her responsibility for conducting the informed consent interview to another individual who is both knowledgeable about the research study and under the Investigator's direct supervision. In addition, the FDA Information Sheets state **"FDA does not require the investigator to personally conduct the consent interview. The investigator remains ultimately responsible, even when delegating the task of obtaining informed consent to another individual knowledgeable about the research."** **"If someone other than the clinical investigator conducts the interview and obtains consent, this responsibility should be formally delegated by the clinical investigator and the person so delegated should have received appropriate training to perform this activity."** However, Wisconsin state law requires the physician-investigator to inform the subject about the availability of all alternate, viable medical modes of treatment and about the benefits and risks of these treatments. This discussion can take place anytime prior to the subject signing the consent document, but any attempt to discharge this responsibility to another individual would constitute a breach of the physician's duty to provide informed consent under state law. The informed consent document contains a place for the investigator to document that this discussion took place. Please contact the Aurora IRB office if you need more information regarding this requirement, or the training of persons designated to obtain informed consent.

- A. List the titles (not names) of individuals who will be involved in the informed consent process (principal investigator, nurses, research assistants, coordinators, etc.) and indicate their roles in the consent process (i.e., screening participants, obtaining informed consent, etc.):
- B. Have you formally delegated the risk/benefit/alternative consent discussion to someone on your research team other than a physician-level investigator? **Choose One** If YES, attach a completed Delegation of Authority worksheet. Indicate N/A if your study does not involve a medical intervention.
- C. Indicate specifically where the initial consent process will take place (e.g., waiting area, exam room, investigator's office). If you intend to conduct any part of the consent process by telephone or mail, provide a description of the intended procedures.
- D. Describe specifically when informed consent will be obtained in relation to the first research-related activity. Include how much time will be allotted for the informed consent process and whether there is any waiting period between informing the subject and obtaining the consent. The IRB recommends that the pre-enrollment discussion with the subject occur at least several days before obtaining the consent and the initiation of the study unless *clinical* considerations preclude this from happening. Describe any foreseeable clinical situations where the informed consent process may be compromised. The IRB also recommends that the unsigned informed consent document be given to the subject to review in private well before the subject is asked to sign the document. If the amount of time is less than one day, please explain the reasons.
- E. Indicate how you will ensure that the potential subject understands the study well enough to enroll (e.g., assessing subject's ability to follow simple commands and ask appropriate questions about the study, asking open ended questions about risks, benefits, alternatives and documenting subject's responses, asking for the subject to summarize aspects of the study, etc.):
- F. What steps will be taken to minimize the possibility of coercion or undue influence during the consent process?
- G. Indicate where subsequent visits will take place and how you intend to ensure the subject continues to be willing to participate in the study:

H. If you are enrolling children in this research study, answer the following questions. If N/A check here .

Provide your plan for obtaining age-appropriate assent:

If you are not planning on obtaining assent, indicate why:

If you are obtaining assent of the children, will assent be documented? **Choose One** (Indicate N/A if you are not obtaining assent.) If YES, how will it be documented?

Based upon the risk level of the research study, the IRB will determine whether the permission of one parent is sufficient or whether permission of both parents is required.

If you intend to obtain permission of both parents for the research study, regardless of risk level, check here . Provide a rationale for your decision.

I. For research involving children in categories 45CFR46.406 or 45CFR46.407 (see <http://www.hhs.gov/ohrp/researchfaq.html>), if you are enrolling children who are wards of the State in this research study, answer the following question. If N/A, check here .

For this research, an advocate is required for a child who is a Ward of the State (this cannot be someone who has already been appointed to act on behalf of the child, e.g., a social worker or a *guardian ad litem*). Indicate your plan for appointing the advocate, and describe their background or experience and their willingness to act in the best interest of the child throughout the child's participation in the research (see <http://www.hhs.gov/ohrp/researchfaq.html#q22>).

