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Section 2.1

Appendix 1: Faculty Senate Resolution

Approved by the: Faculty Senate - December 5, 2013
Administration - February 2014*
Board of Regents - no action required

*The Administration recognizes the Faculty Senate resolution requesting an external review of clinical research on human subjects at the University of Minnesota and is moving forward with this review. The review will be managed by an independent, external firm who is expected to call upon national experts in the field of clinical research on human subjects research and who are widely recognized for their expertise, knowledge and achievement in this field. This review will include a review of relevant standard operating procedures and an assessment of University compliance with regulations and applicable law. It will result in a detailed report outlining strengths and weaknesses of current policies, practices, and oversight and any recommendations for any deficiencies identified. This process will include consultation with faculty and the final report will be public.

Issues Arising from the CAFE Study and the Suicide of Dan Markingson

PREAMBLE:

In May 2004, Dan Markingson, while enrolled in a clinical trial of an antipsychotic drug (the CAFE study) at the University of Minnesota, committed suicide. Since then individuals and groups within and outside the University have raised questions about the study, how Markingson was recruited into it, his treatment during the study, and the circumstances of his suicide.

On October 21, 2013, a letter co-authored by six bioethicists from outside the University, with 175 co-signatories, was addressed to President Eric Kaler and Professor Eva von Dassow, as chair and vice-chair (respectively) of the Faculty Senate, and to members of the University of Minnesota Senate. The letter asked the Senate to endorse and request an independent investigation of the issues arising from the Markingson case and the CAFE study. That letter is available at: http://www1.umn.edu/usenate/fsenate/docs/131205toronto_letter.pdf. The list of additional co-signatories is available at: http://www1.umn.edu/usenate/fsenate/docs/131205toronoto_signatures.pdf.

On November 20, 2013, fourteen faculty senators co-signed a request to the Faculty Consultative Committee to place this matter on the agenda of the December 5 Faculty Senate meeting for discussion, and further requesting that a resolution calling for an independent investigation be presented for discussion and action. That letter is available at: http://www1.umn.edu/usenate/fsenate/docs/131205letter_to_fcc.pdf.

The FCC discussed the letter and the issues it raises at its meetings on Oct. 24, Nov. 14, and Nov. 21. While these discussions have not reached a conclusion, and members of the FCC have varying views, a consensus emerged that it is appropriate to bring the matter before the Faculty Senate at this time. The FCC wishes to emphasize the following points.

First, it is important that those participating in decisions about this matter familiarize themselves, with the history of the case and investigations conducted to date.

Second, as the FCC studied this issue, two things became clear: that the Markingson tragedy specifically had been investigated several times from different perspectives, and that those investigations did not address the broader question of whether the University's current policies, procedures and practices, some of them changed since the Markingson case, reflect both best practices in clinical research on human subjects and the faculty's high ambitions for ethical behavior. Members of the FCC also recognize that external evaluations can have the advantage of fresh perspectives not biased by familiarity with current

practice, and are a way for the public to have the utmost confidence in the integrity of the research conducted at the University of Minnesota.

For this reason, the FCC feels that the way forward is to recommend that an independent and transparent examination be undertaken to evaluate the University's procedures, practices, and policies governing clinical research on human subjects, and in particular clinical research involving adult participants with diminished functional abilities. While the specific charge for such an examination requires further work, FCC believes issues to address may include investigator conflict of interest, institutional conflict of interest, consent policies and procedures, case management of enrolled participants, mechanisms for overseeing such research and mechanisms for addressing adverse events.

Therefore, the FCC suggests to the Faculty Senate the following resolution:

Resolution on the matter of the Markingson case

WHEREAS the faculty of the University of Minnesota are committed to upholding high ethical standards in the conduct of research;

WHEREAS questions continue to be raised about the policies and procedures followed in the case of Dan Markingson, a 26-year-old participant in a clinical trial who committed suicide in 2004;

WHEREAS the University has suffered reputational harm in consequence of this tragic case and its aftermath;

WHEREAS the faculty seek to ensure through independent evaluation that the University's ethical standards for clinical research on human subjects meet or surpass the norm,

BE IT RESOLVED that a panel external to and independent from the University of Minnesota be constituted for the purpose of conducting an inquiry examining current policies, practices, and oversight of clinical research on human subjects at the University, in particular clinical research involving adult participants with diminished functional abilities. The administration, in collaboration with appropriate faculty governance committees, shall initiate the constitution of such an independent panel and shall support its inquiry. The panel shall have authority to obtain any records it deems necessary for a thorough inquiry, to the extent consistent with applicable law. At the conclusion of the inquiry, the panel shall issue a report that will be made publicly available, within the limitations of regulations governing the protection and privacy of individuals, including research participants, and the results will be reported back to the Faculty Senate so that senators have an opportunity to ask questions and discuss the report.

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Section 2.1

Appendix 2: Summary of the Dan Markingson Case

Appendix 2

Summary of Circumstances Related to the Death of Dan Markingson

In 2004, Dan Markingson, age 26, died by suicide while participating in a University of Minnesota research protocol. Mr. Markingson was a subject in a comparative effectiveness study of currently marketed antipsychotic medications. He was enrolled one day after an involuntary commitment was stayed for six months on the condition that he be "cooperative with the treatment plan… and follow all of the aftercare recommendations of the treatment team." [1] His treating psychiatrist, who was also the principal investigator of the study, said in his statement in support of commitment that Mr. Markingson "lacks the capacity to make decisions regarding such treatment." [2]

Mr. Markingson signed a discharge plan from Fairview Health System that was "based upon (his) agreement with the Dakota County Court." The first requirement was that he "keep appointments with [Fairview] CAFÉ study." The discharge plan states that "consequences for not following this plan could result in a court commitment to the hospital." [3] Later, his mother repeatedly left messages or directly contacted the study coordinator, the principal investigator, and the chair of the Department of Psychiatry and requested that her son's deteriorating condition be addressed. "Do we have to wait until he kills himself or someone else before anyone does anything?" she asked in a phone message to the study coordinator several weeks before his death. [4]

As the Faculty Senate noted, the 10 years since Mr. Markingson's death were marked by several investigations, as well as by litigation. A 21-page report by the Food and Drug Administration stated that it did not find "evidence of misconduct or significant violation of the protocol or regulations," [5] and the Minnesota Board of Medical Practice did not find a sufficient basis for disciplinary or corrective action against the physicians involved. [6] In 2012, the Minnesota Board of Social Work required a Corrective Action Plan for the social worker who, under the supervision of the principal investigator, coordinated Mr. Markingson's recruitment and clinical care. [7] No other formal investigations or reports have issued as of the time of this writing, although in 2014, in response to a request by legislators, the Minnesota Auditor of Accounts announced plans to review adverse events dating from 2004 from the Department of Psychiatry. [8] In addition, the Minnesota Legislature passed legislation in 2009 (Minnesota statutes 253B.095(e)) based upon the Markingson case to protect the rights of patients under a stay of commitment, which is a court order requiring a person to follow the court's directives or face commitment to an inpatient facility. The statute requires that a court directly approve the enrollment of such persons in research studies, with specific findings required of the court that a series of criteria have been met that protect voluntary, informed consent. The criteria include: the treating psychiatrist must testify that the patient may benefit because other treatment options have been ineffective; the treating psychiatrist may not be the psychiatrist conducting the drug trial; and the court must make a determination that the patient is competent to choose, is freely choosing to participate, that the compulsion of the stayed commitment is not being used to coerce the person to participate, and that a reasonable person might choose to participate.

Appendix 2

References:

1. In the Matter of the Civil Commitment of Dan Markingson, State of Minnesota, County of Dakota, November 20, 2003.
2. Examiner's Statement in Support of Commitment, November 14, 2003
3. Fairview Hospital discharge plan, December 8, 2003.
4. Establishment Inspection Report, p. 10, Food and Drug Administration, January 26, 2005
5. Establishment Inspection Report, p. 1, Food and Drug Administration, January 26, 2005
6. Letter to Mary Weiss, June 15, 2010 from Helen Patrikus, Medical Regulations Analyst, Minnesota Board of Medical Practice.
7. Agreement for Corrective Action, State of Minnesota Board of Social Work, Nov. 8, 2012.
8. "Auditor to review U's drug trial suicide," Star Tribune, June 18, 2014, http://www.startribune.com/local/263745911.html

Section 2.1

Appendix 3: Charge Letter from President Kaler

UNIVERSITY OF MINNESOTA

Twin Cities Campus | ***Office of the President*** | *202 Morrill Hall, 100 Church Street S.E., Minneapolis, MN 55455*

MEMORANDUM

January 24, 2014

TO: Brian Herman, Vice President for Research

FROM: Eric W. Kaler, President EWK

RE: Human Subject Research Review

On December 5, 2013, the Faculty Senate approved a resolution requesting an external review of clinical research on human subjects at the University of Minnesota. Specifically the Senate resolution stated:

> *BE IT RESOLVED that a panel external to and independent from the University of Minnesota be constituted for the purpose of conducting an inquiry examining current policies, practices, and oversight of clinical research on human subjects at the University, in particular clinical research involving adult participants with diminished functional abilities. The administration, in collaboration with appropriate faculty governance committees, shall initiate the constitution of such an independent panel and shall support its inquiry. The panel shall have authority to obtain any records it deems necessary for a thorough inquiry, to the extent consistent with applicable law. At the conclusion of the inquiry, the panel shall issue a report that will be made publicly available, within the limitations of regulations governing the protection and privacy of individuals, including research participants, and the results will be reported back to the Faculty Senate so that senators have an opportunity to ask questions and discuss the report.*

The intent of this review is to ensure that the University's processes for clinical research on human subjects meet or surpass the established best practices and norms and to instill confidence among faculty and the public that the University of Minnesota research is beyond reproach. It is to be a forward-looking, productive, and independent review of current practice by an external expert panel.

I support the University Senate's resolution. To that end, I am charging you with the responsibility of conducting an inquiry examining policies, practices and oversight of

clinical research on human subjects at the University, in particular clinical research involving adult participants with diminished functional abilities. This review should be managed by an external partner and if any deficiencies in our current practices are found, the review should include recommendations for remedying them.

It is critical that this review be conducted thoroughly, professionally, independently and transparently. Please ensure that reviewers have appropriate access to information, resources and individuals needed to meet their charge. At least one member of the panel should be prepared to speak publicly to their process, findings and any recommendations for improvement. The final report will be public.

I look forward to receiving the report of the independent panel and am confident that the results will demonstrate that our faculty, policies and practices meet the highest quality standards.

EWK:jk

c: Aaron Friedman, vice president of Health Sciences and dean of the Medical School
Professor Will Durfee, chair, Faculty Consultative Committee
William Donohue, general counsel, Office of the General Counsel
Keith Dunder, Academic Health Center counsel, Office of the General Counsel
Amy Phenix, chief of staff, Office of the President

Section 2.1

Appendix 4: University of Minnesota Request for Proposals

University of Minnesota

Bid Information

Bid Owner	Jerry Taintor Category Manager/Contracts Specialist
Email	taint001@umn.edu
Phone	(612) 625-8579
Fax	(612) 626-0366
Bid Number	10714.769997.JST
Title	External Review of Clinical Research on Human Subjects
Bid Type	RFP
Issue Date	02/13/2014
Close Date	3/21/2014 2:00:00 PM

Contact Information

Address

Contact
Department
Building
Floor/Room
Telephone
Fax
Email

Ship to Information

Address

Contact
Department
Building
Floor/Room
Telephone
Fax
Email

Supplier Information

Company Name _____
Contact Name _____
Address _____
_____
_____
Telephone _____
Fax _____
Email _____

Signature _____ Date / /

Supplier Notes

Bid Notes

The University is seeking a contractor to define and manage the process of an expert review of current policies, practices and oversight of clinical research on human subjects. RFP specifications will not be mailed or faxed. RFP specs must be viewed and responses submitted electronically through the MBid system. Suppliers must register or already be registered in MBid in order to view the full RFP and respond. If you are not already a registered supplier go to http://purchasing.umn.edu/mbid/login.html and click New Supplier Registration link to register. If already registered, log in at the above URL to view the RFP and respond.

Bid Activities

Date	Name	Description
2/26/2014 10:30:00 AM	Pre-Proposal Conference Call	A Pre-Proposal conference call will be held to provide an overview of the project. Conference Call Phone in Number: 1-866-865-2157 Code: 9131070954 (press # after)
2/27/2014 2:00:00 PM	Deadline for Questions	Follow the instructions on the Questions Template in the Bid Attachment Section for submitting questions.

Bid Messages

Bid Attachments

The following attachments are associated with this opportunity and will need to be retrieved separately

Line	Filename	Description
Header	References_Attachment.doc	<B>ACTION REQUIRED </B>: References must be submitted using this attachment. Download the attachment, complete the form, label it
Header	Travel Policy.doc	All vendors must adhere to the University Travel Policy if there is travel and expense involved.
Header	Professional Services (501P-4).doc	Contract for Professional Services Terms and Conditions
Header	External_Review_RFP_Questions_Template.doc	Questions Template

Bid Attributes

Please review the following and respond where necessary

#	Name	Note	Response
1	External Review of Clinical research on Human Subjects	On December 5, 2013 the Faculty Senate approved a resolution requesting an external review of clinical research on human subjects at the University of Minnesota. Specifically the Senate resolution stated: BE IT RESOLVED that a panel external to and independent from the University of Minnesota be constituted for the purpose of conducting an inquiry examining current policies, practices, and oversight of clinical research on human subjects at the University, in particular clinical research involving adult participants with diminished functional abilities. The administration, in collaboration with appropriate faculty governance committees, shall initiate the constitution of such an independent panel and shall support its inquiry. The panel shall have authority to obtain any records it deems necessary for a thorough inquiry, to the extent consistent with applicable law. At the conclusion of the inquiry, the panel shall issue a report that will be made publicly available, within the limitations of regulations governing the protection and privacy of individuals, including research participants, and the results will be reported back to the Faculty Senate so that senators have an opportunity to ask questions and discuss the report.	_____ (Required)
2	Rationale for Requesting Services	The intent of this review is to ensure that the University's processes for clinical research on human subjects meet or surpass the established best practices and norms and to instill confidence among faculty and the public that the University of Minnesota research is beyond reproach. It is to be forward looking, productive, transparent and independent review of current practice by an external expert panel.	_____ (Required)

3	Objectives	- Obtain an independent, external assessment of the current policies, practices and oversight of clinical research on human subjects at the University of Minnesota - in particular clinical research involving adult participants with diminished capacity to provide consent. - Select an external contractor with widely recognized expertise and experience in clinical research on human subjects to manage the review process. External contractor selected will empanel an independent team of no less than three experts who will conduct a thorough, professional, independent and transparent review and issue a report that will be made publicly available. - Seek recommendations for any changes, if needed, to policies, practices and oversight of clinical research to align with best practices nationally.	_____ (Required)
4	Outcomes Needed	We expect the contractor selected in response to this RFP to define and manage the process of an expert review of the current policies, practices and oversight of clinical research on human subjects at the University of Minnesota - in particular clinical research involving adult participants with diminished capacity to provide consent. The expert review must include a review of relevant standard operating procedures and an assessment of compliance with regulations and other applicable law. A detailed report outlining the strengths and weaknesses of current policies, practices and oversight of clinical research involving adult participants with diminished capacity to provide consent is required. If any deficiencies in our current practices are found, the review should include recommendations for remedying them. The contractor will select and empanel an independent team of no less than three experts to include an MD who will conduct a thorough, professional, independent and transparent review. The review must examine policies, practices and oversight of clinical research on human subjects at the University, in particular clinical research involving adult participants with diminished functional abilities. At least one member of the panel should be prepared to speak publicly to their process, findings and any recommendations for improvement. The contractor will develop a plan for identifying the data needed, gathering the data and producing a final report that will be public. The contractor will orchestrate site visits and acquisition of materials and data to conduct the review. Key audiences for the results of the review include: University President, Board of Regents, University Faculty Senate, IRB and external stakeholders. The report will also be made publicly available.	_____ (Required)
5	University of Minnesota Obligation	The University of Minnesota will ensure that the panel has appropriate access to information, resources and individuals needed to meet their charge.	_____ (Required)
6	Timeline	The final report shall be delivered on or about July 1, 2014.	_____ (Required)

7	Evaluation Criteria	The selected Respondent will be the Respondent whose Proposal is the most advantageous to the University. The University is not bound to accept the lowest priced Proposal if the Proposal is not in the best interests of the University as determined by the University in its sole discretion. Proposals will be evaluated on the following criteria: <TABLE border =”1”> <tr> <Th> # </TH> <TH> Evaluation Criteria </TH> <TH>Percentage </TH> </tr> <TR> <td> 1 </td> <td> Recognized expertise and experience with clinical trials research and nationally recognized accreditation processes (AAHRP) </TD> <TD> 20% </TD> </TR> <TR> <td> 2 </td> <td> Extensive connections and networks with expertise required to perform this review. </TD> <TD> 10% </TD> </TR> <TR> <td> 3 </td> <td> Experience with managing these types of reviews in a higher education system. </TD> <TD> 20% </TD> </TR> <TR> <td> 4 </td> <td> Total Cost - Provide a Fixed Price for the work as outlined, that includes travel and expenses. </TD> <TD> 30% </TD> </TR> <TR> <td> 5 </td> <td> Quality of the proposed project plan, which could include methods, accountability metrics and communication/dissemination plan. </TD> <TD> 20% </TD> </TR> <TR> <TD> </TD> <td><B><ALIGN=”RIGHT”>TOTAL</td> <TD><b><ALIGN=”RIGHT”>100% </TD> </TR> </TABLE>	_____ (Required)

8	<B> ** VENDOR INSTRUCTIONS **	This RFP contains multiple pages. You can move from page to page by clicking on the numbers or arrows that are located on the maroon bar that appears at the bottom of the Attributes section. Respond with a thorough answer to each question in the space provided unless it is noted that a response may be provided in a separate attachment. Be as brief as possible while still providing pertinent information. If a response is lengthy (e.g. longer than 200 words), summarize your answer in the space provided and include a more detailed answer as an attachment. All attachments should be labeled as 'vendorname_attachmentname'. DO NOT USE A "#" SIGN OR "&" SIGN IN YOUR ATTACHMENT NAME. If you wish to generate a copy of this RFP for review, click on Documents and choose the Invitation Document. A PDF extract of your response will be generated. 	(No Response Required)
9	RFP Deadlines	It is important that you note the RFP Close date and time. The MBid system will not accept a late submission. If you submit early and wish to change an answer, hit RETRACT, make your changes and then resubmit. 	(No Response Required)
10	Questions and Answers	Questions regarding the RFP must be included on the QUESTIONS ATTACHMENT and submitted via email to the buyer responsible for the RFP by the time and date noted in the Bid Events section of the RFP. Responses to questions which involve an interpretation or change to this RFP will be issued as an addendum by Purchasing Services and will be posted electronically in the MBID system. Vendors registered in the MBID system for the specific commodity will be notified via email that the Addendum has been issued. At that time you should review the RFP and any changes/additional information included. Only additional information provided by formal written addenda shall be binding. Oral and other interpretations or clarifications, including those occurring at pre-Proposal meetings, site visits, tours, etc. are not binding unless otherwise stated.	_____ (Required)
11	Addendum	The University reserves the right to issue one or more addenda to the RFP at any time for any reason.	_____ (Required)
12	Withdrawing Proposals	You may withdraw your Proposal at any time prior to the RFP Close Date and Time by viewing your Submitted response in the MBID system and then clicking on RETRACT</B>. The Respondent may submit another Proposal at any time prior to the Close Date and TIme. No Proposal may be withdrawn after the Close Date and Time without approval by the University. Such approval shall be based on Respondent's submittal, in writing, of a reason acceptable to the University in its sole discretion.	_____ (Required)
13	Proposal Submission	All responses must be submitted electronically using the University's MBID system. All supplemental information should be uploaded into the RESPONSE ATTACHMENTS</B> section in your bid response and should be clearly labeled with Respondent's name and content using this format - 'vendorname_attachmentname.'	_____ (Required)

14	Late Submissions	The University will not accept Proposals received after the Close Date and Time. The MBID system will not allow for a late submittal and if Respondent has not submitted their proposal by Clicking on the SUBMIT</B> button, their Response will not be available for review by the University. The Respondent assumes the risk of submitting their Response by the Close Date and Time.	_____ (Required)
15	Ownership of Proposal	All materials submitted in response to this request become the property of the University and may become a part of any resulting contract. Award or rejection of a Proposal does not affect this right.	_____ (Required)
16	Release of Claims, Liability and Preparation Expenses	Under no circumstances shall the University be responsible for any Proposal preparation expenses, submission costs, or any other expenses, costs or damages, of whatever nature incurred as a result of Respondent's participation in this RFP process. Respondent understands and agrees that it submits its Proposal at its own risk and expense and releases the University from any claim for damages or other liability arising out of the RFP and award process.	_____ (Required)
17	Duration of Respondent's Proposal	The Respondent certifies that its Proposal is a valid, firm and irrevocable offer which the University may accept within a minimum of 90 days from the Due Date of this RFP, and that its Proposal, if accepted, shall remain valid for the life of this contract.	_____ (Required)
18	Errors in Proposals	The University shall not be liable for any errors in Respondent's Proposal. Except during negotiations initiated by the University, no modifications to a Proposal shall be accepted after the Close Date and Time. You must ensure that all information, including pricing, is correct and complete. You are responsible for all errors and omissions contained in your proposal; so the University may reject a Proposal based on its erroneous or omitted information, even if the correct or complete information was available to the University elsewhere. Similarly, the University may accept your Proposal based on the erroneous or omitted information, and you will be bound by the information as it appears in the Proposal, even if the correct or complete information was available to the University elsewhere.	_____ (Required)
19	Public Proposal Viewing	After the award has been made and upon finalizing a contract with the selected Respondent(s), the Proposal file may be viewed subject to the University's Record and Information Management policies and procedures.	_____ (Required)

20	Award Process	 - After completion of the RFP review process, an award may be made on the basis of the Proposals submitted, without discussion, clarification or modification, or on the basis of negotiation with any or all of the Respondents. - Issuance of this RFP does not require the University to award or contract. The University reserves the right to reject any or all Proposals, wholly or in part; to waive any technicalities, informalities, or irregularities in any Proposal at its sole option and discretion. The University reserves the right to request clarification or additional information. The University reserves the right to award a contract in whole or in part, to award multiple contracts to multiple Respondents, to re-solicit for Proposals or to temporarily or permanently abandon the procurement. If the University awards a contract, it will award the contract to the Respondent or Respondents whose Proposal(s) is(are) the most advantageous to the University as determined by the University in the exercise of its sole discretion. - If the University awards a contract as a result of this RFP process, the resulting contract shall consist of: - The terms, conditions, specifications and requirements of this RFP and its attachments. - Any addenda issued by the University pursuant to this RFP. - All representations (including but not limited to, representations as to price, specifications, performance and financial terms) made by the Respondent in its Proposal and during any presentations (videotaped or otherwise) or demonstrations for the benefit of the University. - Any mutually agreed upon written modifications to the terms, conditions, specifications, and requirements to this RFP or to the Proposal. 	_____ (Required)

21	Responses Subject to Public Disclosure	The University considers all information, documentation and other materials (collectively "Materials" or "items") submitted in response to this RFP to be non-confidential and/or non-proprietary, and subject to public disclosure after a contract is awarded. By submitting a Proposal, Respondent agrees to release the University from any liability resulting from University's disclosure of such information. If submitting information that you believe to be trade secret materials, as defined by the Minnesota Government Data Practices Act, Minnesota Statute 13.37, subd. 1(b) (MBDPA), you <u>must</u> follow these instructions exactly for information to be considered for confidentiality review: - Confidential Information should be limited to that which is truly confidential under the MGDPA. NOTE: The Department of Administration has opined in several decisions based on Minn Stat. 13.37, Subd, 1(b) that pricing information may not be considered trade secret information. Financial statements can be considered as a trade secret. - Include all Materials that are to be considered "Confidential" in a separate word document which is clearly and conspicuously marked "CONFIDENTIAL." This document must also include the RFP #, the Subject of the RFP and the name of your company. - Include an opinion indicating the legal basis for regarding the Material as a trade secret under the MGDPA. Include the name of the person who has written the opinion. - Upload the document containing BOTH the legal basis for confidentiality and the Confidential Information to the RESPONSE ATTACHMENTS</B> section of the RFP. - NOTE: Confidential Information will be provided electronically to the RFP review committee to be used during the RFP review process. - Prior to release of the files for public viewing, the Office of Records Management will review the Confidential Information to ensure it meets the MGDPA standards. 	_____ (Required)
22	Confidential Information Submission	Respondent acknowledges that if they are submitting confidential information that they have carefully read the above section, Responses Subject to Public Disclosure in the RFP Process and General Instructions Document. Respondent further acknowledges that they have followed the instructions exactly as outlined in that Section and that the confidential information provided is limited to that which is truly confidential and considered a trade secret under the Minnesota Government Data Practices Act. Valid Responses: [Please Select], Confidential Information Submitted, No Confidential Information Submitted	_____ (Required)
23	Oral Presentations/Site Visits	One or more Respondents may be required to do an oral presentation and/or allow the University to visit the Respondent's site. Each Respondent should be prepared to discuss and substantiate any area of its Proposal, its own qualifications for the Goods/and or Work, and any other area of interest relative to its Proposal.	_____ (Required)

24	Testing and Samples	The University reserves the right to request a demonstration of, or to test, any or all Goods and/or Work proposed in response to this RFP. If Respondent fails to provide such demonstration or fails to provide such Goods and/or Work for testing, the Respondent's Proposal may be rejected by the University in its sole discretion. The Respondent warrants that if awarded a contract, the Goods and/or Work delivered under such contract shall meet or exceed the quality of the Goods and/or Work demonstrated or tested. Samples of the quoted products, when requested, must be furnished free of charge and in a timely manner. If not destroyed by testing and if practical, samples may be returned at the Respondent's request and expense following contract award. Respondent should not submit unsolicited samples. If samples are requested in the RFP, Respondent must follow the instructions provided for submitting the samples.	_____ (Required)
25	Subcontracting	Unless otherwise agreed to in writing by the University, the selected Respondent is responsible for performance of any subcontractors. Use of subcontractors in the performance of the contract is subject to University consent. The selected Respondent must ensure that any subcontractors abide by all terms and conditions of the contract.	_____ (Required)
26	Office of Business and Community Economic Development	The Office of Business and Community Economic Development ("BCED") is available to assist Small Business as part of the University's goal of fostering economic growth in urban communities. Businesses owned by women, people of color, people with disabilities, and other historically and currently underrepresented groups are especially encouraged to take advantage of the BCED's services. For inquiries regarding these services, contact BCED at 612-624-0530.	(No Response Required)
27	University Travel Policy Acknowledgment	Respondent acknowledges that they have read and understood the University Travel Policy as provided in the Bid Attachments section of the RFP.	_____ (Required)
28	<B>**RESPONDENT PROPOSAL CERTIFICATIONS**</B>	By agreeing to the certifications listed below, Respondent certifies that they have carefully examined all instructions, requirements, specifications, terms and conditions of this RFP; and hereby offers to furnish the Work and/or Goods, as applicable, at the prices quoted in Respondent's Proposal, and in accordance with the requirements, specifications, terms and conditions of this RFP.	(No Response Required)

29	Certifications	 - RESPONSIBLE RESPONDENTS.<UL> - Respondent certifies that it has the necessary experience, knowledge, abilities, skills, capacity and resources to satisfactorily perform the requirements, specifications, terms and conditions of this RFP. - The University reserves the right to award contracts only to responsible Respondents, defined as companies that demonstrate the financial ability, resources, skills, capability, willingness and business integrity necessary to perform under the contract. The University's determination of whether a Respondent is a responsible Respondent is at the University's sole discretion. </UL> - Respondent certifies that it is aware of, is fully informed about, and is in full compliance with all applicable federal, state and local laws, rules, regulations and ordinances and it is not currently debarred or suspended from doing business with the Federal government, the state of Minnesota, any other state in the United States, or any of their respective agencies. - Respondent certifies that all statements, information and representations prepared and submitted in response to this RFP are current, complete, true and accurate. The Respondent acknowledges that the University will rely on such statements, information and representations in selecting the successful Proposal. - Respondent acknowledges that submission of a Proposal indicates the Respondent's acceptance of the evaluation process described in the RFP and the Respondent's recognition that some subjective judgments may be made by the University as part of the evaluation in its sole discretion. - CONFIDENTIALITY. <UL> <LI>Respondent certifies that it understands and agrees that the University will not treat any information, document, or materials submitted by Respondent as confidential unless the Respondent strictly adheres to the procedures set forth in the RFP Process and General Instructions. - Respondent agrees that the University may disregard confidentiality notices on headers/footers as well as copyright designations that accompany or are contained on material or documents submitted as part of Respondent's Proposal. - It is further understood and agreed that all material and documents not conforming to the procedures set forth in the RFP Process and General Instructions will be made available for immediate public inspection and copying upon completion of the RFP process. - Respondent agrees to defend any action seeking release of the Materials believed to be trade secret, and indemnify and hold harmless the University, its regents, agents and employees ("Releases"), from any judgments or damages awarded against the Releases in favor of the party requesting the materials and any and all costs connected with that defense. 	(No Response Required)
30	Electronic Signatures	<B>IMPORTANT LEGAL NOTICE </B>Subject to state and federal law, the University of Minnesota accepts electronic signatures with the same force and effect as original, physically written signatures. By placing the name of a person on the required signature lines in your response, you are certifying that the person has authority to bind your company and that your company is bound by the statement, representation, or contractual promise.	_____ (Required)

31	Legal Name of the Respondent	Please provide company's legal name.	_____ (Required)
32	Address	What is the address of the office which will fulfill this contract?	_____ (Required)
33	Federal ID Number	Please provide your federal ID number if you have one.	_____ (Optional)
34	Number of years in business	How many years have you been in the business related to this RFP? Valid Responses: [Please Select], 1-5 , 6-10, 11-15, 16-20, more than 20	_____ (Required)
35	Type of Organization	Choose the type of organization. Valid Responses: [Please Select], Individual, Partnership, Corporation, Government, Other: Detail below	_____ (Required)
36	Type of Organization: Other Detail	If you chose OTHER in the Type of Organization, please provide detail as to the type of organization you are.	_____ (Optional)
37	Public or Private	Are you a public or private organization? Valid Responses: [Please Select], Public, Private	_____ (Required)
38	Total Number of Employees	How many employees are in your organization?	_____ (Required)
39	Number dedicated to fulfillment of this RFP	How many employees will be dedicated to the fulfillment of this RFP?	_____ (Required)
40	Company-wide Annual Sales Volume	What is your Company-wide Annual Sales Volume?	_____ (Required)
41	Financial Statements Upon Request	Upon request, Respondent will provide a copy of audited financial statements for the past three (3) years.	_____ (Optional)
42	Financial Ratings	If you have a D&B or other financial rating, please provide it here.	_____ (Optional)
43	Sale or acquisition?	Is Respondent currently for sale or involved in any transaction to expand or to become acquired by another business entity? Valid Responses: [Please Select], Yes: Explain Below, No	_____ (Required)
44	Sale or acquisition detail	If you responded yes to the question above, please describe thoroughly, including, but not limited to parties involved, expansion or acquisition plans and timing.	_____ (Optional)
45	Past or Pending Litigation	Provide details of all past or pending litigation or government action filed or claims made against Respondent that could affect Respondent's performance under a contract with the University.	_____ (Optional)
46	Default	Is Respondent currently in default, or do you foresee going into default, beyond applicable cure periods on any loan agreements or financing agreements with any bank, financial institution or other entity? Valid Responses: [Please Select], Yes: Detail Below, No	_____ (Required)
47	Default Detail	If you answered yes above, specify the dates, details, circumstances and prospects for resolution.	_____ (Optional)
48	Current Relationship with the University	Does any current relationship, whether a relative, business associate, capital funding agreement or any other such kinship, exist between Respondent and any University employee? Valid Responses: [Please Select], Yes: Detail below, No	_____ (Required)
49	Current Relationship Detail	If you answered yes to the question above, please explain the relationship.	_____ (Optional)

50	Performance Circumstances	Are there any circumstances impacting Respondent's ability to perform under any award made through the RFP process? Valid Responses: [Please Select], Yes: Detail below, No	_____ (Required)
51	Circumstances Detail	If the answer was Yes to the above question, please provide the detail.	_____ (Optional)
52	Person to Contact During RFP Process	Please include the name, email address and phone number of the person to contact during the RFP process.	_____ (Required)
53	Award Terms and Conditions Instructions	Any award made as a result of this RFP process will be governed by the terms and conditions included in this RFP. If you take exception or wish to propose an addition or deviation to any term or condition in this document, do so clearly and conspicuously in your proposal. To facilitate your response: Download the terms and conditions found in the Bid Attachment Section of this RFP. Using the ”Track Changes” feature in Microsoft Word, redline the document indicating proposed changes to the University terms and conditions. Explanations as to why you are proposing the changes are appreciated. Upload an unlocked, editable Word version of your proposed changes to BID RESPONSE ATTACHMENTS. If you do not clearly and conspicuously take an exception or propose additional to a specific term or condition, you will be bound by the University's terms and conditions in the event an award is made to you. The University reserves the right in each instance to: Accept any Proposal with deviations, additions, or exceptions; Negotiate deviations, additions or exceptions; or Reject a proposal with deviations, additions, or exceptions the University deems unacceptable at its option and in its sole discretion. NOTE: In the University's terms and conditions included in this RFP, the phrase ”Purchase Order” shall refer to the award made pursuant to this RFP process. The term ”Seller” shall refer to the Respondent receiving an award under this RFP Process.	_____ (Required)

Line Items

Section 2.1

Appendix 5: External Review Team Member Biographies and Disclosures

External Review Team Conflicts of Interest Disclosures

All individuals listed below received consulting fees and reimbursement for travel and expenses paid by the University via its contract with AAHRPP for the performance of this review.

Anne Donahue, JD has no interests, financial or otherwise, to disclose.

Melissa Frumin, MD, MS has no interests, financial or otherwise, to disclose.

Joan Rachlin, JD, MPH has no financial interests to disclose. As the longtime executive director of PRIM&R she had extensive contact with Moira Keane, formerly of the University of Minnesota HRPP/IRB. Ms. Keane was a close colleague, a friend, and has been a longtime PRIM&R Board member. In her capacity as PRIM&R's executive director, Ms. Rachlin was closely involved in its educational programming. Moe than one dozen members of the University faculty were invited to give talks at PRIM&R meetings during her tenure and she met all of them, including, Richard Bianco, Carl Elliott, Cyd Gillette, Dale Hammerschmidt, Michael Oakes, Simon Rosser, Susan Wolf, and of course, Ms. Keane, among them.

Additionally, during her tenure at PRIM&R, the Board of Directors was one of the founders of AAHRPP, the accrediting organization that received the RFP for this external review. AAHRPP was incorporated as an independent nonprofit in 2001 and the two organizations have maintained a professional and collegial relationship since then. AAHRPP's CEOS, Elyse Summers, is a longtime colleague and friend of Ms. Rachlin.

Megan Kasimatis Singleton, JD, MBe, CIP has no interests, financial or otherwise, to disclose.

David Strauss, MD has no financial interests to disclose. As a member of SACHRP and its Subpart A Subcommittee, he had regular professional contact with Moira Keane. Dr. Strauss is also a member of the Board of Directors for PRIM&R on which Moira Keane also serves. Dr. Strauss has a reporting relationship to Dr. Jeffrey Lieberman, Chairman of the Department of Psychiatry at Columbia University. During the course of this review, Dr. Strauss learned that prior to coming to Columbia in 2005, Dr. Lieberman served as principal investigator of the 26 site CAFE study. Dr. Lieberman had no input into this report.

Jeremy Sugarman, **MD**, **MPH**, **MA** receives salary support from Johns Hopkins University. His research is supported by grants from the National Institutes of Health and the Patient Centered Outcomes Research. He receives consulting income from Merck KGaA and Quintiles. He also receives royalty payments from Georgetown University Press and Oxford University Press. Dr. Sugarman is also a member of the Board of Directors for PRIM&R on which Moira Keane also serves.

Anne B. Donahue, JD, has been a Vermont state representative since 2003 where she is the ranking member of the House Health Care Committee and a member of the Joint Legislative Mental Health Oversight Committee. She is the editor of Counterpoint, the state mental health consumer newspaper published by Vermont Psychiatric Survivors, a peer-run advocacy and support organization.
Ms. Donahue is a member of the University of Vermont Medical Center's program quality committee for psychiatry, the Green Mountain Care Board community advisory committee, and the Blueprint for Health, Mental Health and Substance Abuse Advisory Committee. She has served on the Vermont Act 129 Mental Health Insurance Parity committee (2000–2012) and the Vermont State Program Standing Committee for Adult Mental Health (2000–2004).

Her national involvement includes membership on the Subcommittee on the Inclusion of Individuals with Impaired Decision-Making in Research (SIIIDR), which was part of the Secretary's Advisory Committee on Human Research Protections (SACHRP), Department of Health and Human Services in 2007-8. Ms. Donahue has also been a major speaker at several national meetings, including PRIM&R's 2012 annual "Advancing Ethical Research" conference where she gave a plenary talk titled "*IRB Review of Research on Mental Illness: Are Additional Protections Always Appropriate Protections*?" . She presented the conference keynote address at the annual American Psychiatric Nurses Association (2005) meeting, and also presented "*A World Beyond Stigma*" at the American College of Mental Health Administrators (2005).

Both journalist and author, Ms. Donahue has published several journal articles, including: Donahue AB. *Electroconvulsive Therapy and Memory Loss: A Personal Journey;* Journal of ECT. 2000; 16(2):133-143; Donahue AB. *Riding The Mental Health Pendulum: Mixed Messages In The Era Of Neurobiology And Self-Help Movements*, and Social Work. 2000; 45(5):p.427-438; collaborated in Lambert D, Donahue AB, Mitchell M, Strauss R. *Mental Health Outreach: Promising Practices in Rural Areas*, National Association for Rural Mental Health November, 2001, Center for Mental Health Services Substance Abuse and Mental Health Services Administration; and was published in Donahue AB. *Electroconvulsive Therapy And Memory Loss* (letter). JAMA, 2007 Oct 24; 298(16):1862. Ms. Donahue also served as a reviewer for The Practice of Electroconvulsive Therapy, 2nd Ed, American Psychiatric Association (2000).

In recognition of her extraordinary advocacy, Ms. Donahue has received multiple mental health advocacy awards from the Vermont Children's Forum (2006), the Vermont Coalition for Disability Rights (2004), and Vermont Protection and Advocacy (2001). She received the *Jefferson Award*, National Institute for Public Service, for Lifetime Achievement (1997) and for "Greatest Accomplishment by a Person Age 35 or Younger" (1990).

She graduated from Georgetown University Law Center, J.D., cum laude, 1981 receiving the International Academy of Trial Lawyers distinguished advocacy award in juvenile justice. She is an inactive member of the bar in each of the following states: Vermont, New Jersey, and the District of Columbia.

Prior to her legislative and advocacy work in Vermont and nationally, Ms. Donahue worked for nine years in the 1990's at Covenant House, the runaway and homeless youth agency, first as a staff attorney in New York City and then as the founding Executive Director of Covenant House California.

Melissa Frumin, MD, MS, is a neuropsychiatrist and general psychiatrist at Brigham and Women's Hospital in Boston, an IRB chair at Partners (Massachusetts General Hospital and Brigham and Women's Hospital) and an assistant professor of psychiatry at Harvard Medical School. She is board certified in Psychiatry, Forensic Psychiatry, and Behavioral Neurology/Neuropsychiatry.

Dr. Frumin, prior to attending medical school, worked for the California Occupational Safety and Health Administration (Cal OSHA) , as an inspector of work places, applying safety regulations to industries with high rates of injuries. For 2 years, she worked in the Cal OSHA education department, preparing safety education materials and conducting a state-wide educational needs assessment. Following here 6 years at Cal OSHA, she attended the UC San Francisco/UC Berkeley Joint Medical Program, receiving her Masters in Health and Medical Sciences from UC Berkeley in 1990 and her MD from UC San Francisco in 1992. Her Master's thesis was an analysis of the responses of different stakeholders to the proposed OSHA Bloodborne Pathogens Standard. This new standard was partially a response to patient to health care worker HIV seroconversion at the height of the AIDS epidemic.

Dr. Frumin completed her medical internship at UC San Francisco, and her psychiatry residency at Massachusetts General (MGH), followed by a medical psychiatry/neuropsychiatry fellowship at Brigham and Women's Hospital (BWH). For the past 18 years, her clinical work has been in the BWH Neurology Department, caring for people with neuropsychiatric sequelae of dementia, multiple sclerosis and other neurological brain disorders. She also has a private general psychiatry practice.

For 9 years, she worked in a Harvard brain imaging laboratory, identifying structural brain abnormalities in people with psychosis. She performed most of the diagnostic interviews, wrote the IRB protocols, and was the physician engaged in the consent process. This work resulted in the publication of 21 original papers in peer reviewed journals, as well as 3 review articles.

From 2003-2005, she served as a member of the Partners (BWH and MGH) IRB and in 2005, she became an IRB Chair of a Partners medical panel reviewing new protocols. Dr. Frumin also works at the IRB office reviewing amendments, Data Safety Monitoring Board reports, as well as participating in non-compliance investigations. She teaches IRB related topics, to the research staff at both BWH and MGH. She taught a course to Harvard Medical students about the IRB, setting up a mock board with "real" protocols to review. She has also given talks related to the ethics of research, and particularly the IRB process at PRIM&R, Harvard Law School, the International Suicidality Capstone Meeting at Columbia University, and other national organizations.

Joan Rachlin, JD, MPH, served as the executive director of PRIM&R (Public Responsibility in Medicine and Research) from 1975 until her retirement in 2014. She led the organization from its infancy to its current status as the premier educational organization for those conducting and reviewing research both in the United States and globally. PRIM&R has become a unique forum at which every stakeholder group can come together to discuss ethical issues, best practices, and the myriad of controversies that arise in the ever-changing fields of research with human and animal subjects. PRIM&R has a membership of over 4,500 research professionals from around the world.

In addition to planning and organizing more than 300 conferences, short courses, and webinars, Ms. Rachlin also edited the proceedings from most of PRIM&R's conferences. In addition, she produced, in collaboration with two PRIM&R Board members, *Investigator 101*, a CD-ROM for researchers and research staff. *Investigator 101* has been distributed to every major academic health center and university in this country under the aegis of the Office for Human Research Protections (OHRP). Ms. Rachlin was also instrumental in developing PRIM&R's highly acclaimed educational series, which includes *IRB 101 – Biomedical Research*, *IRB 101 – Social Science, Behavioral, and Educational Research*, *IRB 250*, *IRB Administrator 101*, *IRB 201*, as well as seven other short courses.

Under her stewardship, PRIM&R maintained an active and respected Public Policy Committee, which submitted comments on most of the regulatory and policy proposals affecting research over the past four decades. Ms. Rachlin helped launch PRIM&R's certification initiatives, the Certified IRB Professional (CIP®) and the Certified Professional IACUC Administrator (CPIA®) credentials. Among her proudest PRIM&R accomplishments was the creation of "People & Perspectives," an online archive of stories from the research ethics community (www.peopleandperspectives.org). She also was responsible for the development of WISH-net, an online mentoring program for women and girls interested, or already pursuing careers, in science and medicine. This program was developed pursuant to a contract with the Office of Research on Women's Health at NIH.

In addition to her work with PRIM&R, Ms. Rachlin has practiced law, concentrating in the areas of women's health, civil rights, and criminal and civil litigation. She has taught and lectured extensively at several Boston-area colleges on issues relating to women's health, health law, and research ethics. She is a contributor to the well-known book, *Our Bodies, Ourselves* and serves on its Advisory Committee. She is a past member of the editorial board of the journal *IRB: A Review of Human Subjects Research*. Finally, Ms. Rachlin served on two Boston area institutional review boards and one institutional animal care and use committee.

Ms. Rachlin holds a JD from the Suffolk University School of Law and an MPH from the Harvard School of Public Health.

Megan Kasimatis Singleton, JD, MBe, CIP is Associate Director, Human Research Protections at the University of Pennsylvania. In this role she has oversight responsibility for the University's nine IRBs and their associated support staff.

Ms. Singleton serves as a regulatory representative at the convened IRB meetings providing guidance to IRB members and staff regarding applicable regulatory requirements during the course of the IRB review process. Additionally, she serves as the IRB's liaison to the University's Conflicts of Interest Standing Committee and is a member of the University's Human Research Advisory Committee.

She is the lead contact at the IRB for questions related to privacy and security and serves as the institution's HIPAA Research Privacy Officer.

She has primary responsibility for organizing IRB driven educational initiatives for IRB staff, members and the research community.

Ms. Singleton regularly lectures on a range of topics related to research ethics and human subjects protections and serves as co- Course Director for a course in the Master of Translational Research Program at Penn titled *Scientific and Ethical Conduct of Research*. For this course she oversees students serving a six month IRB membership term as part of their course requirement.

Ms. Singleton has served as faculty at PRIM&R's annual conference since 2009 and as guest lecturer for two Quality Improvement workshops sponsored by the Office of Human Research Protections (OHRP).

Ms. Singleton has been involved in several international research ethics training initiatives. In 2010 she served as a faculty reader for a Botswana-based research ethics training initiative, evaluating the efficiency of a 6-week email-based case discussion for improving subjects' efficiency in identifying ethical issues in human subjects research. In 2012, she co-taught a week-long course in nursing ethics in practice to nurse faculty in Botswana that was later used as a basis for curriculum development in ethics for diploma, BSN and MSN students in nursing at the University of Botswana and the Institute of Health Sciences. She currently serves as faculty and IRB Fellows Director on an NIH-Fogarty funded project titled *Building Local Capacities in Ethics Training and IRB Review in Guatemala*. In this role she is responsible for oversight, mentoring and training of three IRB fellows each of whom will complete a 6 month training period in IRB administration at the University of Pennsylvania followed by field placements within designated IRBs in Guatemala.

Ms. Singleton is a licensed attorney in Pennsylvania and a certified IRB professional. She earned her law degree from Temple University and her Masters in Bioethics from the University of Pennsylvania. She has worked in the field of research and research ethics at the University since 2002, joining the IRB in 2008, first as an IRB member, then as Associate Director for Education and Training prior to assuming her current role.

David H. Strauss, MD is Director of Psychiatric Research at the New York State Psychiatric Institute (NYSPI), Associate Professor of Psychiatry at Columbia University Medical Center and Vice Chair for Research Administration, Ethics, and Policy in the Columbia University Department of Psychiatry. He oversees the 23 Research Divisions and 10 Research Centers that comprise Columbia Psychiatry/NYSPI along with its portfolio of more than $100 million in externally sponsored research. Dr. Strauss is responsible for the oversight of NYSPI's core research facilities and research compliance functions, including IRB, IACUC, Conflict of Interest, and Research Integrity.

Dr. Strauss is a graduate of Cornell University Medical College (now Cornell Weill) and trained in psychiatry at New York Presbyterian Hospital (Columbia)/NYS Psychiatric Institute. Dr. Strauss served as an attending psychiatrist and then as Chief of the Schizophrenia Research Unit at NYSPI where he conducted research related to the phenomenology of schizophrenia and putative neuro-immune mechanisms schizophrenia. From 1995 to 2000 Dr. Strauss served as Clinical Director of NYSPI.

From 2000 until 2010, Dr. Strauss was Chair of the NYSPI IRB and Director of the department's Office of Humans Subjects Research. Dr. Strauss currently co-chairs Columbia University's Standing Committee on the Conduct of Research and serves as a member of the University's Conflict of Interest Committee. He formerly co-directed the Ethics, Public Policy and Human Rights Core of the HIV Center for Clinical and Behavioral Studies.

Dr. Strauss is past recipient of two NIH grants on research ethics training and the enhancement of human subjects oversight for psychiatric research. He is a former member of the HHS Secretary's Advisory Committee on Human Research Protections (SACHRP) and completed work as co-chair of its Subcommittee on the Inclusion of Individuals with Impaired Decision-making in Research. He current serves on a SACHRP subcommittee charged with developing recommendations to enhance Subpart A or the "Common Rule." Dr. Strauss is a member of the Board of Directors of PRIM&R and co-chaired PRIM&R's core conference planning committee for the 2012 -2014 annual meetings.