SECTION VI: DECISIONALLY INCAPACITATED SUBJECTS

(COMPLETE THIS SECTION ONLY IF YOU ARE REQUESTING THE USE OF SURROGATE DECISION MAKERS TO ENROLL SUBJECTS INTO THE RESEARCH STUDY)

When mental impairments or other conditions render a potential adult research subject unable to give consent to participate in a prospective research study, federal research regulations state that the investigator must obtain written informed consent from a "legally authorized representative" prior to enrolling the potential subject into the research study. Federal research regulations define a "Legally Authorized Representative" as an "individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research". Federal regulations provide no specific information about who may or may not qualify as a "legally authorized representative." Wisconsin state law is silent about who may provide consent for research participation on behalf of a mentally incapacitated adult, except when experimental treatment is aimed at individuals being treated for mental illness, developmental disabilities, alcoholism or drug dependency. It is the IRB's position that in limited circumstances, as described in Aurora IRB SOP 702, it may be appropriate, and in the subject's best interest, to allow a decisionally incapacitated prospective subject to be enrolled into a research study based on the consent of the subject's guardian, health care agent, or other surrogate decision maker(s).

Are you requesting that a surrogate decision maker (power of attorney for health care, legal guardian, or other surrogate, such as next-of-kin) be allowed to provide permission for a decisionally incapacitated adult (one who is incapable of giving their own informed consent) to be enrolled into this research study? **Choose One** If you are, the following must be completed:

Could the research be conducted with decisional subjects (provide explanation and include discussion of limiting factors)?

Could the subject receive the same medical management they will receive in this study outside the setting of a research protocol? Explain the compelling reasons for conducting the research study with these decisionally incapacitated subjects?

Will participation in this study increase the risk of harm or discomfort compared to that expected with medical management that the subject would receive if they do not participate in this study? Provide an explanation:

Will participating in this study increase the chance that the subject will experience a favorable outcome compared to that expected with the medical management that the subject would receive if they did not participate in this study? Provide an explanation:

What is the magnitude of the benefit that future patients, or society in general, may experience as a result of the subject participating in this research study? Provide an explanation:

Who will be assessing the prospective subject's likely preferences regarding research participation, and how will that assessment be performed?

Who is the independent physician(s) who will be making the incapacity determination and completing Form IC-702A entitled "Declaration of Incapacity for Research Purposes" to be filed in the subject's medical record and the investigator-maintained research record?

You must also complete form SC-502A to request a Waiver of HIPAA Authorization.

Please note, if the prospective research subject has designated a Health Care Agent or has a Legal Guardian, the investigator is not authorized by the IRB to seek consent from another surrogate decision maker (see Aurora IRB SOP 702 Section 1.5.3 for discussion of who can be considered a surrogate decision maker).

If you did not anticipate enrolling subjects with the above conditions at the time of IRB submission but unexpectedly encounter a vulnerable subject during the study, you must contact the RSPP office for guidance before enrolling such subject. The RSPP office can be reached 24 hours by pager 414.222.4792.

SECTION VII: REQUESTS FOR WAIVER

(COMPLETE THIS SECTION ONLY IF YOU ARE REQUESTING A WAIVER OF CONSENT OR DOCUMENTATION OF CONSENT)

If you are requesting a consent procedure that does not include, or alters, some or all of the required elements of informed consent, or you are requesting a waiver of the requirement to obtain a signed consent form, please complete one or the other section below (please note that the IRB must concur that your research involves no more than minimal risk).

I am requesting a waiver of informed consent (some or all of the required elements of informed consent, or an alteration of same).