Dr. Strauss teaches, lectures, and consults widely on matters of human subjects protections and applied research ethics. He maintains a private practice of general psychiatry, psychotherapy and psychopharmacology.

Jeremy Sugarman, **MD**, **MPH**, **MA** is the Harvey M. Meyerhoff Professor of Bioethics and Medicine, professor of medicine, professor of Health Policy and Management, and deputy director for medicine of the Berman Institute of Bioethics at the Johns Hopkins University. He is an internationally recognized leader in the field of biomedical ethics with particular expertise in the application of empirical methods and evidence-based standards for the evaluation and analysis of bioethical issues. His contributions to both medical ethics and policy include his work on the ethics of informed consent, umbilical cord blood banking, stem cell research, international HIV prevention research, global health and research oversight.

Dr. Sugarman is the author of over 250 articles, reviews and book chapters. He has also edited or co-edited four books (*Beyond Consent: Seeking Justice in Research*; *Ethics of Research with Human Subjects: Selected Policies and Resources*; *Ethics in Primary Care;* and *Methods in Medical Ethics*). Dr. Sugarman is a contributing editor for *IRB* and is on the editorial boards of several academic journals.

Dr. Sugarman consults and speaks internationally on a range of issues related to bioethics. He has served as senior policy and research analyst for the White House Advisory Committee on Human Radiation Experiments, consultant to the National Bioethics Advisory Commission, and Senior Advisor to the Presidential Commission for the Study of Bioethical Issues. He also served on the Maryland Stem Cell Research Commission.

He was the founding director of the Trent Center for Bioethics, Humanities and History of Medicine at Duke University where he was also a professor of medicine and philosophy. He is a faculty affiliate of the Kennedy Institute of Ethics at Georgetown University and an Academic Icon of the University of Malaya.

Dr. Sugarman currently serves on the Scientific and Research Advisory Board for the Canadian Blood Service, the Ethics and Public Policy Committee of the International Society for Stem Cell Research, and the Board of Directors of PRIM&R (Public Responsibility in Medicine and Research). He is co-chair of the Johns Hopkins' Institutional Stem Cell Research Oversight Committee. In addition, he is chair of the Ethics Working Group of the HIV Prevention Trials Network and is the ethics officer for the Resuscitation Outcomes Consortium.

Dr. Sugarman has been elected as a member of the American Society of Clinical Investigation, Association of American Physicians, and the Institute of Medicine. He is a fellow of the American Association for the Advancement of Science, the American College of Physicians and the Hastings Center.

Section 2.3

Appendix 6: Documentation Requested for Targeted Protocol List

Appendix:6

Documentation Requested for Targeted Protocol List

For a selected list of 20 protocols, The University of Minnesota was asked to provide:

1. The currently approved version of the protocol, consent and any UMN application documents required to assess approval (e.g. UMN specific application pieces that would address site-specific issues like monitoring, recruitment, etc.)
2. Copies of any videotapes documenting the consent process for these studies, if available.
3. Copies of any auditing/monitoring reports for these studies that specifically comment on the consenting process.
4. Copies of any scientific reviews conducted at the departmental level for these protocols
5. Meeting minutes for the initial review of each of these protocols by the convened IRB including all sets of meeting minutes that led up to the initial protocol approvals.
6. Copies of any continuing review documents, including the IRB meeting minutes related to those reviews
7. Minutes related to specific actions reviewed by the IRB that were of interest to the review team (e.g. review of minutes for an unanticipated problem)
8. Documentation of any follow-up to questions/concerns flagging in monitoring reports

Section 2.3

Appendix 7: Summary of Initial and Follow-up Items Requested for Records Review

Appendix 7: Summary of Initial and Follow-up Items Requested for Records Review

Part A. Initial Document Requests

The following documents were requested and provided prior to the September 2014 site visit:

Request 1:
Requested 7/15/2014
Supplied 7/28/2014- 8/4/2014

1. Organizational Overview explaining the scope of the overall HRPP and the overall human research portfolio. Also describe the landscape of research involving individuals with potentially diminished capacity, how it breaks down in terms of sponsor type (e.g., industry, government, investigator initiated), and a sense of the various stakeholders (including reference to those with diminished capacity who've had positive as well as negative experiences as research subjects at UMN).

2. A list of all protocols active during the past three years that recruit adult and minor subjects from the following diagnostic groups and are more than minimal risk:

    - Autism Spectrum Disorders
    - Other Developmental Disabilities
    - Schizophrenia and schizophrenia spectrum disorders
    - Other psychotic disorders
    - Bipolar disorder
    - Alzheimer's disease
    - Other dementias
    - Acute stroke

    For each protocol above, indicate the following:
    - Study title
    - Abstract (if available)
    - PI and other key personnel and role
    - Sponsor and title of grant (if applicable)
    - Single or multiple site
    - IRB of record
    - Current enrollment status
    - Whether the protocol is approved to enroll subjects who lack consent capacity

3. Key Personnel List (use the AAHRPP supplied Excel spreadsheet) and Organizational Chart along with a detailed description of who the key players and what their roles are within the HRPP.

4. IRB/Institution/HRPP policy on additional safeguards and standard procedures for minimizing risk for adult populations considered "vulnerable" by virtue of impaired decision-making.

5. Applicable State and local policies and procedures related to the inclusion of subjects with impaired consent capacity and surrogate consent.

6. Procedures used when PIs or other research staff receives complaints or hear of concerns from a subject's family or friends about the inclusion of said subject in a given protocol. Information whether such complaints or concerns are brought to anyone other than the PIs.

7. Disciplinary processes and range of penalties for PIs or research staff who are found to have violated the spirit or the regulations pertaining to human subject protections.

8. Circumstances in which said processes and penalties have been levied in the past decade (can be anonymized if not public information).

9. Oversight procedures employed when investigators are known to be resistant to following relevant rules and/or IRB policies.

10. Routine and for-cause monitoring/QA policies and procedures.

11. Credentials and requirements for staff designated to discuss/document consent.

12. Current IRB Roster and resume for each IRB member. Including a list of IRB members and alternates with expertise related the inclusion of subjects with psychiatric and neuropsychiatric disorders and number and backgrounds of community members on each of the IRBs.

13. Six months' worth of minutes for each IRB. If no studies fall into the category of research that involved individuals with limited decision making capacity, please provide 5 examples of minutes for the initial review of protocols involving individuals with limited decision-making capacity, per board. If any of the examples include a study where the decision was tabled or deferred, please provide the follow-up set of minutes.

14. Minutes/details for any potential reports of noncompliance reviewed by a convened IRB.

15. COI policies in IRB context, how COI are managed.

16. External audits of the Institution/IRB [OHRP, FDA, etc.].

17. Internal audit reports for every study involving individuals with limited decision making capacity for the protocols included above.

18. UMN HRPP Policies and Procedures.

19. Any compliance/disciplinary information (including, but not limited to, FDA warning letters, 483s, OHRP correspondence, state AG or medical board reports).

20. Copies of the last notification letters sent to a federal agency (e.g., OHRP, FDA, or other agency and state bodies such as the state AG and medical board) reporting serious or continuing non-

compliance, suspension and termination of IRB approval or an unanticipated problem involving risks to participants or others, including the complete protocol files within the last three years.

21. Minutes and the conflict of interest management plans for the three most recent researcher and research staff financial conflict of interest cases reviewed by the convened IRB, if any.

22. Organizational conflict of interest management plans for the three most recent organizational financial conflict of interest cases related to human research reviewed by the organization or other committee/entity, if any.

23. The results of the three most recent audits of investigators performed by your organization. These may be random/routine audits.

24. Copies of audits of your IRB and IRB records by external consultants for the last year, if any.

25. Documentation of IRB member, IRB staff, researcher, research staff, and key personnel of the HRPP attendance at required training for the last year related to human research protections this may include attendance logs or copies of agendas for the educational sessions. If you use electronic systems describe the method that prevents an individual from proceeding with a submission related to human research protections unless they have completed their required training (e.g. submitting a protocol to the IRB, submitting conflict of interest disclosures, etc.).

Request 2:
Requested 8/12/2014
Supplied 8/14/2014

1. A copy of the 2009 investigation report of the Department of Psychiatry including a copy of any documents outlining the initial complaints that led to the investigation, the report of the investigation and a summary of any corrective action measures taken in response to the report.

2. Additional information regarding the "referral for investigation" discussed in the March 2014 meeting of the IRB Executive Committee including a summary of the events leading up to the investigation and any findings of the sub-group review noted in the excerpted minutes. In the event the review is ongoing, a summary of the progress of this review and any findings to date was requested.

3. An overview of the sites where research activities conducted by the University of Minnesota faculty commonly take place (e.g. is there one primary hospital, multiple hospitals, etc.), particularly for research involving researchers from the Department of Psychiatry.

Request 3:
Requested 8/25/2014
Supplied 8/28/2014

1. A copy of the Jan 2014 Executive Committee meeting minutes related to an ongoing investigation led by the IRB.

2. A summary of the ongoing investigation [Investigation 1] including the current status of the investigation and any available reports/findings, etc.

3. Additional details about a complaint filed with the IRB and documentation related to the decision of the IRB not to pursue further investigation.

4. Copies of the 2006 and 2009 staff surveys of the Department of Psychiatry and the survey results.

5. Additional information regarding the research subject advocate line including a) confirmation as to whether there is a primary point of contact that manages issues that come in through this resource, and b) the process for referring these complaints to other entities, if applicable.

6. A description of how complaints are handled when submitted through UReport or the reporting mechanisms described on the IRB's website. A description outlining how these events are tracked/managed and a summary of the number of complaints in the past three years that relate specifically to human subjects research was requested. Additionally, confirmation was requested as to whether there have been specific reports submitted into either source that have prompted additional investigation.

7. Confirmation as to whether there is a group of clinical research coordinators at UMN that meet regularly through initiatives supported by the CTSI and if so, the name and contact information for the lead contact person this group.

8. Confirmation as to whether WIRB, contracted to help prepare materials for AAHRPP reaccreditation, conducted an evaluation of any policy/practice revisions needed and if so, a copy of any documentation detailing these recommendations was requested.

Request 4:
Requested 9/2/2014
Supplied 9/5/2014

For a selected list of 20 protocols, UMN was asked to provide:

1. The currently approved version of the protocol, consent and any UMN application documents required to assess approval (e.g. UMN specific application pieces that would address site-specific issues like monitoring, recruitment, etc.)
2. Copies of any videotapes documenting the consent process for these studies, if available.
3. Copies of any auditing/monitoring reports for these studies that specifically comment on the consenting process.

Part B. Follow-up Document Requests

The following documents were requested and provided subsequent to the September 2014 site visit:

<u>Request 1:</u>
Requested 10/3/2014
Supplied 10/17/2014- 10/21/2014

1. A detailed description of the size and scope of the post-approval monitoring/auditing program for human subjects' research that preceded the existing program [Office of Research Activities or its equivalent]. The requested description included a summary of the number of studies monitored/audited each year, how studies were selected for monitoring or auditing, what tools, forms & standards were used by auditors/monitors, and how findings were communicated/disseminated.

2. A detailed description of the size and scope of the current post-approval monitoring/auditing program for human subjects' research operated through the IRB at UMN. The requested description included a summary of the number of studies monitored/audited each year, how studies are selected for monitoring or auditing, what tools, forms & standards are used by auditors/monitors, and how findings are communicated/disseminated.

3. A detailed description of any post-approval monitoring/QA of human subjects' research that exists independent of the monitoring/auditing currently conducted through the IRB's office including a description of any monitoring /auditing activities conducted by Fairview of human subjects' research at their facilities.

4. A current list of the number of active protocols covered by the UMN IRB including a breakdown of the number of active studies determined to qualify for exemption, expedited review or require convened review.

5. A count of the number of action items (broken down by type of action, e.g. initial review, continuing review, etc.) reviewed by each convened IRB each month for the past 3 years. Data was provided monthly per board/panel. One sample IRB agenda from each panel was also requested.

6. Confirmation of the current number of IRB members designated to support each convened IRB and commentary on whether this number has changed over the past 5 years [increased/decreased].

7. A description of the compensation structure for IRB members [in terms of both financial compensation and faculty time] including any changes to this structure over the past 5 years.

8. A description of how the HRPP determines what expertise is needed (in terms of IRB membership) to conduct its reviews.

9. A description of how frequently the IRB utilizes consultants, with specific data regarding the number of times a consultant was used for a review in the past 3 years and the specific topic the consultant was asked to address. Documentation of studies [including study title and PI name] for which a consultant has been used to assist in the review of protocols involving adults with the potential for limited decision –making capacity was also requested.

10. A detailed description of how the process for scientific review of protocols is handled at UMN in relation to the IRB review. If this varies across departments, a description was required for each department that supports research involving adults with the potential for limited decision-making capacity. The following information was required related to these descriptions: a) who is involved in the scientific reviews, b) how determinations from these reviews are communicated to the IRB, c) copies of any forms used for the review process and 4) a description of actions available to the IRB if concerns are raised regarding the scientific review. A description of the process by which those responsible for the scientific review address, describe, and mitigate conflicts of interest and how they then communicate those actions to the IRB was also requested. Commentary was requested on how scientific reviews emerging from small departments or scientific reviews of protocols of individuals who hold a leadership role are addressed.

11. For the targeted protocol list identified by the review team on 9/2/2014 the following additional information was requested:

    a. Copies of any scientific reviews conducted at the departmental level for these protocols
    b. Meeting minutes for the initial review of each of these protocols by the convened IRB including all sets of meeting minutes that led up to the initial protocol approvals.
    c. Copies of any continuing review documents, including the IRB meeting minutes related to those reviews

12. A detailed description of how research conducted at Fairview by UMN researchers is implemented, administered and overseen. This description was required to include a summary of any protocol vetting/pre-review required prior to IRB approval as well as a description of the steps required for study start-up, recruitment, enrollment, etc. This description was required to identify how/when Fairview leadership is incorporated in these processes or otherwise informed about UMN research activities including any problems or concerns that may emerge during the conduct of research (such as reportable events, subject complaints, etc.).

13. A list of protocols (include PI name and study title) led by UMN researchers that are currently active/open at the adult in-patient psychiatric unit at Fairview. Additionally, a separate list of protocols that have been conducted within the unit with the past 3 years that may no longer be active was requested.

14. Confirmation as to whether Fairview researchers or researchers within the Departments of Psychiatry and Neurology, create and if so, retain, any video/audio files that capture the consenting process for research. A catalogue of any available videotapes was also requested.

15. A copy of the investigation reports [in draft form if not yet finalized] for the two active IRB investigations a) the investigation into the complaint of subject RH and b) the Fairview investigation.

16. The following were requested related to the new tool recently released by the HRPP that is required for IRB applications where the research involves individuals with the potential for limited decision-making capacity:
    a. A copy of the communication to the research community introducing the change
    b. A copy of any documents researchers/IRB staff/IRB members will now utilize as a result of this change
    c. Copies of the completed tools, study documents and IRB meeting minutes for any studies that have utilized these new documents since implementation. *[This request was responded to on 12/16/2014]*

17. A detailed description of the HRPP's educational program, including a description of all mandatory and optional HRPP- driven educational activities offered in the past 3 years. The response was to include a description of to whom these programs were mandated, offered, and in either case, how they were publicized and to whom.

18. A copy of the current strategic plans created by the Office of the Vice President for Research, the School of Medicine and the Department of Psychiatry.

19. Documentation of any policies/procedures in place to encourage and then to protect whistleblowers. Additionally a description of the channels through which whistleblowers may report concerns to UMN/Fairview related to research and the methods by which these concerns are handled was requested.

20. A copy of the formal review agreement that outlines the responsibilities of the UMN IRB to serve as the IRB of record for research conducted at Fairview facilities.

21. A copy of Fairview records of any research-related complaints by patients, family members or employees in the past three years.

22. Documentation and descriptions of any policies/procedures that identify how an LAR is to be selected when a prospective subject is unable to engage in a dialogue about the proposed study and thus unable to provide informed consent ,or, when an enrolled subject develops impaired capacity during the course of the study. In such cases, the specific hierarchy used to select the LAR was requested including relevant citation(s) to state law, if any, used to establish that hierarchy. Any written materials provided to LARs to explain their role in the decision-making or procedures that require such explanations to be provided, as well as, any policies/procedures for obtaining advance designation of an LAR by an individual who may lose decision-making capacity during the course of a study were also requested. If these documented vary across departments, a description and documents, if any, for each department that supports research involving adults with the potential for limited decision-making capacity was requested.

23. A list of protocols, including study title and PI name, of currently approved protocols that include subjects who lack consent capacity.

<u>Request 2</u>:
Requested 11/21/2014
Supplied: [See below]

1. The response of the Department of Psychiatry, or any individual authorized thereby, to the 2009 internal audit findings letter directed to the Chair; [Provided 11/21/2014]

2. The final report of the IRB's Investigation 1; [Provided 11/21/2014]

3. The final report of the IRB's Investigation 2. [Draft report provided on 12/22/2014]

<u>Request 3</u>:

Requested 12/22/2014
Supplied: [See below]

1. For the new samples of studies utilizing the new tool for research for individuals with limited decision-making capacity, corresponding scientific review documents were requested. [1/9/2015]

2. The number of active protocols reviewed by the convened IRB broken down by division/department

Request 4:

Requested 1/16/2015
Supplied: 1/23/2015

The following previously requested information still in progress was requested again:

1. A copy of any documents outlining the initial complaints of the IRB that led to the 2009 investigation into the Department of Psychiatry.
2. Copies of the 2006 and 2009 staff surveys of the Department of Psychiatry, the survey results and a summary of any actions taken in response.
3. A summary of any outcome of the recent FDA audit of studies of the Department of Psychiatry.
4. A summary of the documentation provided to the state legislative auditor in response to their audit request (e.g. total number of AE events reported, total number of deaths reported, etc).
5. Copy of final "accepted" current version of the SOPS [Many of the versions initially received were under revision at the time they were initially supplied to the team]
6. A copy of the final report of the IRB's Investigation 2, if available.

In follow-up to documents previously reviewed by the external review team, the following additional documents were requested in order for the team to complete its remit:

1. For each health and medical convened board meeting from July through September, the following was requested:
    a. The agenda
    b. A breakdown of the number and type of action items reviewed by the Board
    c. A list of members present per meeting for each Board
2. For a selected sample of reports of unanticipated problems posing risks to subjects or other that were by the convened Board [as noted in the minutes previously provided] the following was requested:
        i. A copy of the initial event report from the study team
        ii. A copy of any IRB correspondence with the team related to the event included any email correspondence
        iii. A copy of all convened IRB meeting minutes discussing the event
        iv. A copy of any follow-up provided by the team in response to the convened IRB's review.
3. Evidence of conflict of interest Committee and IRB review and action regarding any financial disclosures that met the institutional financial disclosure threshold and were deemed related to a Department of Psychiatry human subjects' research protocol for the past 3 years.
4. Copies of any CTSI monitoring reports for greater than minimal risk studies involving adults with the potential for limited decision making capacity for the past 3 years. Additionally a copy of any forms, templates or tools used by CTSI to perform their monitoring functions was requested.
5. A summary of the topics covered in ongoing IRB member training at the convened IRB meetings in 2014

6. Documentation of the final IRB determination, if any thus far on the select protocols deferred at the time of initial review from the Department of Psychiatry.
7. Any follow-up that occurred in response to a PAR report that suggested further education on the consent process for a specific study and for the investigator and IRB more broadly.
8. A copy of any IRB discussion of a May 2010 unanticipated problem report for a selected Psychiatry protocol.
9. For a specific study from the Department of Psychiatry where the scientific review raised a concern regarding withdrawal of the current medication, any documentation that the IRB considered/addressed the concern and any evidence that the protocol was modified in response.
10. Documentation of any follow-up to concerns raised in a specific PAR report.

Materials Supplied to the Review Team:
The following is a sample of the types of materials the external review team received from individuals directly [not solicited by the external review team]:

- Links to current stories in the local media regarding research at the University
- Copies of complaint letters filed with the University
- Copies of complaint letters filed with medical boards, the Board of Regents or legal authorities outside of the University
- Materials related to the lawsuit filed by Dan Markingson's mother, Mary Weiss
- Blogs covering issues related to the Markingson case

Section 2.3

Appendix 8: Summary of Site Visit Interviews

Appendix 8: Site Visit Interview Summary

A. Text of Targeted Email Invitations for Selected Interviewees:

Dear XXXX

In response to the December 2013 resolution of the Faculty Senate [See : http://www1.umn.edu/usenate/resolutions/131205panelres.html] an external independent panel will examine the current policies, practices and oversight of clinical research on human subjects at the University of Minnesota, with emphasis on research involving adults who may have impaired decision-making ability. The external review team will be on campus on September 9th-10th to conduct interviews and review records.

The external review team has identified you as someone with whom they would like to meet. Please contact Megan Singleton at UMNReview@gmail.com to arrange this meeting.

The review team will take care not to reference comments/concerns shared by individuals in a way that identifies them directly.
We apologize for the time- sensitive nature of this request and thank you in advance for your willingness to participate in the review process.

B. Text of Broad Email Invitation for the UMN Research Community**

**Distributed through the UMN clinical research coordinator and investigator listservs

Dear XXXX [suggested this come from the IRB office]

In response to the December 2013 resolution of the Faculty Senate [See : http://www1.umn.edu/usenate/resolutions/131205panelres.html] an external independent review team will examine the current policies, practices and oversight of clinical research on human subjects at the University of Minnesota, with emphasis on research involving adults who may have impaired decision-making ability. The external review team will be on campus on September 9th-10th to conduct interviews and review records.

The external review team invites persons interested in providing information to contact them at UMNReview@gmail.com.

Follow-up from the review team may occur by telephone, email or a request for an in-person meeting.

The review team will take care not to reference comments/concerns shared by individuals in a way that identifies individuals directly.

We apologize for the time-sensitive nature of this request and thank you in advance for your willingness to participate in the review process.

C. Interview Summary Information:

1. Total Number of In-Person Interviewees: 53
2. Total Number of Telephone Interviews: 5
3. Total Number of individuals who contacted the review team to request an interview: 2 [both interviewed; 1 by phone]
4. Total Number of Individuals who did not response to a targeted invitation: 1
5. Total Number of Individuals who declined an interview in response to an targeted invitation: 1

D. Summary of Entities Interviewed:

University of Minnesota:

1. Clinical Translational Science Institute
2. Office of General Counsel
3. Office of Internal Audits
4. Office of Institutional Compliance
5. Office of the Vice President for Research
    a. IRB
    b. Research Education and Oversight
6. School of Medicine
    a. Bioethics
    b. Diabetes Endocrinology & Medicine
    c. Emergency Medicine
    d. Epidemiology & Community Health
    e. Neurology
    f. Pediatrics
    g. Psychiatry
    h. Pulmonary, Allergy & Critical Care Medicine

External Entities:

1. Fairview Health System
2. National Association of Mental Illness (NAMI) – Minneapolis/St. Paul Chapter

E. Types of Individuals Interviewed (By Role):

1. Clinicians
2. Clinical staff
3. Faculty/Investigators
4. Family members of individuals with mental illness
5. HRPP leadership
6. Institutional leadership
7. IRB Chairs

8. IRB members including unaffiliated IRB members and members of the IRB's Executive Committee
9. IRB staff
10. Research Personnel including administrators, project managers and study coordinators

Section 2.3

Appendix 9: Online Survey Questions and Dissemination Strategy

Appendix 9: Survey of Research Participants and Their Family Members

Enclosures:

1. Copy of Online Survey Questions
2. Copy of Flyer Announcing the Availability of the Survey

According to UMN the following strategy for posting flyers was used:

a) Fairview posted 25 flyers in the behavioral health areas on the Riverside campus.

b) UMN engaged a service to post flyers in the biomedical areas of this campus (this, on the recommendation of the recruitment specialist in our Clinical and Translational Science Institute). 110 flyers were posted by this service.

3. Copy of the Email to Deans/Directors of the Academic Health Center announcing the availability of the survey
4. Copy of Craig's List Posting announcing the availability of the survey.

UMN Research Participant Survey

(untitled)

Have you or a family member participated in UMN research?

Was the research done at the University of Minnesota (UMN) campus, at one of the Fairview Hospitals, or in any other location at which UMN research takes place? If so, we would like you to complete a brief questionnaire to learn about your experiences in research.

We are a group of independent consultants conducting a review of research at UMN at the request of the Faculty Senate. This brief questionnaire will provide important information for the review since we think it is critical to include the perspectives and opinions of people like you who have participated in research. We will not collect your name or other identifying information, so your responses cannot be associated or linked to you. Because this survey is anonymous, we will not be able to respond to you directly. If you have concerns about your experiences as a research subject and would like to speak to someone, please contact the UMN IRB. Contact information can be found at the following link.

Thank you in advance for answering this questionnaire. The questionnaire contains 6 questions and will take approximately 5-10 minutes to complete.

Please only complete this questionnaire one time.

Please note that you must click on the arrow in the bottom right corner of the screen in order to proceed to the next page.

1. Please choose one of the following below: *

- I am answering this questionnaire because I took part in UMN research
- I am answering this questionnaire because my family member took part in UMN research

2. How many research studies have you/your family member participated in at the University of Minnesota, at one of the Fairview Hospitals, or in any other location at which UMN research takes place?

- One
- Two
- Three
- Four
- Five
- More than Five

3. If “more than five,” please estimate the number of studies in which you have participated as a research subject.

4. What types of research studies did you/your family member participate in? [If you remember the name(s) of the research study/studies, please include it/them here; if not, please provide a short description, such as “a survey study on my exercise habits,” etc.]:

5. At the time you/your family member agreed to be in the research, did you feel that you had enough information to make an informed choice about participating in it?

- Yes
- No
- Not sure

6. Please explain.

7. How would you describe your/your family member's experience(s) as a research subject here?

- The overall experience was positive (good)
- The overall experience was negative (bad)
- The overall experience was neither positive (good) nor negative (bad)

8. Please describe why you selected that description:

9. If you would like to share any additional information about your/your family member's experience(s) as a research subject please include it below:

Thank You!

Thank you for taking our survey. Your response is very important to us.

Have you or a family member participated in UMN research?

Was the research done at the **University of Minnesota (UMN)** campus, at one of the Fairview Hospitals, or in any other location at which UMN research takes place? If so, we would like you to complete a brief questionnaire to learn about your experiences in research.

We are a group of independent consultants conducting a review of research at UMN at the request of the Faculty Senate. We are currently seeking feedback from current or former research participants and their family members.

If you are willing to share your experiences with UMN research, please consider completing a brief anonymous questionnaire developed by the review team.

The questionnaire will take approximately 5-10 minutes to complete.

The questionnaire will be available online at the following link http://www.surveygizmo.com/s3/1927159/UMN-Research-Participant-Survey through **Monday January 5, 2015**.

Thank you for considering responding to this informal survey.

From:	William Durfee
To:	Megan Kasimatis Singleton
Subject:	Fwd: Inquiry panel outreach to current or former biomedical research participants
Date:	Monday, December 29, 2014 10:19:40 AM
Attachments:	ResearchParticipantSurvey_Flyer-1.pptx

Megan,

The memo sent to AHC deans (minus vet-med).

Will

---------- Forwarded message ----------
From: **Debra Dykhuis** <dykhu001@umn.edu>
Date: Tue, Dec 16, 2014 at 10:10 AM
Subject: Inquiry panel outreach to current or former biomedical research participants
To: Brooks Jackson <jacksonb@umn.edu>, Leon Assael <assael@umn.edu>, Connie Delaney <delaney@umn.edu>, Marilyn Speedie <speed001@umn.edu>, sphdean SPH Deans Office <sphdean@umn.edu>

Dear Deans Jackson, Assael, Delaney, Speedie and Finnegan,

I am writing to call your attention to the recent posting of flyers which ask, "Have you or a family member participated in UMN research?" A copy of the flyer is attached.

The goal of the questionnaire listed on the poster is to gather feedback from "current or former research participants and their families." All responses to the questionnaire will be received by the independent review team, not the U of M, nor AAHRPP (the IRB accrediting body).

The survey and flyer were organized by the independent inquiry review panel conducting a review of the human protections program at the University of Minnesota. This review, as you may recall, was requested by the University Faculty Senate. You can read more about the University Faculty Senate request here http://www.research.umn.edu/news/documents/Senate_Review_RFP.pdf.

I just wanted to make you aware of the nature and reason for the posting of these flyers in case you see them, or your faculty members raise questions. Please contact me if you have any further questions or concerns about this email.

Sincerely,

Debbie

_____

--
Debra Dykhuis
Director
Human Research Protection Program
University of Minnesota

Have you or a family member participated in UMN research?

Was the research done at the University of Minnesota (UMN) campus, at one of the Fairview Hospitals, or in any other location at which UMN research takes place? If so, we would like you to complete a brief questionnaire to learn about your experiences in research.

We are a group of independent consultants conducting a review of research at UMN at the request of the UMN Faculty Senate. We are currently seeking feedback from current or former research participants and their family members.

If you are willing to share your experiences with UMN research, please consider completing a brief anonymous questionnaire developed by the review team. The questionnaire will take approximately 5-10 minutes to complete.

The questionnaire will be available through Monday January 12, 2015 at the following link:

http://www.surveygizmo.com/s3/1927159/UMN-Research-Participant-Survey

Thank you for considering responding to this informal survey.

- do NOT contact me with unsolicited services or offers

post id: 4817745192

posted: 2014-12-23 4:13pm

Section 3.3.2

Appendix 10: Scientific Review Documents

UNIVERSITY OF MINNESOTA

IRB: Scientific Review and Resource Assessment

Policy number: 904

Date: 06/01/2014

References:
45 CFR 46.111
AAHRPP I.1.F.

Cross References:
800 Principal Investigator Responsibilities
800A, B, C, D, E, F, G Additional Investigator Responsibilities for Federally Funded (DoD, DOJ, EPA, DOE, ED, FDA) and Industry-Sponsored Research ICH-GCP E6
802 Signature Requirements for Researchers

Policy Owner:
Executive Director, HRPP

Definitions:
None

1.0 Reason for Policy

Describe the procedure for ensuring that appropriate review for sound scientific design takes place prior to initial IRB review of Health and Biological/Medical applications and that all researchers have the resources necessary to protect participants.

2.0 Scope of Policy

This policy applies to the University research community and its healthcare components.

3.0 Policy Statement

In order to approve research, the IRB must determine that risks to subjects are minimized by using procedures which are consistent with sound research design.

For projects involving not greater than minimal risk and reviewed by expedited review, scientific review is performed by the IRB reviewer.

For projects involving greater than minimal risk, reviewed by the social and behavioral sciences IRB panels, the IRB members perform scientific review.

For projects involving greater than minimal risk in the medical areas and reviewed by the full IRB committee, scientific review is to be performed by independent peer reviewers. Researchers are required to provide documentation of fulfillment of the scientific review requirement as well as assurance that they have the resources necessary to protect participants.

Procedures:
Independent scientific review is to be performed by one of the following methods:

1. Nationally-based, federal funding organizations (NIH, NSF) when research projects have been subjected to full peer review (e.g., review by a study section or grant committee).

The actual protocol being submitted to the IRB must have been reviewed in its current form. Peer review of a grant that describes a clinical trial in general terms does not satisfy this criterion. Industry-sponsored clinical trials designed by the sponsor with or without external consultants do not satisfy this criterion for independent peer-review.

2. Nationally based non-federal funding organizations (March of Dimes, American Academy of Pediatrics) employing peer review mechanisms for awarding of funding

The actual protocol being submitted to the IRB must have been reviewed in its current form. Peer review of a grant that describes a clinical trial in general terms does not satisfy this criterion. Industry-sponsored clinical trials designed by the sponsor with or without external consultants do not satisfy this criterion for independent peer-review.

3. Locally constituted mechanisms using peer review for awarding of funding, or for permission to use resources, including:

Cancer Protocol Review Committee (CPRC)
Clinical and Translational Science Institute (CTSI) pilot funding awards
Departmental peer review

4. All other applicable medical research not reviewed under one of the methods above: HRPP scientific assessment information, including a job aid and link to the portal to request HRPP scientific assessment, may be found on the HRPP website.

Features of an Appropriate Review Committee

A minimum of two reviewers
Consensus regarding the scientific acceptability of the project (if there is not initial consensus, some group discussion regarding the project must take place)
Documentation of the review process (dates, participants, method of review and discussion, decision).

Review Requirements for Method 3

Is the rationale for the study clearly stated and is the rationale scientifically sound?

Are the aims and corresponding hypothesis clearly stated?
Is the primary outcome (and secondary outcomes, as appropriate) clearly defined?
Are there adequate preliminary data in the literature (or from the investigator) to justify the proposed research? Has an adequate literature review been done to support this study?
Is the question or hypothesis being tested providing important knowledge to the field?
Is the design of the study appropriate for the questions that are posed?
Have the validity and reliability of measures been established or are there methods proposed for establishing validity and reliability?
Is the proposed subject population appropriate?
Are statistical considerations, including sample size and justification, estimated accrual and duration, and statistical analysis clearly described and adequate to meet the study objectives?
Are all the proposed tests or measurements requested necessary to answer the scientific question?
Are the investigators well qualified to conduct this study?

Review Requirements for Method 4

Review by a biostatistician is required for all applicable research prior to scientific assessment under Method 4. This will permit an initial foundation that allows further assessment; reviewers know as they initiate assessment that the study is powered to yield results. With that foundation, reviewers will consider two fundamental questions, considering the bulleted issues for each as they answer the questions:

1. Is the scientific question reasonable?

   The question is precisely articulated
   The research has the potential to provide new and/or useful knowledge
   The potential to provide useful knowledge is supported by literature review

2. Will the methods described in the protocol answer the question?

   Research tests and procedures are appropriate to answer the scientific question
   Research measures are valid and reliable, or there are methods proposed to establish validity and reliability
   The proposed subject population is appropriate
   The principal investigator is qualified to conduct the research

Procedures to Satisfy Review

Select one of the four scientific review methods
Document fulfillment of the scientific review requirement and include with the IRB application submission.
Note: Medical applications requiring full committee IRB review will not be assigned to a meeting until documentation of scientific review is provided.

The IRB evaluates that individual research studies have the resources necessary to protect participants by asking the reviewer to determine if the researcher has provided the following information

- Is there adequate time to conduct and complete the research?
- Does the researcher have an adequate number of qualified staff?
- Does the researcher have adequate research facilities?
- Does the researcher have access to a population that will allow recruitment of the necessary number of participants?
- Are medical or psychosocial resources available if participants need them as a consequence fo the research?

Further, by providing their signature as principal investigator on an IRB application, researchers explicitly assure the IRB that they have the resources necessary to protect participants, such as adequate funding, appropriately trained staff and necessary facilities and equipment. By his/her signature on the initial IRB application, the principal investigator assures the IRB of the following:

As Principal Investigator of this study, I assure the IRB that the following statements are true:

- The information provided in this form is correct.
- I have evaluated this protocol and determined that I have the resources necessary to protect participants, such as adequate funding, appropriately trained staff, and necessary facilities and equipment.
- I will seek and obtain prior written approval from the IRB for any substantive modifications in the proposal, including changes in procedures, co-investigators, funding agencies, etc.
- I will promptly report any unexpected or otherwise significant adverse events or unanticipated problems or incidents that may occur in the course of this study.
- I will report in writing any significant new findings which develop during the course of this study which may affect the risks and benefits to participation.
- I will not begin my research until I have received written notification of final IRB approval.
- I will comply with all IRB requests to report on the status of the study.
- I will maintain records of this research according to IRB guidelines.
- The grant that I have submitted to my funding agency which is submitted with this IRB submission accurately and completely reflects what is contained in this application.
- If these conditions are not met, I understand that approval of this research could be suspended or terminated.

4.0 Required approvals for this document

Title
Executive Director, HRPP

5.0 Revision History

Revision	Reason for change	Date of release
06/01/14	Update options and reformat PI attestation	09/02/14
01/05/11	Update cross references	01/05/11
02/01/10	Revision	02/01/10
10/15/09	Update AAHRPP references	10/15/09
08/31/09	Revision	08/31/09
08/24/09	Reformat, Revision	
05/16/07	Policy Development	

To obtain a copy of a historical policy, e-mail the IRB at irb@umn.edu or call 612-626-5654.

ct
w
ng
Guidance
What Every Researcher Needs To Know
Protecting Human Subjects Guide
Frequently Asked Questions
Members only
Report complaints
eResearch
eProtocol
Subscribe & connect ›

Guidance & FAQs

Scientific Consultation and Assessment

Scientific Assessment of Proposals Submitted to the IRB

Since July 1, 2007, evidence of scientific review for medical research involving human subjects deemed by the Institutional Review Board (IRB) to be greater than minimal risk has been required at the time of submitting an application to the IRB. A new scientific assessment option will be added to other available options effective July 1, 2013.

The purpose of scientific assessment is to encourage the development of scientifically sound medical research. To justify the inclusion of human subjects in research, and to assess the balance between any risks that may be imposed upon human subjects with the utility of the outcomes of the investigation, an assessment is required to evaluate the scientific question and appropriateness of the methods planned to answer the scientific question.

After receiving documented acceptance of the protocol via an approved scientific assessment process, the IRB will continue to determine that the following requirements will be satisfied:

- Risks to subjects are minimized
- Risks to subjects are reasonable in relation to anticipated benefits
- Selection of subjects is equitable
- Informed consent will be sought from each subject or the subject's legally authorized representative
- Informed consent will be appropriately documented
  - Adequate provisions to protect privacy and maintain confidentiality are in place

Applicability

Scientific assessment is required for medical research that is not exempt under CFR 45 §46.101 (b) or does not qualify for expedited review under CFR 45 §46.110.

Acceptable Methods for Scientific Assessment

1. Nationally-based, federal funding organizations (NIH, NSF) when research projects have been subjected to full peer review (e.g., review by a study section or grant committee).

- The actual protocol being submitted to the IRB must have been reviewed in its current form. Peer review of a grant that describes a clinical trial in general terms does not satisfy this criterion.
- Industry-sponsored clinical trials designed by the sponsor with or without external consultants **do not** satisfy this criterion for independent peer-review.

2. Nationally based non-federal funding organizations (March of Dimes, American Academy of Pediatrics) employing peer review mechanisms for awarding of funding

- The actual protocol being submitted to the IRB must have been reviewed in its current form. Peer review of a grant that describes a clinical trial in general terms does not satisfy this criterion.
- Industry-sponsored clinical trials designed by the sponsor with or without external consultants do not satisfy this criterion for independent peer-review.

3. Locally constituted mechanisms using peer review for awarding of funding, or for permission to use resources, including:

- Cancer Protocol Review Committee (CPRC)
- Clinical and Translational Science Institute (CTSI) pilot funding awards
- Departmental peer review

4. All other applicable medical research not reviewed under one of the methods above: o HRPP scientific assessment – information, including a joib aid and link to the portal to request HRPP scientific assessment, may be found on the HRPP website.

Features of an Appropriate Review Committee

- A minimum of two reviewers

+More Information

On This Page

For More on Scientific Review

As with any IRB related matters, for more information you may contact Patrice Webster at irb@umn.edu or 612-626-5654.

Consensus regarding the scientific acceptability of the project (if there is not initial consensus, some group discussion regarding the project must take place)
- Documentation of the review process (dates, participants, method of review and discussion, decision).

Review Requirements for Method 3

- Is the rationale for the study clearly stated and is the rationale scientifically sound?
- Are the aims and corresponding hypothesis clearly stated?
- Is the primary outcome (and secondary outcomes, as appropriate) clearly defined?
- Are there adequate preliminary data in the literature (or from the investigator) to justify the proposed research? Has an adequate literature review been done to support this study?
- Is the question or hypothesis being tested providing important knowledge to the field?
- Is the design of the study appropriate for the questions that are posed?
- Have the validity and reliability of measures been established or are there methods proposed for establishing validity and reliability?
- Is the proposed subject population appropriate?
- Are statistical considerations, including sample size and justification, estimated accrual and duration, and statistical analysis clearly described and adequate to meet the study objectives?
- Are all the proposed tests or measurements requested necessary to answer the scientific question?
- Are the investigators well qualified to conduct this study?

Review Requirements for Method 4

Review by a biostatistician is required for all applicable research prior to scientific assessment under Method 4. This will permit an initial foundation that allows further assessment; reviewers know as they initiate assessment that the study is powered to yield results. With that foundation, reviewers will consider two fundamental questions, considering the bulleted issues for each as they answer the questions:

Is the scientific question reasonable?

- The question is precisely articulated
- The research has the potential to provide new and/or useful knowledge
- The potential to provide useful knowledge is supported by literature review

Will the methods described in the protocol answer the question?

- Research tests and procedures are appropriate to answer the scientific question
- Research measures are valid and reliable, or there are methods proposed to establish validity and reliability
- The proposed subject population is appropriate
- The principal investigator is qualified to conduct the research

Procedures to Satisfy Review

1. Select one of the four scientific review methods
2. Document fulfillment of the scientific review requirement and include with the IRB application submission.
   Note: Medical applications requiring full committee IRB review will not be assigned to a meeting until documentation of scientific review is provided.

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Last modified on January 7, 2014

Documentation of departmental or collegiate scientific review of clinical research protocol

NOTE: Attach written documentation of the review process (dates, participants, method of review and discussion, decision. These documents should also be filed with the associate dean for research of the appropriate college (or assistant vice president for research for AHC-level reviews).

We, the undersigned, attest that the below-named clinical research protocol has been evaluated for the following items:

- The rationale for the study is clearly stated and the rationale is scientifically sound.
- The aims and corresponding hypothesis are clearly stated.
- The primary outcome (and secondary outcomes, as appropriate) is clearly defined.
- There are adequate preliminary data in the literature (or from the investigator) to justify the proposed research. An adequate literature review has been done to support this study.
- The question or hypothesis being tested is providing important knowledge to the field.
- The design of the study is appropriate for the questions posed.
- The validity and reliability of measures have been established or there are methods proposed for establishing validity and reliability.
- The proposed subject population is appropriate.
- Statistical considerations, including sample size and justification, estimated accrual and duration, and statistical analysis are clearly described and adequate to meet the study objectives.
- All the proposed tests or measurements requested are necessary to answer the scientific question.
- The principal and any other investigators are well qualified to conduct this study.
- The resources necessary to conduct this study are adequate and that these criteria have been addressed sufficiently such that the human subject research described is scientifically valid.

_____

Reviewer 1 (signature) print name Date

_____

Reviewer 2 (signature) print name Date

_____

Reviewer 3 (signature) print name Date

Title of research protocol:

_____

Name of scientific review committee _____

Method 4 Process for doing Scientific Assessment

1. Check CTR Portal for new submissions (https://ctsi.ahc.umn.edu/portal/)
2. Review submission to be sure contact information is complete and documents are downloadable and readable.
3. Assign 2 reviewers from the list, according to availability and expertise. Make sure to check for recorded conflicts of interest.
4. Change status of submission from 'Submitted' to 'In Review.' Notifications will automatically go out to assigned reviewers with information regarding access to materials for review.
5. Record information in Tracking Spreadsheet.
6. Send reminder email to reviewer(s) after 5 business days.
    a. If no response received from reviewer(s) after 7 business days, contact regarding reason for delay in completing review. Send notification email with this reason to PI.
7. Once determination has been made by both reviewers, create appropriate documentation and send to PI via email.
    a. If stipulations are made by reviewer(s), create stipulation letter and send to PI.
    b. If approved as submitted, send approval letter to PI and change status in CTR to 'Completed.'
8. Record determination information and dates in Tracking Spreadsheet.

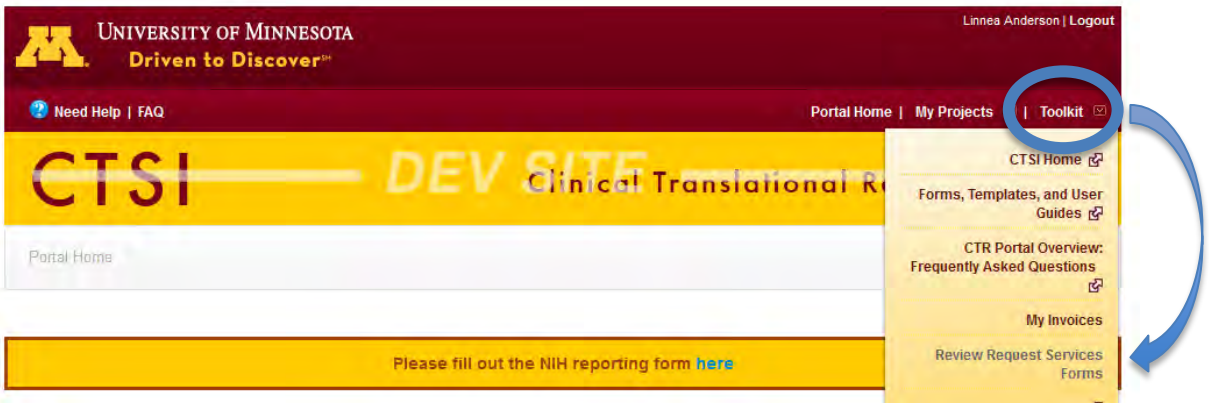
Scientific Assessment Reviewer

Job aid to document how to access projects to which you have been assigned and how to record your review decisions.

Notification of Review Pending
You will receive an email notification when a project is assigned to you. A sample of the email notification is below:

> You have been assigned a request for scientific assessment that is ready for your review.
>
> Log-in with your X.500 credentials at https://samplelink.ahc.umn.edu/portal/app/index.cfm/requests/list and navigate to the Review Request Services Forms by following these steps:
>
> - Hover over Toolkit link in top menu
> - Click Review Request Services Forms
> - Requests that have been assigned to you will be listed
>
> As a reminder the HRPP pledges to deliver a prompt response which requires reviewers to note their response within 7 business days
>
> If you have any questions respond to this email or call 612-626-5654

Accessing Project Information
Click the link provided in the email -https://ctsi.ahc.umn.edu/portal/ and log in to the portal. As indicated in the email notification, hover over the toolkit link and select "Review Request Services Forms"

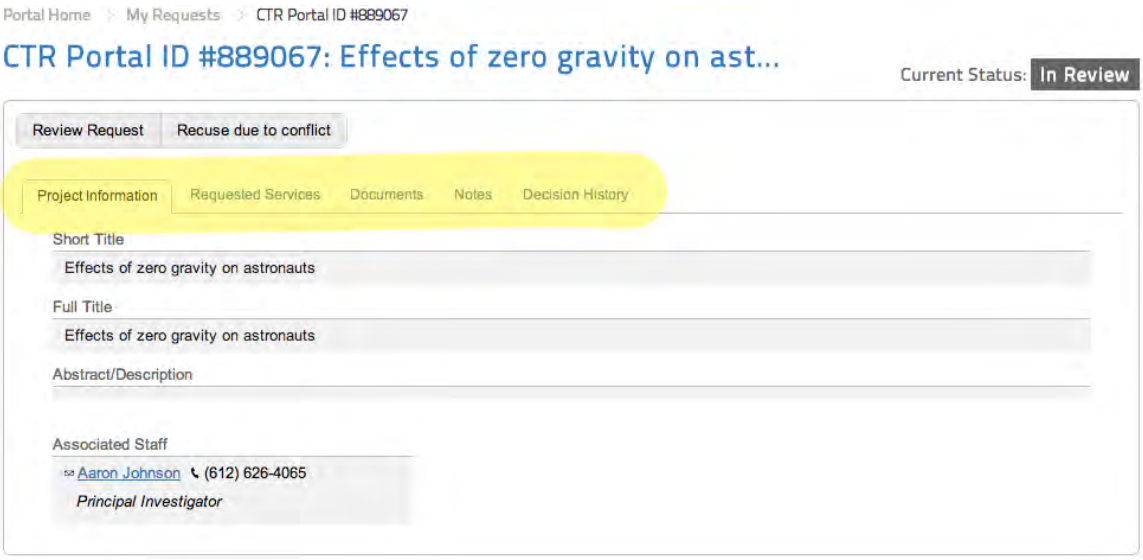


The “Review Request Services Forms” link will take you to the reviewer dashboard. An example of the dashboard is below. Clicking the “In Review” or “Completed” header (example circled below) allows you to choose to what displays below. In the example below projects “In Review” display and projects with the status “Completed” are hidden.

Click the hyperlinks under the **CTR Portal ID** or **Short Title** columns to begin the review process.

If you have a potential conflict of interest with this request click **Recuse due to conflict** button.