In order for the IRB to grant (a) a waiver of informed consent, or (b) a waiver of the consent procedure requirement to include all or alter some or all of the elements of informed consent [45CFR46.116(d)], please complete the following:

➤ In your opinion, does the research involve no more than minimal risk? **Choose One**

- Check the appropriate box(es) indicating why the waiver of informed consent will not adversely affect the rights and welfare of the subjects:
- The clinically indicated intervention or tests were already completed, or would be completed, regardless of this research activity.
 - Results of this research activity would not affect clinical decisions about the individual's care because they are being analyzed after the fact.
 - Subjects are not being deprived of clinical care to which they would normally be entitled.
 - Other (describe):
- Describe why the waiver is necessary and how it would not be practicable to conduct the research without the waiver/alteration:
- Describe how you will provide subjects with additional pertinent information after their participation, or why it is not appropriate:
- Explain whether the entire informed consent is being waived or only certain required elements are being waived (and if so, list which ones):

You must also request a Waiver of HIPAA Authorization. Please submit Form SC-502A along with this submission.

Note: If the IRB finds that your research involves no more than minimal risk and a waiver of informed consent is granted under the above conditions, documentation of informed consent (i.e., signed consent form) is also waived. Even if a waiver is granted, the IRB may require other conditions. The IRB may require you to provide subjects with an information sheet (written summary) about the research.

I am requesting a waiver of documentation of informed consent

In order for the IRB to grant a waiver of the requirement to obtain a signed consent form for some or all subjects [45CFR46.117(c)], you must be able to answer **YES** to at least one of the following questions, and describe the reason(s) the waiver is necessary below.

- Is the only record linking the subject and the research is the consent document, and the principal risk is potential harm resulting from a breach of confidentiality (subjects should be asked whether they want documentation linking them to the research, and their wishes should be followed)? **Choose One**
- In your opinion, does the research involve no more than minimal risk of harm **AND** involve no procedure for which written consent is normally required outside of the research context? **Choose One**
- Describe the reason(s) the waiver is necessary:

You must also request an Alteration of HIPAA Authorization. Please submit Form SC-502A along with this submission.

NOTE: If the IRB finds that your research involves no more than minimal risk and a waiver of documentation of informed consent is granted, the IRB may still require other conditions. For example, the IRB may require the investigator to provide subjects with an information sheet (written summary) about the research.

SECTION VIII: INVESTIGATOR ASSURANCE FOR RESEARCH INVOLVING HUMAN SUBJECTS

- A. **Research Involving Human Subjects:** By signing below, I acknowledge and accept primary responsibility for protecting the rights and welfare of human research subjects, and that such rights and welfare take precedence over the goals and requirements of the research. I hereby represent that I have reviewed the following documents and agree to conduct my research in compliance with: (1) the Belmont Report; (2) the Department of Health and Human Service's ("HHS") and Food and Drug Administration's ("FDA") regulations; (3) the Federalwide Assurance applicable to this research study; and (4) the Aurora IRB policies and procedures governing human subject research (above named documents, including Aurora IRB policies and procedures are available for review on the Aurora RSPP Web site: <http://www.aurorahealthcare.org/misc/irb/index.asp>).
- B. **Conduct of the Study:** This research study or project will be performed in the manner described in this proposal, and in accordance with Aurora IRB policies and procedures, applicable laws, regulations, and guidelines. I hereby agree to refrain from enrolling subjects into this proposed research study prior to its review and approval by the Aurora IRB. Notwithstanding the previous statement, I understand that emergency medical care using investigational articles may be delivered to patients who are in a life-threatening situation without IRB approval to the extent permitted under federal regulations, state law, and Aurora IRB policies and procedures (SOP EU 1301). However, data and information obtained as a result of such emergency medical care may not be included as part of the research. I understand that any modification from the procedures detailed herein must be submitted to the IRB and be approved by the IRB prior to implementation.
- C. **Protected Health Information:** I hereby agree that I will not reuse or disclose to any other person protected health information obtained or accessed by virtue of this research except as authorized by the subject, or permitted or required by law and shall require my research staff to also comply with this section.
- D. **Informed Consent:** I hereby agree to obtain, document, and maintain records of informed consent from each subject (or legally authorized representative) as required under HHS and FDA regulations, applicable laws, Aurora IRB policies and procedures, and as stipulated by this IRB.
- E. **Training:** I hereby assure that all personnel working with human subjects described in this protocol ("research personnel") are technically competent, and have a working knowledge of the Belmont Report and applicable federal regulations regarding human subject research [45 CFR 46 and 21 CFR 50 and 56]. I agree to complete and require any research personnel participating in this research study under my direction and control to complete any and all educational training required by Aurora Health Care or the Aurora IRB prior to initiating this research study.