If you do not have a known conflict use the series of tabs beginning with **Project Information** (highlighted below in yellow) to review the information submitted by the researcher about the project.

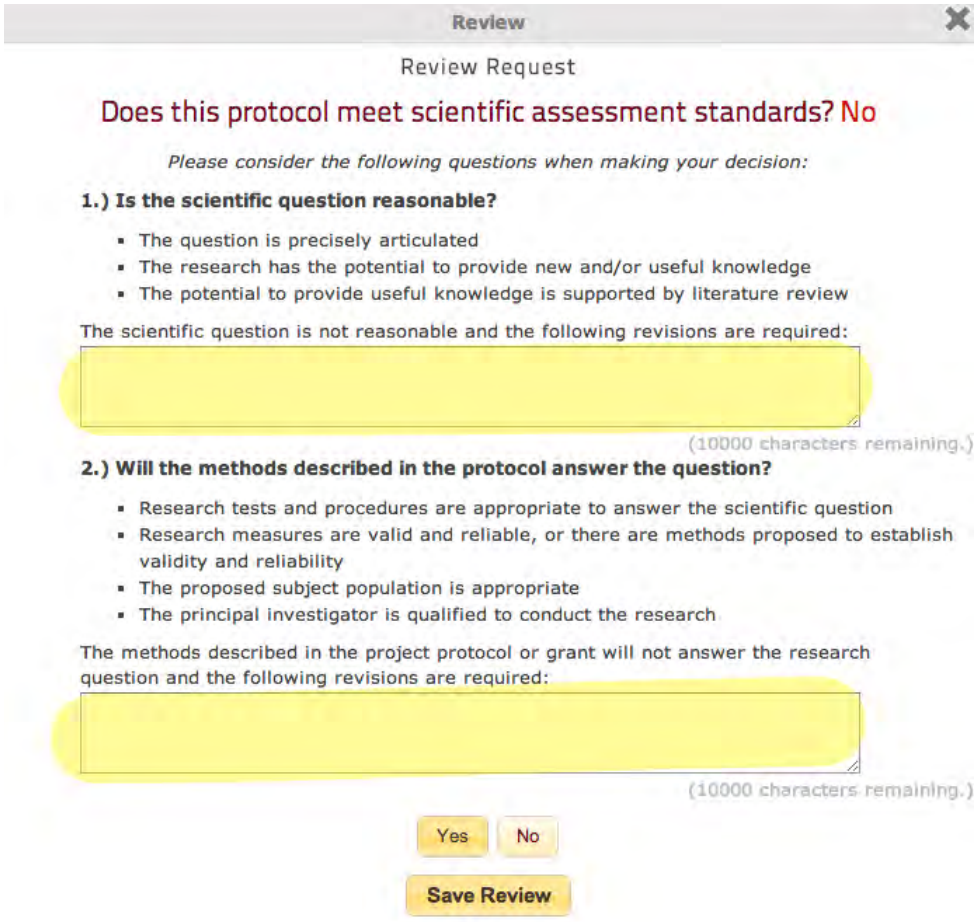


The **Requested Services** tab contains information provided by the investigator when requesting review including the biostatistician’s name, credentials and contact information. The **Documents** tab will contain any file attachments the requester uploaded. **Notes** are messages HRPP staff and reviewers can share with each other during the review process. Please make sure to review the note section for any

questions or special instructions from HRPP staff regarding the submission. These notes are never displayed to the investigator.

Documenting your Review Decision

After reviewing the information provided on Requested Services and Documents tabs, click "Review Request" to record your decision. This will reveal a window asking if the protocol meets scientific assessment standards. You are asked to consider only two questions when making this judgment, "Is the scientific question reasonable?" and "Will the methods described in the protocol answer the question?" An example of the window is below.



If the answer is **Yes** no further input is necessary.

If the answer is **No** you are required to provide revisions that the investigator must make to meet the assessment standard. Click **Save Review** after indicate yes or no. If you are satisfied with your decision no additional action is required.

If you change your mind or decide to update the answers provided you may update you review at any time but again clicking Review Request button.

After you save your review, you may now see other reviews in the Decision History tab and correspond via the Notes interface. The **Decision History** tab reveals other reviewer's decisions only after you complete your review (each project will be assigned two reviewers).

If you determine the protocol does not meet scientific assessment standards HRPP staff will communicate to the investigator your finding and any changes or clarifications you require. The investigator may choose to amend or withdraw the project. You will receive notification when the investigator submits revisions requiring your review. The process for reviewing a revised protocol is the same as reviewing a new submission.

If you have any questions not addressed by this job aid, please contact the HRPP office at 612-626-5654 or, via email, at hrpp@umn.edu

Section 3.3.3

Appendix 11: Post Approval Review (PAR) Program Description

The University of Minnesota's

Human Research Protection Program (HRPP)

Post Approval Review (PAR)

Program Introduction & Goals

Under the direction of the Vice President for Research and the IRB Executive Committee, the continuing review procedures of the IRB were expanded in 2011 to include a Post Approval Review (PAR) function. This function is housed within the Human Research Protection Program (HRPP) office, the administrative home of the IRB.

The purpose of the PAR program is to provide internal oversight on compliance issues associated with the performance of human subjects research conducted at the University. The PAR program is also intended to provide a mechanism for assuring the quality of human subjects' research by supplementing existing HRPP quality improvement and educational initiatives.

The PAR program takes a collaborative review approach with researchers, key study personnel, other supporting institutional programs and internal/external entities toward a common goal of protecting human research subjects.

PAR Categories

Review is primarily conducted via the following three mechanisms: 1) Risk Based Review, 2) Supplemental Compliance Review, and 3) Researcher Self-Assessment. All reviews and assessments are designed to assess compliance with organizational policies and procedures and applicable laws, regulations, code and guidance. Reviews provide an opportunity to identify areas for improvement in the research as well as suggest recommendations to enhance the quality, efficiency, and effectiveness of the Human Research Protection Program.

Additional PAR activities include quality improvement initiatives and management of the Research Subject Advocate Telephone Line.

The following information outlines current PAR activities:

- **Risk Based Review:**
  - PAR review of IRB approved studies that are selected, at random or targeted, in response to an identified concern (e.g. complaint, information or event) and conducted to assess investigator compliance with federal, state, and local law, and IRB policies. PAR reports of observations/finding are forwarded to the convened IRB.

    All "for- cause" reviews based on concerns, complaints or allegations of non-compliance are performed in accord with HRPP 408 Managing Allegations of Non-Compliance with IRB Policies and Procedures policy.

    Examples of criteria prompting Risk Based review:

    - Any directive or concern from the convened IRB;
    - Higher risk studies identified through the IRB Executive Committee's defined risk profile (e.g. SI research, vulnerable populations, use of controlled substances);
    - Studies where concerns have been raised about possible material changes occurring without IRB approval based upon information provided in continuing review reports or other sources;
    - A response to an externally initiated complaint (OHRP, FDA or Sponsor) of potential protocol violations or regulatory non-compliance;
    - A response to an internally initiated complaint or concern (a participant, a family member, Institutional personnel); or
    - A researcher or department with a history of poor adherence to IRB policies and procedures.

- **Supplemental Compliance Review:**
  - PAR review of IRB Approved studies, selected at random or targeted, to assess investigator compliance with federal, state, and local law, and IRB policies. Conducted using systematic methods, such as on-site review and/or informed consent review. Results of Supplemental Compliance Reviews are reported to the convened IRB or, if applicable, to a designated reviewer for expedited review.

    Supplemental Compliance Review activities may include but are not limited to the following:

- Review of studies to verify from sources other than the researcher that no unapproved changes have occurred;
- Review of studies to verify informed consent compliance and practices;
- Review of regulatory documents, including correspondence with the IRB, to verify file accuracy and researcher IRB reporting compliance; or
- Verification that protocol deviations, adverse events and unanticipated problems involving risks to subjects have been appropriately reported.

- **Self-Assessment:**
  - Self-Assessments are developed by PAR at the direction of the IRB Executive Committee, Executive Director, or in response to new/changing regulation. Self-Assessments are distributed to researchers for completion and reporting. Results of Self-Assessments are reported to the convened IRB or, if applicable, to a designated reviewer for expedited review.

    A wide range of topics may be evaluated via Self-Assessment including, but not limited to, the following:

    - Consent process and documentation procedures;
    - IRB approval and start date compliance;
    - Protocol adherence;
    - PI verification of study funding; or
    - PI training/qualifications assessment.

- **Quality Improvement:**
  - The PAR program supports continuous quality improvement through evaluation, assessment, and action. PAR quality improvement reviews may be conducted based on IRB request, departmental needs, and/or PAR findings. Quality improvement projects are initiated to improve existing processes and to enhance compliance with regulatory requirements and/or IRB policies. Results of these reviews are shared with the Executive Director and/or IRB Executive Committee. Reports including observations resulting in potential changes to existing, IRB approved research will be reviewed by convened IRB and subsequently reported to the researcher.

- **Research Subject Advocate Telephone Line & Complaint Management:**
  - PAR program staff also respond to complaints/concerns from research subjects received via the Research Subjects Advocate Line. Concerns/complaints may also be submitted verbally, by e-mail or letter, through the UMN Confidential Reporting Service, and via electronic report available on the IRB website. All

communication is logged by PAR staff, promptly reviewed and follow-up with subjects conducted. Summary reports of complaints/concerns received via current reporting mechanisms are shared with the IRB Executive Committee.

IRB Policy 107 Voicing Concerns is followed when managing complaints from research subjects.

PAR Notices

Written notices are sent directly to researchers prior to initiation of all Risk Based and Supplemental Compliance Reviews. Notices are typically sent two weeks in advance of the requested visit date. Notices include details regarding the PAR program, identifies whether the study was selected at random or via directed review, and outlines materials that must be available during the site review. A second notice is sent several days in advance of the site visit to confirm the visit schedule and outline any additional items that must be made available to PAR reviewers.

In the case of "for cause" reviews, the site visit is scheduled as soon as possible.

All other PAR activities include formal notification to researchers, as appropriate.

PAR Elements

The scope of PAR review of research includes a wide range of topics as appropriate to the type of study and/or "for-cause" directive. These areas may include:

1. Adequacy of the Consent Form
2. The Consent Process
3. HIPAA (Data Privacy and Security Procedure)
4. Correspondence with the IRB:
    a. Continuing review
    b. Protocol changes/deviations
5. Correspondence to/from sponsor/PI
6. Protocol Adherence
7. Protocol/Investigational plan
    a. Protocol SOP
    b. Protocol Specific Procedures
8. Data and Safety Monitoring
    a. Data safety monitoring plan
    b. DSMB, documentation
    c. Monitoring plan
    d. Monitoring report, issues, corrective action plan
9. Unanticipated Problems
    a. UPIRTSO reporting
    b. Complaints

c. Follow-up of FDA communication, if applicable
10. Data Collection and Source Documentation
    a. Case Report Forms
    b. Data Confidentiality Procedures
11. Subject Recruitment and Subject Selection
12. Training Requirements
    a. HIPAA
    b. Human Subject Training
    c. Study Specific Training
    d. Current CVs, Certificates, Registrations etc
13. Required Forms/Essential documents
    a. Allocation of Responsibilities – Signature log
    b. Training log
    c. Screening/Enrollment logs
    d. Documentation of subject payment
    e. Forms 1571, 1572,
14. Conflict of Interest
15. Investigational product accountability
16. Required Ethics/Scientific committee approval
17. Record Retention Requirements
18. TASCS
19. Funding Materials

Review emphasis is also placed on verifying whether or not the PI complied with IRB requirements, post approval.

Self-Assessment review elements vary depending on department needs, IRB Executive Committee directive and/or changing guidelines. However, self-assessments are typically topic based, researcher lead, and would not involve full site review by PAR staff unless concerns are identified.

Quality improvement activities and reviews will be conducted in response to IRB Executive Committee directive, departmental needs, in response to internal/external compliance concerns, or PAR reports.

Report of Findings

PAR reports associated with completion of Risk Based and Supplemental Reviews are prepared for IRB review and forwarded for consideration. While researchers do not receive the PAR report, they will receive all observations/findings requiring response via written letter following IRB review. Every effort is made to finalize reports promptly to minimize wait time between site visit and IRB determination.

All other findings from PAR activities, such as quality improvement initiatives, are shared with the IRB Executive Committee and IRB Executive Director. IRB staff are also provided updates of PAR activities and findings during staff meetings.

PAR staff conduct trending analysis to determine whether systemic issues or patterns of concern can be identified. Frequent issues and/or common themes are then examined to determine root cause and reported to the IRB Executive Committee and Executive Director. This process serves to identify HRPP program or researcher weaknesses to allow for correction and quality improvement initiatives.

Other Sources of Compliance Information

In addition to PAR, there are other departments within the University that gather valuable information on human subjects research compliance. These include:

A. Office of Internal Audit :

The Office of Internal Audit (OIA) routinely audits high-risk areas within the institution. They typically perform audits by department or administrative function. When auditing departments who conduct research with human subjects, the OIA team will also look at compliance areas such as consent, appropriate completion of study files, study data confidentiality, training, and data security (http://www1.umn.edu/audit/).

The internal audit reports are copied to the department administration and other offices such as the Office of the Vice President for Research, as appropriate. Appropriate follow-up and corrective action plans are monitored by the Internal Audit team.

B. Clinical Monitors:

The Clinical and Translational Science Institute's (CTSI) Clinical Research Associates (CRAs) help investigators assure study adherence to protocol requirements, FDA regulations, compliance with Good Clinical Practice (GCP) guidelines pertaining to study management, and compliance with the guidelines of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), as applicable. Clinical trial monitoring activities include overseeing the progress of a trial, and ensuring that it is conducted, recorded, and reported in accordance with the protocol and GCP guidelines. (http://www.ctsi.umn.edu/research/services-resources/regulatory-support/index.htm).

C. Clinical Trials Office:

The Masonic Cancer Center Clinical Trials Office (CTO) at the University of Minnesota provides the infrastructure necessary to assist investigators in performing high-quality clinical research, insure the validity and integrity of data, and fulfill all National Cancer Institute (NCI) and regulatory requirements.

This infrastructure includes state-of-the-art information systems and database facilities, expertise in the development and management of clinical trials, and development of IND/IDE applications and monitoring plans.

D. Research Education & Oversight

The Research, Education and Oversight (REO) program staff provide institutional expertise in the analysis, reporting, management and resolution of financial compliance issues. REO also reviews processes related to the use of humans and animals in research.

Regulatory Requirements & Accreditation Standards

45 CFR 46.109(e); 21 CFR 56.109(f);

"An IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research."

OHRP recommends that IRBs have a specific procedure for describing how the IRB determines which projects need verification from sources other than the researchers that no material changes have occurred since previous IRB review, including specific criteria used to make these determinations (e.g., such criteria could include some or all of the following:

(a) randomly selected projects;

(b) complex projects involving unusual levels or types of risk to subjects;

(c) projects conducted by researchers who previously have failed to comply with the requirements of the HHS regulations or the requirements or determinations of the IRB; and

(d) projects where concern about possible material changes occurring without IRB approval have been raised based upon information provided in continuing review reports or from other sources);

45 CFR 46.111(a)(6); 21 CFR 56.111(a)(6); 32 CFR 219

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Federalwide Assurance:

TERMS OF THE FEDERALWIDE ASSURANCE (FWA) OHRP strongly recommends that the Institution and the designated IRB(s) establish educational training and oversight mechanisms (appropriate to the nature and volume of its research) to ensure that research researchers, IRB members and staff, and other appropriate personnel maintain continuing knowledge of, and comply with relevant federal regulations; written IRB procedures; OHRP guidance; other applicable guidance, state and local laws; and institutional policies for the protection of human subjects.

AAHRPP Accreditation Standards:

Standard I-5: The Organization measures and improves, when necessary, compliance with organizational policies and procedures and applicable laws, regulations, codes, and

guidance. The Organization also measures and improves, when necessary, the quality, effectiveness, and efficiency of the Human Research Protection Program.

Element I.5.A. The Organization conducts audits or surveys or uses other methods to assess compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The Organization makes improvements to increase compliance, when necessary.

Element I.5.B. The Organization conducts audits or surveys or uses other methods to assess the quality, efficiency, and effectiveness of the Human Research Protection Program. The Organization identifies strengths and weaknesses of the Human Research Protection Program and makes improvements, when necessary, to increase the quality, efficiency, and effectiveness of the program.

Element I.5.C. The Organization has and follows written policies and procedures so that Researchers and Research Staff may bring forward to the Organization concerns or suggestions regarding the Human Research Protection Program, including the ethics review process.

Element I.5.D. The Organization has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. The Organization works with the Institutional Review Board or Ethics Committee, when appropriate, to ensure that subjects are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate.

Section 3.3.3

Appendix 12: Templates/Audit Forms used by the PAR Program

Site Visit Date:
Study HSC#

subject ID or Code	Adult consent version Date	Adult consent signature date	Adult consent PI signature date	Parent consent version date	Parent consent signature date	Parent consent PI signature date	Assent signature date	Assent PI signature date	Assent 8-11 or 12-17?	HIPAA version date	HIPAA signature date	Screening date	In Screening Log?	matches expected approved date? (Y/N)	Any additional consents?	Observations?	baseline

Post Approval Review (PAR)

Medical and Biological Sciences Research Guide

PI Name: Approval Date:

HSC #: Expiration Date:

Study Title:

Funding: ☐Yes ☐No Funding Type:

IRB Review Level:

Expedited Review ☐ Full Committee Review ☐

Type of PAR: Risk Based ☐ For Cause ☐

Post Approval Reviewer:

Reviewer COI: ☐ Yes ☐ No

Regulatory Documentation

☐Yes ☐No	Appropriate signatures?		
☐Yes ☐No	Training documented for each research staff?		
☐Yes ☐No	Funding		
	☐Yes ☐No	Funding source(s) match IRB materials	
	☐Yes ☐No	If grant/protocol is applicable, version matches IRB approval and study plans.	
☐Yes ☐No	Multi-Site Study?	If yes, name of participating institutions:	
☐Yes ☐No	Other committees to review?	If yes, list committees:	
☐Yes ☐No	PI indicates Conflict of Interest		
	☐Yes ☐No	If applicable, COI Management Plan is on file with IRB	

PAR Reviewer Comments:

Approval and Record Keeping

☐Yes ☐No	All IRB Related Documents (approval letter(s), application, consent materials, etc.) accessible and complete.
☐Yes ☐No	All changes to the IRB approved study have been submitted to the IRB
☐Yes ☐No	IRB approved consent (s) version was used when enrolling subjects

☐Yes ☐No	IRB approval lapses during conduct of the study (e.g. continuing renewal not submitted ina timely manner?)
PAR Reviewer Comments:	

Participant Population	
Total number of subjects enrolled at time of PAR:	
☐Yes ☐No	Age range matches IRB approved range
☐Yes ☐No	Protected Populations***/Vulnerable Populations Included? (indicate below)
	☐ Mentally/emotionally/developmentally disabled*
	☐ Minority group(s) and non-English speakers*
	☐ Persons who are in the process of commitment*
	☐ Elderly Subjects
	☐ Patients (clinical patients of the investigator?)
	☐ Children (Subpart D)***
	☐ Students
	☐ Employees
	☐ Pregnant Women (Subpart B)***
	☐ Prisoners (Subpart C)***
	☐ Other
☐Yes ☐No	IRB approved inclusion of protected/vulnerable populations
PAR Reviewer Comments:	

Recruitment		
☐Yes ☐No	Subjects were identified and recruited according to the methods approved by the IRB?	
☐Yes ☐No	Advertising or recruitment materials used to recruit were approved by the IRB	
☐Yes ☐No	Inclusion/Exclusion requirements as listed and approved by the IRB were followed?	
	If no, were deviations reported to the IRB?	☐Yes ☐No
☐Yes ☐No	If subjects received compensation is there documentation?	
PAR Reviewer Comments:		

Compensation/ Inducement	
☐Yes ☐No	Subjects Receive Compensation for study participation
☐Yes ☐No	Any change to compensation or subject participation/parameters since last continuing renewal?

☐ Yes ☐ No	Matches consent?
PAR Reviewer Comments:	

Confidentiality of Data		
☐ Yes ☐ No	Are direct identifiers recorded and/or maintained?	
	If yes, list direct identifiers:	
☐ Yes ☐ No	Does PI's IRB approved plan to protect identifiers match practice?	
	Confirm Practice (check all that apply):	
	☐ Paper based records: secure location with limited personnel access	
	☐ Paper based records: no direct ID's on study forms; random code used	
	☐ Computer based records: limited access, passwords, encryption	
	☐ Computer based records: PI adheres to UMN OIT Guidelines	
☐ Yes ☐ No	Have any breaches in confidentiality occurred during the conduct of the study?	
	If yes, was the breach reported to the IRB?	☐ Yes ☐ No
☐ Yes ☐ No	Does study include a COC?	
	If yes, does CF(s) accurately describe COC?	☐ Yes ☐ No
	Are data storage and collection practices consistent with COC?	☐ Yes ☐ No
PAR Reviewer Comments:		

Informed Consent/HIPAA Review	
☐ Yes ☐ No	Is written informed consent required for this project?
	If no, check applicable IRB approved consent waiver
	☐ Waiver of signed documentation of consent (45CFR46.117(c))
	☐ Waiver of consent (45CFR46.116(d))
☐ Yes ☐ No	Does Consent form/material match IRB approved documents?
☐ Yes ☐ No	Are all consent forms available for review?
	If so, do forms include (check applicable):
	☐ Participant Signature/LAR/PG
	☐ Date of Consent
	☐ Signed by subject prior to enrollment?
	☐ IRB approved consent obtainer?
☐ Yes ☐ No	Are children included?
	If so,
	☐ Assent obtained
	☐ Assent/information Sheet Waived by IRB
	☐ Information Sheet Used
	☐ Parent/Guardian Consent
	☐ Parent/Guardian Consent Waived by IRB
	☐ Parent/Guardian Consent obtained before child assent
☐ Yes ☐ No	Is HIPAA Applicable to the research?

	If yes, check applicable IRB approved HIPAA compliance process
	☐ HIPAA Authorization
	☐ Waiver of HIPAA
	☐ Alteration of HIPAA

PAR Reviewer Comments:

Additional Comments and Notes

PAR Reviewer Comments:

Protocol Version		Comments
☐Yes ☐No	Is the most recent version of the protocol on file?	
☐Yes ☐No	Are there previous versions of the protocol?	
☐Yes ☐No	If yes, are they on file?	
☐Yes ☐No	Are you able to identify each version and date of the protocol?	
FDA Regulated Research		**Comments**
☐Yes ☐No	Is this an FDA regulated study?	
☐Yes ☐No	If yes, is there a signed 1572 on file at the IRB?	
☐Yes ☐No	Is the Clinical Investigator Financial Disclosure form (FDA 3455 or 3454) on file for each investigator?	
☐Yes ☐No	Is all the correspondence to and from the sponsor on file with the IRB?	
Federally-Sponsored Research		**Comments**
☐Yes ☐No	Is this research activity federally sponsored or submitted for federal sponsorship?	
☐Yes ☐No	Is the protocol as originally submitted to the IRB congruent with the federal application?	
Additional Comments Miscellaneous		
PI Sponsor-Investigator		**Comments**
☐Yes ☐No	Is the PI the sponsor-investigator (i.e. IND/IDE holder)?	
☐Yes ☐No	If yes, is there a signed FDA 1571 on file (IND only)?	
☐Yes ☐No	If yes, are there 1571s on file for the following:	
☐Yes ☐No	Original application?	
☐Yes ☐No	All amendments?	
☐Yes ☐No	Annual Reports?	

☐Yes ☐No	Who (organization or individual) is listed as the monitor in Section 14 of the 1571?	***Organization/Individual:***

Training and Experience		Comments
☐Yes ☐No	Have all key study personnel (including PI, Sub/Co-PIs, and all other staff who interact/intervene with research participants or their identifiable data) completed the Basic CITI course in either Biomedical or Social-Behavioral Research? OR Has the IRB approved an alternative training program?	
☐Yes ☐No	Have all key personnel received appropriate training on execution of the protocol?	
☐Yes ☐No	Are there CVs of PI/CO-PI and all study staff on file?	
☐Yes ☐No	Are CVs updated within the past two years and signed and dated?	

Enrollment		Comments
☐Yes ☐No	Is there a subject enrollment log?	
☐Yes ☐No	If yes, is the subject enrollment log up to date?	

Monitoring		Comments
☐Yes ☐No	Is the study site externally monitored (by sponsor or DSMB)?	
☐Yes ☐No	If yes, is there a monitoring log?	
☐Yes ☐No	Is the monitoring log up to date?	
☐Yes ☐No	How frequently is the site monitored?	

Staff Signature Log		Comments
☐Yes ☐No	Is there a staff signature log? ***(If no, go to 1.10)***	
☐Yes ☐No	If yes, is the staff signature log up to date?	
☐Yes ☐No	Does the staff signature log include information regarding delegation of responsibility?	

Investigational Drugs, Devices, Biologics		Comments
☐Yes ☐No	Is this an investigational drug or device study? ***(If no, go to next section)***	

☐Yes ☐No	If yes, are all versions of the Investigator Brochure, Labeling, or Device Manual on file?	
☐Yes ☐No	Is there package insert/product information on file? (Other labeling)?	
Laboratory Records		**Comments**
☐Yes ☐No	Are lab tests required? ***(If no, go to next section)***	
☐Yes ☐No	Is a copy of the normal lab values on file?	
☐Yes ☐No	Is lab certification on file, (e.g. CLIA)? If this is an IND study, documentation for all laboratories listed on the FDA form 1572 must be on file.	
☐Yes ☐No	Is the lab director's CV on file (signed and dated)?	
Data Safety Monitoring		**Comments**
☐Yes ☐No	Is there a data safety monitoring board (DSMB) for this study?	
☐Yes ☐No	Has the DSMB met in accordance with the IRB approved protocol?	
☐Yes ☐No	Are appropriate DSMB reports or indication of DSMB reviews and recommendations on file?	
☐Yes ☐No	Has the DSMB report or review been submitted to the U of MN IRB?	

Please describe any areas of concern identified, action(s) to take or taken, and other notes:

Post Approval Review Sheet (PAR)
Social and Behavioral Sciences Research Guide

PI Name: Approval Date:

HSC #: Expiration Date:

Study Title:

Funding: ☐Yes ☐No Funding Type:

IRB Review Level:

Expedited Review ☐ Full Committee Review ☐

Type of PAR: Risk Focused ☐ For Cause ☐

Post Approval Reviewer:

Reviewer COI: ☐ Yes ☐ No

Regulatory Documentation

☐Yes ☐No	Appropriate signatures?		
☐Yes ☐No	Training documented for each research staff?		
☐Yes ☐No	Funding		
	☐Yes ☐No	Funding source(s) match IRB materials	
	☐Yes ☐No	If grant/protocol is applicable, version matches IRB approval and study plans.	
☐Yes ☐No	Multi-Site Study?	If yes, name of participating institutions:	
☐Yes ☐No	Other committees to review?	If yes, list committees:	
☐Yes ☐No	PI indicates Conflict of Interest		
	☐Yes ☐No	If applicable, COI Management Plan is on file with IRB	

PAR Reviewer Comments:

Approval and Record Keeping

☐Yes ☐No	All IRB Related Documents (approval letter(s), application, consent materials, etc.) accessible and complete. **Notes:**
☐Yes ☐No	All changes to the IRB approved study have been submitted to the IRB **Notes:**
☐Yes ☐No	IRB approved consent (s) version was used when enrolling subjects **Notes:**

☐Yes ☐No	IRB approval lapses during conduct of the study (e.g. continuing renewal not submitted ina timely manner?) **Notes:**
PAR Reviewer Comments:	

Participant Population	
Total number of subjects enrolled at time of PAR:	
☐Yes ☐No	Age range matches IRB approved range
☐Yes ☐No	Protected Populations***/Vulnerable Populations Included? (indicate below)
	☐ Mentally/emotionally/developmentally disabled*
	☐ Minority group(s) and non-English speakers*
	☐ Persons who are in the process of commitment*
	☐ Elderly Subjects
	☐ Patients
	☐ Children (Subpart D)***
	☐ Students
	☐ Employees
	☐ Pregnant Women (Subpart B)***
	☐ Prisoners (Subpart C)***
	☐ Other
☐Yes ☐No	IRB approved inclusion of protected/vulnerable populations
PAR Reviewer Comments:	

Recruitment	
☐Yes ☐No	Subjects were identified and recruited according to the methods approved by the IRB?
☐Yes ☐No	Advertising or recruitment materials used to recruit were approved by the IRB
☐Yes ☐No	Inclusion/Exclusion requirements as listed and approved by the IRB were followed?
If no, were deviations reported to the IRB?	☐Yes ☐No
☐Yes ☐No	If subjects received compensation is there documentation?
PAR Reviewer Comments:	

Compensation/ Inducement	
☐Yes ☐No	Subjects Receive Compensation for study participation

☐ Yes ☐ No	
☐ Yes ☐ No	

PAR Reviewer Comments:

Confidentiality of Data		
☐ Yes ☐ No	Are direct identifiers recorded and/or maintained?	
	If yes, list direct identifiers:	
☐ Yes ☐ No	Does PI's IRB approved plan to protect identifiers match practice?	
	Confirm Practice (check all that apply):	
	☐ Paper based records: secure location with limited personnel access	
	☐ Paper based records: no direct ID's on study forms; random code used	
	☐ Computer based records: limited access, passwords, encryption	
	☐ Computer based records: PI adheres to UMN OIT Guidelines	
☐ Yes ☐ No	Have any breaches in confidentiality occurred during the conduct of the study?	
	If yes, was the breach reported to the IRB?	☐ Yes ☒ No
☐ Yes ☐ No	Does study include a COC?	
	If yes, does CF(s) accurately describe COC?	☐ Yes ☐ No
	Are data storage and collection practices consistent with COC?	☐ Yes ☐ No

PAR Reviewer Comments:

Informed Consent/HIPAA Review	
☐ Yes ☐ No	Is written informed consent required for this project?
	If no, check applicable IRB approved consent waiver
	☐ Waiver of signed documentation of consent (45CFR46.117(c))
	☐ Waiver of consent (45CFR46.116(d))
☐ Yes ☐ No	Does Consent form/material match IRB approved documents?
☐ Yes ☐ No	Are all consent forms available for review?
	If so, do forms include (check applicable):
	☐ Participant Signature/LAR/PG
	☐ Date of Consent
	☐ Signed by subject prior to enrollment?
	☐ IRB approved consent obtainer?
☐ Yes ☐ No	Are children included?
	If so,
	☐ Assent obtained
	☐ Assent/information Sheet Waived by IRB
	☐ Information Sheet Used

	☐ Parent/Guardian Consent
	☐ Parent/Guardian Consent Waived by IRB
	☐ Parent/Guardian Consent obtained before child assent
☐ Yes ☐ No	Is HIPAA Applicable to the research?
	If yes, check applicable IRB approved HIPAA compliance process
	☐ HIPAA Authorization
	☐ Waiver of HIPAA
	☐ Alteration of HIPAA

PAR Reviewer Comments:

Additional Comments and Notes

PAR Reviewer Comments:

Post Approval Review
Title:
IRB/HSC #: Click here to enter a date. **PI:** Click here to enter text.
Date of Review : Click here to enter text.
Contact Information: PAR Reviewer: Email: Phone:

Post Approval Review

Site Visit

Presented to the Medical and Biological Committee

Month, DD, 2014

Study Summary	
Principal Investigator:	
Research Coordinator:	Click here to enter text.
Study Overview:	
Funding:	
# Subjects Approved:	**# Subjects Currently Enrolled:**
Date of Initial Approval:	**Date of Most Recent Approval:**
Type of Review:	**Original Level of Review:**
Current Study Status: Choose an item.	**Notes:**

Post Approval Review
Title:
IRB/HSC #: Click here to enter a date. **PI:** Click here to enter text.
Date of Review : Click here to enter text.
Contact Information: PAR Reviewer: Email: Phone:

Recommendations for Committee Discussion

Issues summarized and presented in order by degree of risk. Regulations will be cited to support recommendations, as applicable:

Risk Area: Choose an item.

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Risk Area: Choose an item.

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
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Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Risk Area: Choose an item.

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Observation Description

Observation Observation Observation Observation Observation Observation Observation Observation

Post Approval Review
Title:
IRB/HSC #: Click here to enter a date. **PI:** Click here to enter text.
Date of Review : Click here to enter text.
Contact Information: PAR Reviewer: Email: Phone:

Observation Observation Observation Observation Observation Observation Observation Observation Observation Observation Observation Observation Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Post Approval Review
Title:
IRB/HSC #: Click here to enter a date. **PI:** Click here to enter text.
Date of Review : Click here to enter text.
Contact Information: PAR Reviewer: Email: Phone:

Review Summary

This section will be reviewed by staff and leadership and not at convened IRB:

# Subjects Approved:	**# Subjects Currently Enrolled:**	
Monitored by:	**Date of Most Recent Monitoring Visit:**	
Current Study Status: Enrolling		
Safety Monitoring	Y/N/NA	
Laboratory Records	Y/N/NA	
Staff Signature Log	Y/N/NA	
Monitoring	Y/N/NA	
Enrollment	Y/N/NA	
Training documentation	Y/N/NA	
Delegation Log	Y/N/NA	
Regulatory Binder	Y/N/NA	
Screening Logs	Y/N/NA	
Screening Fails	Y/N/NA	
Additional Patient Materials	Y/N/NA	
IRB Files at study site	Y/N/NA	
Consent form review	Y/N/NA	**%**
Subject Record Review	Y/N/NA	**%**

Post Approval Review
Title:
IRB/HSC #: **PI:**
Date of Review :
PAR Reviewer:

Post Approval Review

For-Cause Site Visit

Presented to the <Medical Committee/Social Sciences Committee>

<DATE>

Study Summary	
Principal Investigator:	
Research Coordinator:	
Study Summary:	
Funding:	
# Subjects Approved:	**# Subjects Currently Enrolled:**
Date of Initial Approval:	**Date of Most Recent Approval:**
Type of Review: For Cause	**Original Level of Review:**
Current Study Status:	**Notes:**

Summary of Non-Compliance

Summarize issue(s):

Post Approval Review
Title:
IRB/HSC #: **PI:**
Date of Review :
PAR Reviewer:

Corrective & Preventive Action Plan (CAPA)

The CAPA issues, included below, identify the key problems occurring during the conduct of the research, as observed by the PAR reviewer, notes the potential root cause, and confirms recommendations for corrective action (subject to IRB agreement) to prevent recurrence.

Summarize CAPA:

CAPA Recommendations

CAPA Issue 1:

Description:

Root Cause:

- **Recommendation**:
- **Recommendation:**

CAPA Issue 2:

Description:

Root Cause:

- **Recommendation**:
- **Recommendation:**

Root Cause:

CAPA Issue 3:

Description:

Root Cause:

- **Recommendation**:
- **Recommendation:**

Post Approval Review
Title:
IRB/HSC #: **PI:**
Date of Review :
PAR Reviewer:

PAR Recommendations for Committee Discussion

PAR review and site visit observations summarized and presented in order by degree of risk. Regulations will be cited to support recommendations, as applicable:

Risk Area: Choose an item.

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Risk Area: Choose an item.

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Observation Description

Observation Observation

- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)
- **Recommendation:** Recommendation Recommendation Recommendation Recommendation Recommendation Recommendation (high, medium, low)

Post Approval Review
Title:
IRB/HSC #: **PI:**
Date of Review :
PAR Reviewer:

Review Summary

This section will be reviewed by staff and leadership and not at convened IRB:

# Subjects Approved:	**# Subjects Currently Enrolled:**	
Monitored by:	**Date of Most Recent Monitoring Visit:**	
Current Study Status: Enrolling		
Safety Monitoring	Y/N/NA	
Laboratory Records	Y/N/NA	
Staff Signature Log	Y/N/NA	
Monitoring	Y/N/NA	
Enrollment	Y/N/NA	
Training documentation	Y/N/NA	
Delegation Log	Y/N/NA	
Regulatory Binder	Y/N/NA	
Screening Logs	Y/N/NA	
Screening Fails	Y/N/NA	
Additional Patient Materials	Y/N/NA	
IRB Files at study site	Y/N/NA	
Consent form review	Y/N/NA	**%**
Subject Record Review	Y/N/NA	**%**

University of Minnesota

New Medical Application Review (Full Committee)

Staff pre-review comments are intended to assist the primary reviewer. Email completed reviews to irb@umn.edu

HSC#:		PI Name:	
Date of pre-review:	Click here to enter a date.	Date received:	
Staff reviewer:		Meeting Date	
Reviewer:			

HOLD for:		
☐ Federal Grant	☐ TASCS Billing Grid	☐ Scientific Assessment
☐ Appendix A/EFS info	☐ COI Management Plan	☐ Other: Click here to enter text.
Date hold applied Click here to enter a date.	Date hold lifted: Click here to enter a date.	

Important Note to IRB Member Reviewers:
Staff Pre-review findings are for guidance only. Any actions to be taken regarding pre-review findings, must be stipulated/suggested by the IRB Member reviewer

Section 1 – Principal Investigator/Faculty Advisor Consider if those responsible for conducting/overseeing the proposed research have the training, expertise and necessary institutional affiliation to execute that role.		
Staff Pre-review:	☐ HIPAA training required	☐ Sponsor-investigator training required
☒ Human Subjects training not documented	☐ HIPAA training not documented	☐ Sponsor-Investigator training not documented
Staff Pre-review Comments:		
IRB Member review: Staff Pre-review findings are for guidance only. Any actions to be taken regarding pre-review findings, must be stipulated/suggested by the IRB Member reviewer		
Stipulations:		
Suggestions:		
For committee discussion:		
☐ Meets UMN HRPP standards – PI has the required training and expertise to conduct this study		

Section 2 – Summary of Activities Consider if there are any ethical issues regarding the study's design and plan for conduct	
Staff Pre-review:	
Staff Pre-review Comments:	
IRB Member review: ☐ Procedures are NOT consistent with sound research design and/or unnecessarily expose subjects to risk. (provide detail below)	☐ Use of human subjects **does NOT** have research relevance When appropriate, are procedures already being performed on subjects for diagnostic or treatment purposes?

☐Yes ☐No ☐N/A

Provide a 1-3 sentence summary of the project for presentation at meeting:

Stipulations:

Suggestions:

For committee discussion:

☐ Meets UMN HRPP and regulatory standards – no concerns noted

Section 3 – Risks and Benefits

Consider if risks (physical, emotional, financial, legal) to subjects have been minimized and if those risks are reasonable in relation to any anticipated benefit.

Staff Pre-review:

Staff Pre-review Comments: Click here to enter text.

IRB Member review:

☐Risks to subjects are NOT minimized.

Are risks to subjects described consistently in the application, consent form, protocol and any other supporting material?
☐**Yes** ☐**No**

Does the risk/benefit ratio justify proceeding?
☐**Yes** ☐**No**

Stipulations:

Suggestions:

For committee discussion:

☐ Meets UMN HRPP and regulatory standards – risks to subjects are reasonable in relation to the anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result.

Section 4 – Subject Profile

Staff Pre-review:
Protected populations include:
☐Prisoners
☐Pregnant women
☐Non-English speakers
☐Minority group(s) targeted
☐Diminished capacity to consent
☐Economic/educationally disadvantaged

Number of subjects requested:
Click here to enter text.
Number of subjects required to enroll:
Click here to enter text.

Staff Pre-review Comments: .

IRB Member review:

☐Subject Selection is NOT equitable for the reasons stated below

☐Use of human subjects does not have research relevance

Are children excluded?
☐ No
☐ yes. If exclusion is not justified, explain:

Stipulations:

Suggestions:

For committee discussion:

☐ Meets UMN HRPP standards – no concerns noted

Section 5 – Study Location(s)	
Staff Pre-review:	☐ Letters of support/permission missing: Click here to enter text.
Staff Pre-review Comments: Click here to enter text.	
IRB Member review: ☐ Stip for appendix ☐ stip for letter of support/permission	
Stipulations:	
Suggestions:	
For committee discussion:	

☐ Meets UMN HRPP standards – no concerns noted

Section 6 – Recruitment & Compensation		
Staff Pre-review: ☐ Recruitment methods are not described	☐ Screening procedures are not included	☐ Recruitment materials are missing
Staff Pre-review Comments: Click here to enter text.		
IRB Member review: ☐ Payments/reimbursements are potentially coercive/unduly influential	☐ Recruitment is potentially coercive/undue influence on subjects to participate	
Stipulations:		
Suggestions:		
For committee discussion:		

☐ Meets UMN HRPP standards – no concerns noted

Section 7 – Confidentiality & Privacy	
Staff Pre-review: ☐ Certificate of confidentiality requested	
Staff Pre-review Comments: Click here to enter text.	
IRB Member review: ☐ Adequate provisions to protect the privacy of subjects and to maintain confidentiality of data is NOT documented.	☐ Privacy protections measures and confidentiality measures are not clearly described
Stipulations:	
Suggestions:	
For committee discussion:	

☐ Meets UMN HRPP standards and regulatory requirements.– research plans make adequate provisions to protect the privacy of subjects and to maintain confidentiality of data.

Section 8 – Expedited Review
Staff Pre-review:
☐ This research meets expedited review eligibility, category: Click here to enter text.
IRB Member review:
☐ This research meets expedited review eligibility, category:

Section 9 – Informed Consent Process		
Staff Pre-review: ☐ PI not identified along with affiliation with U of M	☐ Not stated that subjects can withdraw at any time	☐ No out of study contact listed ☐ Study sponsor not identified
Staff Pre-review Comments: Click here to enter text.		
IRB Member review: ☐ Informed consent process **does not** conform to requirements stated in 21 CFR 50 and/or 45 CFR 46.116 ☐ Documentation of informed consent **does not** conform to requirements stated in 21 CFR 50.27 and/or 45 CFR 46.117	☐ Third party observation of the consent process required	
Stipulations:		
Suggestions:		
For committee discussion:		
☐ Meets UMN HRPP standards and regulatory requirements		

Consent/Assent/Info Sheet			
Staff Pre-review:			
Staff Pre-review Comments:			
IRB Member review:			
CONSENT FORM			
Required consent form elements. Missing items should be stipulated or waived.			
Is the PI identified?	☐ STIP	Are benefits clearly and fully stated?	☐ STIP
Is the affiliation with the University of Minnesota identified?	☐ STIP	Are privacy concerns address?	☐ STIP
Is the study sponsor identified?	☐ STIP	Is there an out of study contact?	☐ STIP
Is the drug manufacturer identified?	☐ STIP	Is it stated that subjects can withdraw at any time?	☐ STIP

Does the consent form state the study purpose accurately?	☐ STIP	Is there standard language regarding injury/compensation?	☐ STIP
Is it clear what the subject will be asked to do?	☐ STIP	Is the consent understandable at an 8th grade level?	☐ STIP
Are risks clearly and fully stated?	☐ STIP	Are alternatives listed? (treatment only)	☐ STIP ☐ Waive
Reviewer justification for waiving required elements:			
ASSENT FORM			
Is the assent form one page or less?	☐ STIP ☐ Waive	Is the language simple and the sentences short?	☐ STIP ☐ Waive
ADDITIONAL ELEMENTS OF CONSENT Check the box to indicate if any of the items in the table below should be included in the consent form			
Treatment or procedure may involve risks which are currently not foreseeable.	☐	Consequences of a subject's decision to withdraw from the research and procedures for the orderly termination of participation by the subject.	☐
Circumstances under which subject's participation may be terminated by the investigator without regard to the subject's consent	☐	Significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.	☐
Any additional costs to the subject that may result from participation in the research	☐	Approximate number of subjects involved in the study.	☐
Stipulations:			
Suggestions:			
For committee discussion:			

Section 10 – Funding

Staff Pre-review:
Funding type is:
☐ B&I ☐ Federal ☒ Foundation
☐ Other: Click here to enter text.

Multi-site, competitive enrollment?
☐ Yes ☐ No

Staff Pre-review Comments: Click here to enter text.

IRB Member review:
Funding

Stipulations:

Suggestions:

For committee discussion:

☐ Meets UMN HRPP standards – no concerns noted

Section 11 – Conflict of Interest

Staff Pre-review:
☐ Conflict of interest indicated

COI management plan
☐ Approved ☐ Pending

Staff Pre-review Comments: Click here to enter text.

IRB Member review:

Stipulations:

Suggestions:

For committee discussion:

☐ Meets UMN HRPP standards – no concerns noted

Section 12 – Research Services, Assessment & Oversight

Staff Pre-review:

☐ Protocol is greater than minimal risk and PI has indicated no need for a DSMP

☐ Clinicaltrials.gov registration decision/number pending

Will the investigational product be provided free of charge?
☐ Yes ☐ No ☐ N/A

Is this a Qualifying Clinical Trial?
☐ Yes ☐ No
if no, research charges cannot be billed to insurance

Staff Pre-review Comments: Click here to enter text.

IRB Member review:

☐ Adequate provisions for monitoring the data collected to ensure the safety of subjects **are NOT** documented

Stipulations:

Suggestions:

For committee discussion:

☐ Meets UMN HRPP standards and regulatory requirements – research plans make adequate provisions for monitoring the data collected to ensure the safety of subjects.

Section 13 – Study Personnel

Consider if those responsible for conducting/overseeing the proposed research have the training, expertise and necessary institutional affiliation to execute that role.

Staff Pre-review:

☐ HIPAA training required

☐ Human Subjects training not documented

☐ HIPAA training not documented

Staff Pre-review Comments: Click here to enter text.

IRB Member review:

Stipulations:

Suggestions:

For committee discussion:

☐ Meets UMN HRPP standards – Personnel have the required training and expertise to conduct this study

Appendices submitted:

☐ **A** ☐ **B** ☐ **C** ☐ **D** ☐ **E** ☐ **F** ☐ **G** ☐ **H** ☐ **I** ☐ **J** ☐ **K** ☐ **L** ☐ **M** ☐ **N** ☐ **Q** ☐ **T** ☐ **Y**

Appendices required – not submitted
☐A ☐B ☐C ☐D ☐E ☐F ☐G ☐H ☐I ☐J ☐K ☐L ☐M ☐N ☐Q ☐T ☐Y

Appendix Y:

Staff Pre-review:

Staff Pre-review Comments: Click here to enter text.

IRB Member review:
Children included under
☐**404** ☐**405** ☐**406** ☐**407**

Assent:
☐**Required**
☐**Assent waived – info sheet provided**
☐**Assent waived**

Stipulations:

Suggestions:

For committee discussion:

Appendix:
☐A ☐B ☐C ☐D ☐E ☐F ☐G ☐H ☐I ☐J ☐K ☐L ☐M ☐N ☐Q ☐T ☐Y

Staff Pre-review:

Staff Pre-review Comments: Click here to enter text.

IRB Member review:

Stipulations:

Suggestions:

For committee discussion:

Appendix:
☐A ☐B ☐C ☐D ☐E ☐F ☐G ☐H ☐I ☐J ☐K ☐L ☐M ☐N ☐Q ☐T ☐Y

Staff Pre-review:

Staff Pre-review Comments: Click here to enter text.

IRB Member review:

Stipulations:

Suggestions:

For committee discussion:

IRB Member Recommendation:

☐ **APPROVED AS SUBMITTED**

☐ **APPROVED WITH STIPULATIONS as noted**
Response to stipulations review

☐ **APPROVAL DEFERRED – ADDITIONAL INFORMATION REQUIRED**

☐ **APPROVED WITH SUGGESTIONS as noted**

☐ **Must be sent to original reviewer** ☐ **NOT APPROVED**
☐ **May be reviewed administratively**

For **continuing review** and approval, federal regulations state that studies need to be reviewed no less than yearly but the reviewer may set continuing review at a more frequent interval. Indicate the appropriate interval below

☐ Annually
☐ Every six months
☐ Quarterly
☐ Other (i.e. reviewed after 5 subjects enrolled). Specify renewal interval:

Reviewer:	Study code #:

UMN Review Guide: Industry-Sponsored Research – ICH-GCP E6

☐ The PI has confirmed that he/she has fulfilled requirements for and will conduct the research in a manner consistent with ICH-GCP E6 requirements.

☐ Researchers' current curriculum vitae or other documentation evidencing qualifications is provided. *(ICH-GCP 3.1.2)*

☐ The research is scientifically sound and described in a clear, detailed protocol. *(ICH-GCP 2.5)*

☐ The study includes the resources necessary to protect participants including:

- Adequate numbers of qualified staff
- Adequate facilities

(ICH-GCP 4.2.3)

Use of Investigation Product/Article

Is an investigational product/article used in this study?