All investigators are required to complete the training tutorial: <http://phrp.nihtraining.com/users/login.php>.

No submission will receive final IRB approval until the Aurora RSPP office has received documentation that all investigators have completed this required training.

- F. **Credentials:** If the research involves medical treatment or intervention, a qualified clinician responsible for all study-related health care decisions must be an involved as an investigator. In addition, the qualified clinician must provide for referrals for needed healthcare during the research and for follow-up after the research has ended, as necessary.

For studies involving procedures and/or devices, what clinical privileges are necessary to perform this procedure? _____

Do all listed investigators hold the necessary clinical privileges to perform this procedure at all Aurora institutions where the study is being conducted?

Choose One

If no, have all investigators applied for the necessary privileges to perform this procedure? **Choose One**

This submission will be sent to the Aurora Credentials Department for verification, if applicable.

- G. **Conflict of Interest:** All investigators and research staff are required to comply with Aurora IRB SOP GA 104. All investigators listed on this submission are required to submit a *Study Specific Investigator Conflict of Interest Statement* (Form GA 104A). Research staff conducting any research activities (as delegated by the Principal Investigator) are also required to disclose a conflict of interest. Research staff employed through the Aurora Department of Clinical Research must also follow DCR SOP 002 and disclose the conflict of interest to their research manager. Research staff that are not employed through the Aurora Department of Clinical Research are required to comply with Aurora IRB policy GA 104 and disclose any conflict of interest by submitting the *Study Specific Investigator Conflict of Interest Statement* (Form GA 104A).

No submission will receive final IRB approval until the Aurora RSPP office has received a signed original for each investigator.

- H. **Malpractice Insurance** (if applicable): I agree to notify my malpractice carrier that I am conducting human subject research and will participate in the Wisconsin State Patient's Compensation Fund.
- I. **Billing:** If any research subject services are delivered at an Aurora Health Care facility and a bill for those services will be submitted to a third-party payor, I understand that I or my representative must contact the Research Medical Auditor at Aurora's Medical Audit Office (414.649.6855) prior to IRB submission to initiate all required and appropriate billing procedures.
- J. **Extramural Funding:** If funded by an extramural source, I assure that this application accurately reflects all procedures involving human subjects as described in the grant/contract proposal to the funding agency. I also assure that I will notify the Aurora IRB and the funding/contract entity if there are modifications or changes made to the protocol after the initial submission to the funding agency.
- K. **Continuing Obligations:** I understand that it is the responsibility of the Aurora IRB to conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. I also understand that as continuing review is conducted, it is my responsibility to provide timely and accurate information when pertinent or requested, and to notify the Aurora IRB in a timely manner when my study has been revised, amended, or modified in any way, placed on hold, suspended, completed, or otherwise is no longer active to subject enrollment or follow-up.

(Principal Investigator Signature) **The original signature must be on file in the IRB office.**

(Date)

- L. **Facilitator:** For studies being conducted by an investigator who is not an employee of Aurora Health Care, Inc. or who does not have staff privileges at an Aurora Health Care facility, a facilitator is required (see SOP FO 301). For protocols involving the "practice of medicine and surgery" a physician is required. If applicable, please provide the name and contact information of the facilitator.

Not applicable

Name:

Department: _____ / Telephone: _____ / E- mail address: _____

Facilitator's signature (if applicable)

(Date)