☐ No. **If no, go to Reporting Requirements**

☐ Yes. **If yes, confirm the requirements below are met. These requirement are in addition to requirements imposed by FDA.**

☐ Available nonclinical and clinical information provided is adequate to support the proposed research. *(ICH-GCP 2.4)*

☐ Where allowed or required, the Principal Investigator may assign some or all duties for investigational articles accountability at the trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the Principal Investigator. *(ICH-GCP 4.6.2)*

☐ Qualified research personnel will maintain records that adequately document the participants are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor. *(ICH-GCP 4.6.3)*

☐ Qualified study personnel will maintain records of the investigational product's delivery to the trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused products. These records should include:

a. Dates
b. Quantities
c. batch/serial numbers
d. expiration dates (if applicable)
e. unique code numbers assigned to the investigational products and trial participants

Reporting Requirements

☐ The study materials confirm that the following will be promptly reported to the IRB:

- New information that may affect adversely the safety of the participants or the conduct of the clinical trial.
- Any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.

Consent Form Requirements

☐ The consent form(s) includes language regarding the following:

- Alternative procedures or treatment that may be available to the participant, including their important potential benefits and risks.
- Study monitor(s), auditor(s), the IRB, and any regulatory authorities will be granted direct access to the participant's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the participant or the participant's legally acceptable representative is authorizing such access.
- The study has been reviewed and received approval by the IRB.

(ICH-GCP 4.8.10)

Inclusion of Adults Lacking Capacity to Consent or Adults with Diminished Capacity to Consent

When the research proposes to include adults lacking capacity to consent *one of the following must be true*:

☐ If the study is a non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the participant), only participants who personally give consent and who sign and date the written consent document are included as subjects.

-----OR-----

☐ Consent of a legally acceptable representative may be used, provided *all of the following conditions are fulfilled*:

- The objectives of the clinical trial cannot be met with only participants who can give consent personally.
- The foreseeable risks to the participants are low.
- The negative impact on the participant's wellbeing is minimized and low.
- The clinical trial is not prohibited by law.
- The opinion of the IRB is expressly sought on the inclusion of such participants, and the written opinion covers this aspect.
- Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. (Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.)
  (ICH-GCP 4.8.14)

☐ The study lists procedures for ensuring that the subject or the subject's legally acceptable representative are informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. *(ICH-GCP 4.8.12)*

Staff Reviewer:	Study code #:
Reviewer:	Meeting Date:

UMN IRB Review Guide: Adults Lacking Capacity to Consent or with Diminished Capacity to Consent

This worksheet is used to review non-exempt Human Research that includes or may include adult subjects lacking capacity to consent.

Section 1 - Considerations Applied to All Research

Does the population targeted for recruitment represent the population with the least degree of impairment compatible with the aims of the study?

☐ Yes ☐ No

Comments:

Have appropriate procedures for assessing capacity to consent to enroll in the study been described in the protocol?

☐ Yes ☐ No

Comments:

Does the research involve risks or discomforts that are greater for subjects who lack capacity than unimpaired subjects?

☐ Yes ☐ No

Comments:

Does the process to assess capacity provide reasonable assurances that the evaluator's judgments will be impartial?

☐ Yes ☐ No

Comments:

Should the investigator follow a consent process so that individuals who are not capable under routine procedures might be capable?

☐ Yes ☐ No

Comments:

Examples of IRB requirements for the consent process might include:

- *Designing a stepwise consent process, which involves a waiting period between each phase of the process: capacity assessment, initial presentation of information, and obtaining consent;*
- *Enhanced presentation of consent information during initial presentation and/or immediately prior to obtaining consent including: repetition of information), both oral and written presentation of information, multi-media presentation of information, interactive questioning, and written study summaries;*
- *Continuous dissemination of consent information throughout the course of the study; and*
- *Conducting the consent process in an environment in which the subject is comfortable.*

Section 1a - Considerations Applied When Subjects Might Experience Fluctuating Functional Abilities

Does the consent process include plans to avoid, if feasible, periods during which subjects are likely to experience greater than normal impairment?

☐ Yes ☐ No

Comments:

Should provisions be included to anticipate fluctuations in capacity?

☐ Yes ☐ No

Comments:

Examples of IRB requirements for the consent processes might include:

- *Re-evaluating subjects' capacity over the course of the study*
- *Designation of an individual to serve as a legally authorized representative (LAR) (see Policy 703)*
- *Involving potential LARs in the consent process*
- *Asking subjects to document their wishes regarding participation*
- *Avoiding consent when subjects are likely to experience greater than normal impairment*
- *Obtaining consent of subjects who regain capacity*

Section 2 - Considerations for All Research Involving Greater than Minimal Risk to Subjects

Has the experimental intervention been tested on animals, or humans with unimpaired functional abilities?

☐ Yes ☐ No

Comments:

Does the protocol include a written description of procedures for minimizing risk?

☐ Yes ☐ No

Comments:

Is there documentation of the importance of knowledge to be obtained by answering the research question?

☐ Yes ☐ No

Comments:

Check the box indicating if one or more monitors listed below must be appointed to assist with various aspects of the study

☐ A subject advocate such as a member of the target population or family member thereof; or an employee of an organization that advocates for the target population;

☐ An individual with expert knowledge of the relevant psychological or physical condition who will monitor the consent of subjects;

☐ A health care professional to serve as a consultant to subjects

Should a list of resources and referrals be offered to subjects to assist them in coping with any foreseeable harm?

☐ Yes ☐ No

Comments:

Should there be a written rationale for the inclusion of subjects with diminished functional abilities?

☐ Yes ☐ No

Comments:

Should continuing review be conducted more frequently than annually?

☐ Yes ☐ No

If yes, how frequently:

Should there be a description of procedures for withdrawing subjects or terminating the study?

☐ Yes ☐ No

Comments:

Should there be procedures for screening LARs and informing them of their responsibilities?

☐ Yes ☐ No

Comments:

Section 2a - Choose the appropriate category below. The research must meet *all* criteria in the appropriate category for the research to be approved.

☐ **Research with Anticipated Direct Benefit to the Subject (must meet *all* criteria below):**

- One of the following is true: a) the knowledge likely to be gained will improve the understanding of the condition, disease or behavior affecting the subject population or b) there is a compelling argument for including individuals who lack decision-making capacity in the research
- One of the following is true: a) the research involves no more than minimal risk to the subjects or b) the research holds out the prospect of direct benefit for the individual subject where the relation of the anticipated benefit to the risk is at least as favorable as that presented by available alternative approaches
- The research is not prohibited by law
- Subjects will be closely monitored and withdrawn from the research if they appear to be unduly distressed
- There are adequate provisions for soliciting the permission of a LAR

☐ **Research with No Anticipated Direct Benefit to the Subject (must meet *all* criteria below):**

- The objective cannot be met with research involving subjects who can give consent personally
- Unless an exception is justified, subjects have a disease or a condition relevant to the research
- One of the following is true: a) the foreseeable risks to the subjects are no greater than a minor increase over minimal risk or b) the research is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition
- The negative impact on the subject's well-being is minimized and low
- The research is not prohibited by law
- Subjects will be closely monitored and withdrawn from the research if they appear to be unduly distressed
- There are adequate provisions for soliciting the permission of an LAR

Section 3 - Provisions for Soliciting Assent

The content of the assent process will depend on the degree of risk and the extent of likely impairments to subjects' functional abilities. The assent process will increase in rigor as risk and functional abilities increase.

Assent is required of:

☐ All subjects

☐ All subjects determined by the investigator to be capable of assent

☐ None of the subjects

Written documentation of assent:

☐ Is not required

☐ Will be documented by a statement of the research team on the consent form

☐ Will be documented by an assent form

Section 3.4

Appendix 13: Documents/policies regarding consent capacity, including lists of study types

Appendix 13

Documents and materials used in the review of policies and practices for research involving adults with the potential for limited decision-making capacity

Key words used to identify protocols active during the past three years that posed more than minimal risk, and that also recruited subjects from diagnostic groups that may include individuals with impaired decision-making capacity:

Autism Spectrum Disorders; other developmental disabilities; schizophrenia and schizophrenia spectrum disorders; other psychotic disorders; bipolar disorder; Alzheimer's disease; other dementias; and acute stroke.

Cross section of 20 protocols (from among the 89 studies identified by key word search) received in September as selected by the External Review Team for more intensive review:

Those protocols selected included studies on schizophrenia or other psychotic disorders (11), acute stroke (4), autism (3), Amyotrophic lateral sclerosis (ALS) (1), and Alzheimer disease (1). Each of these protocols was read by at least two members of the external review team. In addition, the corresponding IRB minutes were also reviewed, along with any and all materials related to scientific review (in those cases where departmental scientific reviews had been conducted) or to continuing review.

In response to a request for materials from all protocols from September through December that came under any of the new policies pertaining to potential subjects whose decision-making might be impaired, materials for an additional 24 studies were provided.

These included studies on oncology (12), developmental or intellectual disabilities (4), schizophrenia (3), major depression (1), anorexia nervosa (1), epilepsy (1), nephrology (1), neurology (1), and geriatrics.

Revisions to other policies relevant to potential subjects whose decision-making might be impaired were also reviewed, along with the policies they replaced. The key policies are attached. This group included:

- 501 on Vulnerable Populations; (Attachment A)
- 506 on Adults Lacking Capacity to Consent; (Attachment B)
- 703 on Research Involving Human Participants Unable to Consent – Surrogate Consent; (Attachment C)
- 403c on Minnesota State Laws that Affect Research. (Attachment D)

The following tools and information were reviewed:

- Appendix I on Populations with Additional Considerations (updated September, 2014) (Attachment E)
- IRB reviewer guide for Appendix I (Attachment F)
- Updated study application form
- Guidance on the University's Human Research Protection Program HRPP/Institutional Review Board (IRB) website related to informed consent.

In addition, any substantive discussion by the IRB that related to informed consent was reviewed using, but not limited, to:

- Materials on studies suspended or terminated in the past decade;
- Minutes of all IRB panels from January to June, 2014;
- Minutes regarding noncompliance reviews;
- External and internal audits;
- Compliance disciplinary information and reports to federal agencies;
- Post approval monitoring reviews;
- Complaints received via reporting mechanisms at Fairview.

UNIVERSITY OF MINNESOTA

IRB: Vulnerable Populations

Policy number: 501

Date: 04/21/2014

References:

45 CFR 46.111(b), 45 CFR 46 Subparts B-D, 45 CFR 46.205

21 CFR 50.3, 21 CFR 50 Subpart D, 21 CFR 56.111(b),(c)
AAHRPP II.4.A

Cross References:

203 C Consultants

Policy Owner: Executive Director, HRPP

Definitions:

None

1.0 Reason for Policy

To define the University of Minnesota IRB approach to research with potentially vulnerable human subjects who are not covered by policies for prisoners, pregnant women, or children.. The policy describes the requirements concerning review of research that involves groups which could be vulnerable to coercion in regard to autonomy or situational vulnerability, but are not specifically protected by a Subpart to 45CFR 46 and 21 CFR 56 and present conditions that may affect the criteria for approval of research.

2.0 Scope of Policy

The scope of this policy is the University community and its partners.

3.1 Policy Statement

In order to ensure the protection of subjects and the fair and equitable selection of subjects, the IRB systematically reviews each research proposal to determine if the proposed subject population may include vulnerable populations. Potentially vulnerable individuals or groups who are not protected with specific sub parts to 45 CFR 46 and 21 CFR 56 may include but are not limited to:

- the decisionally impaired
- students

- employees

Other considerations regarding the status of potential subjects that are reviewed in the specific context of the research include:

- Economic disadvantage

- Educational disadvantage
- Language barriers or cultural values
- Involvement in potentially emotional or otherwise sensitive current events or incidents
- Health status and/or chemical use
- Terminal illness

Research may also involve otherwise healthy, normal subjects but propose to address sensitive topics, including:

- Sexual practices
- Substance use/abuse
- Illegal behavior
- Religion
- Immigration status
- Race/Ethnicity
- Physical emergency conditions in a community or geographic area
- Economic status of the subject or subject's family
- Perceived sanctions for participation/non-participation

Procedures for Additional Protections:

- The IRB must ensure that there are appropriate safeguards to protect the rights and welfare of vulnerable participants.
- Reviewers of research that proposes to include vulnerable populations may be chosen for expertise in working with or having additional expertise with the subject population. If no member of the IRB has the background required with the population to be studied, a consultant may be sought.
- If through review, the IRB determines that additional protections are required of the researcher, these will be recorded in the minutes.

4.0 Required approvals for this document

Title	Name
Executive Director, HRPP	Debra Dykhuis

5.0 Revision History

Revision	Reason for change	Date of release

04/21/2014	revision for AAHRPP	
01/04/2011	Update categories	01/04/2011
11/02/09	Update AAHRPP references	11/02/09
06/22/09	Reformat	06/22/09
09/29/06		

To obtain a copy of a historical policy, e-mail IRB at irb@umn.edu or call 612-626-5654

UNIVERSITY OF MINNESOTA

IRB: Adults Lacking Capacity to Consent

Policy number: 506

Date: 05/04/2014

References:
AAHRPP II.4.B

Cross References:
403C Minnesota Laws
501 Vulnerable Populations
703 Surrogate Consent

Policy Owner:
Executive Director, HRPP

Definitions:
Consent Capacity: denotes the specific abilities necessary for a prospective research participant to understand and use information relevant to consent.

1.0 Reason for Policy

This policy describes the requirements concerning review of research that involves adults lacking decision making capacity who could be vulnerable to coercion in regard to autonomy, but are not specifically protected by a Subpart to 45CFR 46 and 21 CFR 56 and present conditions that may affect the criteria for approval of research. The policy provides guidance on how to determine and document whether non-exempt human research involving adults lacking decision making capacity can be approved..

2.0 Scope of Policy

The scope of this policy is the University community and its partners.

3.0 Policy Statement

This policy is applied when the research includes individuals who have a condition of a type and a severity likely to affect capacity to consent such as: acute medical conditions, psychiatric disorders, neurologic disorders, developmental disorders and behavioral disorders.

The IRB will require applicants to provide information about whether the research involves participants whose decision-making capacity is in question. When any of the participants are likely to have diminished decision-making capacity, the IRB will consider whether additional safeguards are needed.

Prospective adult subjects with impairments to functional abilities are presumed to be capable of providing consent unless there is substantial evidence otherwise. The presence of a condition that leads to diminished functional abilities should not be considered as indicative of a lack of capacity to consent.

When an application for non-exempt research is received by the IRB, pre-review evaluation will include a determination about whether adults lacking capacity to consent are proposed to be included. When adults lacking capacity to consent will be included, IRB staff will ensure that answers and determinations to the applicable following points are documented in IRB review.

Considerations Applied to All Research

The IRB will apply the following considerations for all research:

- Does the population targeted for recruitment represent the population with the least degree of impairment compatible with the aims of the study?
- Have appropriate procedures for assessing capacity to consent to enroll in the study been described in the protocol?
- Does the research involve risks or discomforts that are greater for subjects who lack capacity than unimpaired subjects?
- Does the process to assess capacity provide reasonable assurances that the evaluator's judgments will be impartial?
- Should the investigator follow a consent process so that individuals who are not capable under routine procedures might be capable?

Examples of IRB requirements for the consent process might include:

- Designing a stepwise consent process, which involves a waiting period between each phase of the process: capacity assessment, initial presentation of information, and obtaining consent;
- Enhanced presentation of consent information during initial presentation and/or immediately prior to obtaining consent including: repetition of information), both oral and written presentation of information, multi-media presentation of information, interactive questioning, and written study summaries;
- Continuous dissemination of consent information throughout the course of the study; and
- Conducting the consent process in an environment in which the subject is comfortable.

Considerations Applied When Subjects Might Experience Fluctuating Functional Abilities

- Does the consent process include plans to avoid, if feasible, periods during which subjects are likely to experience greater than normal impairment?
- Should provisions be included to anticipate fluctuations in capacity?

Examples of IRB requirements for the consent processes might include:

- Re-evaluating subjects' capacity over the course of the study
- Designation of an individual to serve as a legally authorized representative (LAR) (see Policy 703)
- Involving potential LARs in the consent process
- Asking subjects to document their wishes regarding participation
- Avoiding consent when subjects are likely to experience greater than normal impairment
- Obtaining consent of subjects who regain capacity

Considerations for All Research Involving Greater than Minimal Risk to Subjects

- Has the experimental intervention been tested on animals, or humans with unimpaired functional abilities?
- Does the protocol include a written description of procedures for minimizing risk?

- Is there documentation of the importance of knowledge to be obtained by answering the research question?
- Should one or more monitors be appointed to assist with various aspects of the study, such as:
  a) A subject advocate such as a member of the target population or family member thereof; or an employee of an organization that advocates for the target population;
  b) An individual with expert knowledge of the relevant psychological or physical condition who will monitor the consent of subjects;
  c) A health care professional to serve as a consultant to subjects
- Should a list of resources and referrals be offered to subjects to assist them in coping with any foreseeable harm?
- Should there be a written rationale for the inclusion of subjects with diminished functional abilities?
- Should continuing review by conducted more frequently than annually?
- Should there be a description of procedures for withdrawing subjects or terminating the study?
- Should there be procedures for screening LARs and informing them of their responsibilities?

After these considerations are made, research will be evaluated to meet criteria based on whether the proposed research is without anticipated direct benefit to the subject or the proposed research has anticipated direct benefit to the subject. The research must meet all criteria in the appropriate category for the research to be approved:

Research with Anticipated Direct Benefit to the Subject (must meet all criteria below):

- One of the following is true: a) the knowledge likely to be gained will improve the understanding of the condition, disease or behavior affecting the subject population or b) there is a compelling argument for including individuals who lack decision-making capacity in the research
- One of the following is true: a) the research involves no more than minimal risk to the subjects or b) the research holds out the prospect of direct benefit for the individual subject where the relation of the anticipated benefit to the risk is at least as favorable as that presented by available alternative approaches

- The research is not prohibited by law
- Subjects will be closely monitored and withdrawn from the research if they appear to be unduly distressed
- There are adequate provisions for soliciting the permission of a LAR

Research with No Anticipated Direct Benefit to the Subject (must meet all criteria below):

- The objective cannot be met with research involving subjects who can give consent personally
- Unless an exception is justified, subjects have a disease or a condition relevant to the research
- One of the following is true: a) the foreseeable risks to the subjects are no greater than a minor increase over minimal risk or b) the research is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition
- The negative impact on the subject's well-being is minimized and low
- The research is not prohibited by law
- Subjects will be closely monitored and withdrawn from the research if they appear to be unduly distressed
- There are adequate provisions for soliciting the permission of an LAR

Provisions for Soliciting Assent

The content of the assent process will depend on the degree of risk and the extent of likely impairments to subjects' functional abilities. The assent process will increase in rigor as risk and functional abilities increase.

The IRB will determine whether assent is required of:

- All subjects
- All subjects determined by the investigator to be capable of assent
- None of the subjects

The IRB will determine whether written documentation of assent:

- Is not required
- Will be documented by a statement of the research team on the consent form
- Will be documented by an assent form

4.0 Required approvals for this document

Title	Name
Executive Director HRPP	Debra A. Dykhuis

5.0 Revision History

Revision	Reason for change	Date of release
05/04/2014	Clarification of new practice	
07/07/2011	Change to guidance	07/07/2011
11/02/09	Update AAHRPP references	11/02/09
	New policy	08/24/09

To obtain a copy of a historical policy, e-mail irb@umn.edu or phone 612-626-5654

UNIVERSITY OF MINNESOTA

IRB: Research Involving Human Participants Unable to Consent- Surrogate Consent

Policy number: 703

Date: 05/16/14

References:

45 CFR 46.204, 45 CFR 46.205, 45 CFR 46.305, 45 CFR 46.402(a)-(c), 45 CFR 46.408,

21 CFR 50.3(l), (n), 21 CFR 50.55, 21 CFR 50.20

Minn. Stat. Ch. 145C (Health Care Directives) AAHRPP II.4.A and B

AAHRPP II 3.F and G

Policy Owner:

Executive Director, HRPP

Definitions:

None

1.0 Reason for Policy

To ensure that informed consent is obtained and documented appropriately in instances where a subject's capacity to consent does not allow true informed consent of the subject.

2.0 Scope of Policy

The scope of this policy is the University community and its healthcare components.

3.0 Policy Statement

The IRB assures that provisions are made to obtain legally effective informed consent prospectively from each research participant or permission from the participant's legally authorized representative (LAR).

Research involving subjects with impaired decision-making capacity warrants special attention. Research involving these populations frequently presents greater than minimal risk, may not offer direct medical benefit to the subject, and may include a research design that calls for washout, placebo or

symptom provocation. In addition, these populations are considered to be vulnerable to coercion. In all instances, the IRB will follow the guidelines for review outlined in Policy 506.

Investigators' Responsibilities:

- Investigators must apply to the IRB for use of surrogate consent that is specific to the particular study being reviewed.

    - Surrogate consent may be considered only in research studies relating to the cognitively impaired, those who lack capacity, or have serious or life-threatening disease and conditions
    - Upon approval of the IRB for use within a specific protocol, the investigator shall apply the use of surrogate consent on a case by case basis
- If an adult participant is identified and is incompetent or lacks decision-making capacity for healthcare decisions and consent, the treating physician, and/or consulting physician(s) must document in the medical record:
    - The basis for their determination that the patient lacks decision-making capacity.
    - The identity of the legally authorized representative and if none, the next-of-kin. A copy of the legal form authorizing the healthcare power of attorney must be maintained in the research records.
    - The process by which the participant was enrolled or declined to be enrolled in the research.

IRB Responsibilities:

- Surrogate consent is a protocol specific request of the investigator, and must be reviewed and approved accordingly by the IRB
- Surrogate consent may be considered only in research studies relating to the cognitively impaired, those who lack capacity, or have serious or life-threatening disease and conditions
- The IRB membership shall include at least one member who is familiar with the population to be recruited. One member shall be an expert in the area of the research. Consideration may be given to adding a member of the study population or a family member of such a person or a representative of an advocacy group for that population, but this is not an absolute requirement.
- The IRB shall use consultants, as necessary, to assure appropriate expertise. Such consultant members may not vote with the IRB or contribute to the quorum.
- The IRB will consider whether and when to require a reassessment of the participants' decision making capacity, periodic re-consenting of the participants and the study's renewal period

Guidelines for IRB approval:

Study design limited to incompetent persons or persons with impaired decision making capacity. Competent persons are not suitable for the proposed research. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision making capacity must not be subjects in research simply because they are readily available.

Favorable risk/benefit ratio. The proposed research entails no significant risks, tangible or intangible or, if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision making capacity will not be subjects of research that poses a risk of injury unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

Voluntary participation. In situations where the potential research subject is incompetent to provide informed consent, the investigator should still attempt to obtain assent from the potential subject. Some persons may resist participating in a research protocol that has been approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

Well-informed representatives. Procedures have been devised to assure that participant's representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health care agents (appointed under a Health Care Power of Attorney) and for VA Research, next-of-kin or guardians must be given descriptions of both proposed research studies and the obligations of the person's representatives. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest.

IRB Determination and Documentation

The IRB shall make a determination in writing; the IRB may approve the inclusion of incompetent subjects or subjects with impaired decision making capacity in research projects on the basis of informed consent from legally authorized representatives or if none exists, next-of-kin, following medical practice guidelines and Minnesota statute.

4.0 Required approvals for this document

Title
Executive Director HRPP

5.0 Revision History

Revision	Reason for change	Date of release
05/17/14	Update cross reference and minor edits	09/02/14
11/02/09	Update AAHRPP references	11/02/09
08/24/09	Revision and Reformat	08/24/09
	New policy	09/29/06

To obtain a copy of a historical policy, e-mail IRB at irb@umn.edu or call 612-626-5654

UNIVERSITY OF MINNESOTA

Policy number: 403 C	**Date: 3/21/2014**

References:
45 CFR 46.101(e)-(f), 45 CFR 46.102(c), 45 CFR 46.402(d)-(e)
38 CFR 17.32(e), (g)
21 CFR 50.3(l), (o), (s), 21 CFR 56.103(c)
Minnesota Laws (see below) https://www.revisor.leg.state.mn.us/pubs/
Minn. Stat. 626.556, 626.557, 144.341, 144.343, 14 and 151.461
AAHRPP I.1.G
AAHRPP I-3
AAHRPP II.3.F
AAHRPP II.4.B

Cross Reference:
412A Investigational Drugs
501 Vulnerable populations
501D, Research with Children
701 Documentation of Consent
703 Surrogate Consent
704 Assent of Subjects

Policy Owner:
Executive Director, HRPP

Definitions:
None

1.0 Reason for Policy

The purpose of this policy is to explain how Minnesota Law affecting research is applied by the Human Research Protection Program. The research community is expected to follow all state or local regulations or laws when conducting research with human subjects.

Policy number: 403 C	**Date: 3/21/2014**

References:
45 CFR 46.101(e)-(f), 45 CFR 46.102(c), 45 CFR 46.402(d)-(e)
38 CFR 17.32(e), (g)
21 CFR 50.3(l), (o), (s), 21 CFR 56.103(c)
Minnesota Laws (see below) https://www.revisor.leg.state.mn.us/pubs/
Minn. Stat. 626.556, 626.557, 144.341, 144.343, 14 and 151.461
AAHRPP I.1.G
AAHRPP I-3
AAHRPP II.3.F
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Cross Reference:
412A Investigational Drugs
501 Vulnerable populations
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701 Documentation of Consent
703 Surrogate Consent
704 Assent of Subjects

Policy Owner:
Executive Director, HRPP

Definitions:
None

2.0 Scope of Policy

This policy is University-wide. All components of the University of Minnesota and its healthcare components must adhere to State laws that affect research.

3.0 Policy Statement

Policy number: **403 C**

Date: 3/21/2014

References:
45 CFR 46.101(e)-(f), 45 CFR 46.102(c), 45 CFR 46.402(d)-(e)
38 CFR 17.32(e), (g)
21 CFR 50.3(l), (o), (s), 21 CFR 56.103(c)
Minnesota Laws (see below) https://www.revisor.leg.state.mn.us/pubs/
Minn. Stat. 626.556, 626.557, 144.341, 144.343, 14 and 151.461
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Cross Reference:
412A Investigational Drugs
501 Vulnerable populations
501D, Research with Children
701 Documentation of Consent
703 Surrogate Consent
704 Assent of Subjects

Policy Owner:
Executive Director, HRPP

Definitions:
None

The research community is expected to follow all federal regulations, which by definition do not supersede any state or local regulations or laws that also may apply. Minnesota law is silent on many

Policy number: **403 C**

Date: 3/21/2014

References:
45 CFR 46.101(e)-(f), 45 CFR 46.102(c), 45 CFR 46.402(d)-(e)
38 CFR 17.32(e), (g)
21 CFR 50.3(l), (o), (s), 21 CFR 56.103(c)
Minnesota Laws (see below) https://www.revisor.leg.state.mn.us/pubs/
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Cross Reference:
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501D, Research with Children
701 Documentation of Consent
703 Surrogate Consent
704 Assent of Subjects

Policy Owner:
Executive Director, HRPP

Definitions:
None

research related issues and the research community must extrapolate in some areas from laws that affect treatment decisions. Researchers are advised of particular applicability of Minnesota statutes through electronic email newsletters routinely sent by the Office for the Vice President for Research and through information on the HRPP web site. IRB committee members have training materials, prepared by the Office of the General Counsel (OGC), which address specific issues. Training sessions are held periodically to ensure that HRPP staff, IRB members and researchers are current with the legal requirements.

The HRPP has access to counsel through the OGC of the University of Minnesota. Any IRB questions related to research and State law should be reviewed by OGC.

Minnesota Laws

Reporting Requirements (Minnesota Statute 626.556 and 626.557)
Under Minnesota law, professionals engaged in education, health care, social services and other professions are required to report known or suspected instances of child neglect or physical or sexual abuse. When research is likely to reveal this type of information, such as interviews about personal behavior, child-rearing practices, and discipline, or when talking to others about the child or specific familial relationships, both the parental permission form and the assent form should clearly indicate that the investigator is required to report known or reasonable suspicion of abuse or neglect of a child. Similar reporting requirements also exist when vulnerable adults are involved in research and a researcher learns or reasonably suspects the vulnerable adult has been subjected to maltreatment through abuse, neglect, or financial exploitation.

Parental Consent for Minors (Minnesota Statutes 144.341 – 347, and 524.5- 207)
Although Minnesota law does not specifically address the issue of parental consent for minors to participate in research, based on legal advice and established practice, the research community follows the rules that apply to parental consent for treatment. The consent of one parent is sufficient to provide treatment to a minor except where the minor is undergoing an abortion. Any study involving care or treatment to a minor in connection with an abortion would need the consent of both parents if they are living. Other studies may proceed with the consent of one parent under Minnesota law. However, the IRB still must determine whether consent of both parents is necessary when research is covered by 45 CFR 46, Part D.

Under Minnesota law, a minor who has a court appointed guardian may not receive experimental treatment of any kind without a court order.

Consent by Minors (Minnesota Statute 144.341,342, 343, 344, and 253B.03)
Minnesota law permits emancipated minors to give effective consent for any medical services. Emancipated minors are those living apart from their parents and managing their own affairs, minors who have been married, those who have borne a child, and those declared by a court to be emancipated. Also, minors may give effective consent without parental permission to receive services in connection with: pregnancy, sexually transmitted diseases, drug or alcohol abuse, Hepatitis B vaccination, and inpatient mental health care if the minor is age 16 or older. If a minor receives these services, including pregnancy testing, as part of a research study with parental/guardian consent, the study physician may

not inform the parent or legal guardian of the treatment/testing information without the minor's consent unless failure to do so would seriously jeopardize the health of the minor.

Consent by minors for research participation may be valid under Minnesota law where the minor is emancipated or the research consists principally of providing treatment to the minor related to a condition for which the minor has authority to consent. However, because this issue is unsettled under state law, the IRB is generally advised to consult legal counsel and/or consider whether the research qualifies for a waiver of parental permission under federal regulations before approving such research based on minor consent only.

Consent for Incompetent Adults (Minnesota Statute 524.5-313, 144.291, 13.384)
Under Minnesota law, an incapacitated adult who has a court appointed guardian or conservator may not receive experimental treatment of any kind without a court order. Except for this requirement, Minnesota law does not address the issue of research participation by incapacitated adults. Based on legal advice and established practice, the research community follows the rules that apply to surrogate consent for treatment. Legally authorized representatives of incompetent or incapacitated adults are determined in the following order of priority: healthcare agent previously appointed by the individual through a health care power of attorney; spouse; parents; adult children; and finally, adult siblings.

As a matter of subjects' protection, assent should be obtained from incompetent adults for research participation to the extent they are able to provide assent. Even where a legally authorized representative has consented to the research participation, an incompetent adult may not be included over his or her objection.

Clinical Drug Trials and Inclusion of Persons who are in the process of Commitment (Minnesota Statute 253B.095 Subdivision 1)
Under Minnesota Law, a person who is in the process of commitment, including release by a court prior to issuance of a commitment order, is prohibited from participating in a psychiatric clinical drug trial unless the court specifically authorizes the participation. The court must make specific findings as to the ability of the person to participate in a clinical drug trial as follows: "The court must determine that, under the circumstances of the case, the patient is competent to choose to participate in the trial, that the patient is freely choosing to participate in the trial, that the compulsion of the stayed commitment is not being used to coerce the person to participate in the clinical trial, and that a reasonable person may choose to participate in the clinical trial."

Labeling of Investigational Drugs (Minnesota Statute 151.212 subdivision 1; Minnesota Rule 6800.3400, subpart 1)
Minnesota regulations for labeling prescription drugs apply to investigational drugs; however, there is flexibility for labeling of investigational drugs due to the unique nature of investigational studies, particularly studies involving a placebo. Additional information regarding labeling requirements appears in policy 412A.

Disclosure of Health Records for External Research (Minnesota Statute 144. 295,)
Minnesota law is more restrictive than HIPAA in certain respects regarding access to health records for research purposes. Researchers external to the University who obtain an IRB waiver of the HIPAA authorization requirement still must meet state law requirements (an authorization signed by patients

permitting access to their records for research purposes generally) in order to access health records. IRB staff is knowledgeable about the differences between Minnesota law and HIPAA in the research context and applies the appropriate standard when reviewing research applications.

Gifts to Researchers (Minnesota Statute 151.461)
Under Minnesota law, practitioners with authority to prescribe drugs are prohibited from accepting gifts from drug manufacturers and wholesale distributors valued at more than $50 per year. There are certain exceptions including payments for consulting and honoraria. Consistent with this law and University policy generally, researchers may not accept gifts, such as finders' fees or recruitment bonuses, paid by research sponsors or others to the researcher personally in connection with University research activity. This prohibition is reflected in IRB application forms.

Patients Bill of Rights (Minnesota Statute 144.651, subdivision 13)
There is a patients bill of rights under Minnesota law that affords hospital patients and residents of health care facilities certain rights, including, the right to refuse participation in experimental research. This provision does not preclude emergency research conducted in conformance with federal guidelines.

Minnesota Genetic Privacy Act (Minnesota Statute 13.386)
Minnesota law classifies genetic information as private data. The Minnesota Supreme Court has interpreted the definition of genetic information to include blood samples. Researchers must have written informed consent to collect, use, store or disseminate genetic information, including blood samples, for research.

4.0 Required approvals for this document

Title
Executive Director
Counsel to the IRB

5.0 Revision History

Revision	Reason for change	Date of release
03/21/14	AAHRPP	09/02/14
10/23/12	Update minor consent reference	10/23/12
10/14/09	Update AAHRPP reference	10/14/09
04/27/09	Reformat/revision	07/08/09
		09/29/06

To obtain a copy of a historical policy, e-mail at irb@umn.edu or call 612-626-5654

PI Name:	Date:
Project title or IRB #:	

Appendix I - Populations with Additional Considerations

The targeting or inclusion of potentially vulnerable populations in research requires special considerations. Complete this appendix if the proposed research includes or targets:

- Subjects who are mentally, emotionally or developmentally disabled
- Adults lacking capacity to consent and/or adults with diminished capacity to consent.
- Non-English speakers
- Economically or educationally disadvantages populations
- Minority groups

Special protections apply and additional information is required if the research project includes children, pregnant women, or prisoners. See links below for more information and IRB forms

Children	Appendix Y	Pregnant women	Appendix B	Prisoners	Appendix C

Section 1 – Targeting or Including Adults Lacking Capacity to Consent and/or Adults with Diminished Capacity to Consent.

1.1 Does this research include or specifically target subjects who are mentally, emotionally or developmentally disabled or may otherwise have impaired decision making ability?

☐ No – section 1 complete, go to section 2

☐ Yes

☐ Included, but not targeted ☐ Targeted

1.2 Provide justification for including or targeting this population. Include a description of the importance of the knowledge to be gained for the population(s) under study.

1.3 Does the population included or targeted represent the population with the least degree of impairment compatible with the aims of the study?

1.4 Specify how risks are minimized for this population:

1.5 Explain how capacity to provide consent will be evaluated

Attach any instrument or tools used to evaluate capacity.

1.6 Provide the name(s) and credentials of all those who will evaluate capacity to consent. Explain

how each evaluator's judgment will be impartial.

1.7 Will risks or discomforts be greater for the adults who lack capacity to consent than unimpaired subjects?

☐ **No**

☐ **Yes, explain how:**

☐ **Not applicable**

1.8 Explain plan to reassess ability to consent if capacity fluctuates:

1.9 Document plans, if any, to avoid seeking consent during periods of greater than normal impairment.

1.10 If subjects lacking capacity to consent will be enrolled, document the plan for obtaining surrogate consent from a legally authorized representative.

1.11 If surrogate consent will occur, explain whether the researcher will obtain the assent of prospective participants with impaired capacity.

1.12 Is this research a clinical psychiatric drug trial?

☐ No – section 1 complete, go to section 2

☐ Yes

1.13 Are persons who are in the process of commitment excluded or included in the potential subject population pool?

☐ Excluded - section 1 complete, go to section 2

☐ Included - requirements of Minnesota Statute 253B.095 Subdivision 1 apply

Under Minnesota Law, a person who is in the process of commitment, including release by a court prior to issuance of a commitment order, is prohibited from participating in a psychiatric clinical drug trial unless the court specifically authorizes the participation. The court must make specific findings as to the ability of the person to participate in a psychiatric clinical drug trial as follows: "The court must determine that, under the circumstances of the case, the patient is competent to choose to participate in the trial, that the patient is freely choosing to participate in the trial, that the compulsion of the stayed commitment is not being used to coerce the person to participate in the clinical trial, and that a reasonable person may choose to participate in the clinical trial."

1.14 Provide justification for inclusion of person in the process of commitment.

1.15 Provide plan for obtaining consent compliant with Minnesota Statute 253B.095 Subdivision 1.

If requirements of Minnesota Statute 253B.095 Subdivision 1 apply a copy of the court order(s) authorizing participation must be provided to the IRB.

Section 2 – Including and/or Targeting Non-English Speakers for Participation

2.1 Are non-English speakers specifically targeted for inclusion?

☐ No, **non-English speakers will be included but are not specifically targeted.** Review guidance regarding inclusion of non-English speakers section 2 complete, go to section 3

☐ Yes

2.2 Provide justification for targeting non-English speakers for inclusion.

2.3 Provide plan for obtaining consent.

Consent forms in the language(s) spoken by participants and in English must be provided with your application.

Section 3 - Targeting Economically or Educationally Disadvantaged Populations

3.1 Are economically or educationally disadvantaged populations specifically targeted for inclusion?

☐ No – section 3 complete, go to section 4

☐ Yes

3.2 Provide justification for targeting economically or educationally disadvantaged populations for inclusion

3.3 Specify how risks are minimized for this population.

Section 4 – Targeting Minority Groups for Participation

4.1 Are minority groups specifically targeted for participation?

☐ No – section 4/appendix I complete

☐ Yes

4.2 Provide justification for targeting minority groups for participation.

4.3 Specify how risks are minimized for this population.

Staff Reviewer:	Study code #:
Reviewer:	Meeting Date:

UMN IRB Review Guide: Adults Lacking Capacity to Consent or with Diminished Capacity to Consent

This worksheet is used to review non-exempt Human Research that includes or may include adult subjects lacking capacity to consent.

Section 1 - Considerations Applied to All Research

Does the population targeted for recruitment represent the population with the least degree of impairment compatible with the aims of the study?

☐ Yes ☐ No

Comments:

Have appropriate procedures for assessing capacity to consent to enroll in the study been described in the protocol?

☐ Yes ☐ No

Comments:

Does the research involve risks or discomforts that are greater for subjects who lack capacity than unimpaired subjects?

☐ Yes ☐ No

Comments:

Does the process to assess capacity provide reasonable assurances that the evaluator's judgments will be impartial?

☐ Yes ☐ No

Comments:

Should the investigator follow a consent process so that individuals who are not capable under routine procedures might be capable?

☐ Yes ☐ No

Comments:

Examples of IRB requirements for the consent process might include:

- *Designing a stepwise consent process, which involves a waiting period between each phase of the process: capacity assessment, initial presentation of information, and obtaining consent;*
- *Enhanced presentation of consent information during initial presentation and/or immediately prior to obtaining consent including: repetition of information), both oral and written presentation of information, multi-media presentation of information, interactive questioning, and written study summaries;*
- *Continuous dissemination of consent information throughout the course of the study; and*
- *Conducting the consent process in an environment in which the subject is comfortable.*

Section 1a - Considerations Applied When Subjects Might Experience Fluctuating Functional Abilities

Does the consent process include plans to avoid, if feasible, periods during which subjects are likely to experience greater than normal impairment?

☐ Yes ☐ No

Comments:

Should provisions be included to anticipate fluctuations in capacity?

☐ Yes ☐ No

Comments:

Examples of IRB requirements for the consent processes might include:

- *Re-evaluating subjects' capacity over the course of the study*
- *Designation of an individual to serve as a legally authorized representative (LAR) (see Policy 703)*
- *Involving potential LARs in the consent process*
- *Asking subjects to document their wishes regarding participation*
- *Avoiding consent when subjects are likely to experience greater than normal impairment*
- *Obtaining consent of subjects who regain capacity*

Section 2 - Considerations for All Research Involving Greater than Minimal Risk to Subjects

Has the experimental intervention been tested on animals, or humans with unimpaired functional abilities?

☐ Yes ☐ No

Comments:

Does the protocol include a written description of procedures for minimizing risk?

☐ Yes ☐ No

Comments:

Is there documentation of the importance of knowledge to be obtained by answering the research question?

☐ Yes ☐ No

Comments:

Check the box indicating if one or more monitors listed below must be appointed to assist with various aspects of the study

☐ A subject advocate such as a member of the target population or family member thereof; or an employee of an organization that advocates for the target population;

☐ An individual with expert knowledge of the relevant psychological or physical condition who will monitor the consent of subjects;

☐ A health care professional to serve as a consultant to subjects

Should a list of resources and referrals be offered to subjects to assist them in coping with any foreseeable harm?

☐ Yes ☐ No

Comments:

Should there be a written rationale for the inclusion of subjects with diminished functional abilities?

☐ Yes ☐ No

Comments:

Should continuing review be conducted more frequently than annually?

☐ Yes ☐ No

If yes, how frequently:

Should there be a description of procedures for withdrawing subjects or terminating the study?

☐ Yes ☐ No

Comments:

Should there be procedures for screening LARs and informing them of their responsibilities?

☐ Yes ☐ No

Comments:

Section 2a - Choose the appropriate category below. The research must meet *all* criteria in the appropriate category for the research to be approved.

☐ **Research with Anticipated Direct Benefit to the Subject (must meet *all* criteria below):**

- One of the following is true: a) the knowledge likely to be gained will improve the understanding of the condition, disease or behavior affecting the subject population or b) there is a compelling argument for including individuals who lack decision-making capacity in the research
- One of the following is true: a) the research involves no more than minimal risk to the subjects or b) the research holds out the prospect of direct benefit for the individual subject where the relation of the anticipated benefit to the risk is at least as favorable as that presented by available alternative approaches
- The research is not prohibited by law
- Subjects will be closely monitored and withdrawn from the research if they appear to be unduly distressed
- There are adequate provisions for soliciting the permission of a LAR

☐ **Research with No Anticipated Direct Benefit to the Subject (must meet *all* criteria below):**

- The objective cannot be met with research involving subjects who can give consent personally
- Unless an exception is justified, subjects have a disease or a condition relevant to the research
- One of the following is true: a) the foreseeable risks to the subjects are no greater than a minor increase over minimal risk or b) the research is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition
- The negative impact on the subject's well-being is minimized and low
- The research is not prohibited by law
- Subjects will be closely monitored and withdrawn from the research if they appear to be unduly distressed
- There are adequate provisions for soliciting the permission of an LAR

Section 3 - Provisions for Soliciting Assent

The content of the assent process will depend on the degree of risk and the extent of likely impairments to subjects' functional abilities. The assent process will increase in rigor as risk and functional abilities increase.

Assent is required of:

☐ All subjects

☐ All subjects determined by the investigator to be capable of assent

☐ None of the subjects

Written documentation of assent:

☐ Is not required

☐ Will be documented by a statement of the research team on the consent form

☐ Will be documented by an assent form

Section 3.4

Appendix 14: OHRP FAQs & OHRP Determination Letter to Vanderbilt University

APPENDIX (Section D – Interim Number S)

Office for Human Research Protections, Department of Health and Human Services

(http://www.hhs.gov/ohrp/policy/faq/informed-consent/index.html)

Frequently Asked Questions

OHRP FAQs: What is informed consent and when, why, and how must it be obtained? (introduction)

The HHS regulations at 45 CFR part 46 for the protection of human subjects in research require that an investigator obtain the legally effective informed consent of the subject or the subject's legally authorized representative, unless (1) the research is exempt under 45 CFR 46.101(b); (2) the IRB finds and documents that informed consent can be waived (45 CFR 46.116(c) or (d)); or (3) the IRB finds and documents that the research meets the requirements of the HHS Secretarial waiver under 45 CFR 46.101(i) that permits a waiver of the general requirements for obtaining informed consent in a limited class of research in emergency settings. When informed consent is required, it must be sought prospectively, and documented to the extent required under HHS regulations at 45 CFR 46.117. [Food and Drug Administration (FDA) regulations at 21 CFR part 50 may also apply if the research involves a clinical investigation regulated by FDA.]

The requirement to obtain the legally effective informed consent of individuals before involving them in research is one of the central protections provided for under the HHS regulations at 45 CFR part 46. This requirement is founded on the principle of respect for persons, one of the three ethical principles governing human subjects research described in the Belmont Report. The principle of respect for persons requires that individuals be treated as autonomous agents and that the rights and welfare of persons with diminished autonomy be appropriately protected. The Belmont Report states that an autonomous agent is "an individual capable of deliberation about personal goals and of acting under the direction of such deliberation." Respect for persons requires that prospective research subjects "be given the opportunity to choose what shall or shall not happen to them" and thus necessitates adequate standards for informed consent.

The informed consent process involves three key features: (1) disclosing to potential research subjects information needed to make an informed decision; (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether or not to participate in the research. Informed consent must be legally effective and prospectively obtained. HHS regulations at 45 CFR 46.116 and 45 CFR 46.117 describe the informed consent requirements.

J. OHRP FAQs: What does it mean to minimize the possibility of coercion or undue influence?

The HHS regulations state that "An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence" (45 CFR 46.116). This

requirement applies to all nonexempt human subjects research not eligible for a waiver of the consent requirements.

Coercion occurs when an overt or implicit threat of harm is intentionally presented by one person to another in order to obtain compliance. For example, an investigator might tell a prospective subject that he or she will lose access to needed health services if he or she does not participate in the research.

Undue influence, by contrast, often occurs through an offer of an excessive or inappropriate reward or other overture in order to obtain compliance. For example, an investigator might promise psychology students extra credit if they participate in the research. If that is the only way a student can earn extra credit, then the investigator is unduly influencing potential subjects. If, however, she offers comparable non-research alternatives for earning extra credit, the possibility of undue influence is minimized.

In addition to undue influence that can arise with the offering of rewards, undue influence also can be subtle. For example, patients might feel obligated to participate in research if their physician is also the investigator, or students might feel pressure to participate in research if everyone else in the class is doing so. Because influence is contextual, and undue influence is likely to depend on an individual's situation, it is often difficult for IRBs to draw a bright line delimiting undue influence. It is up to the IRB to use its discretion in determining which circumstances give rise to undue influence. For example, an IRB might consider whether the informed consent process will take place at an appropriate time and in an appropriate setting, and whether the prospective subject may feel pressured into acting quickly or be discouraged from seeking advice from others.

Because of their relative nature and lack of clear-cut standards on the boundaries of inappropriate and appropriate forms of influence, investigators and IRBs must be vigilant about minimizing the possibility for coercion and undue influence. Reasonable assessments can be made to minimize the likelihood of undue influence or coercion occurring. For example, IRBs may restrict levels of financial or nonfinancial incentives for participation and should carefully review the information to be disclosed to potential subjects to ensure that the incentives and how they will be provided are clearly described. Known benefits should be stated accurately but not exaggerated, and potential or uncertain benefits should be stated as such, with clear language indicating how much is known about the uncertainty or likelihood of these potential benefits.

The regulatory requirements for IRB review and approval also specify the need for the IRB -- in order to approve research covered by the HHS regulations -- to ensure that "When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects" (45 CFR 46.111(b)). Thus, inducements that would ordinarily be acceptable in some populations may become undue influences for these vulnerable subject groups.

K. OHRP FAQs: Who can be a legally authorized representative (LAR) for the purpose of providing consent on behalf of a prospective subject?

Legally authorized representative (LAR) means 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 (45 CFR 46.102(c)). The regulations state that "no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative" (45 CFR 46.116). The issue as to who can be an LAR is determined by the laws of the jurisdiction in which the research is conducted (e.g., local or state law). Some states have statutes, regulations, or common law that specifically address consent by someone other than the subject for participation in research. Most states have no law specifically addressing the issue of consent in the research context. In these states, law that addresses who is authorized to give consent on behalf of another person to specific medical procedures or generally to medical treatment may be relevant if the research involves those medical procedures or medical treatment.

When the laws of the jurisdiction in which the research is being conducted provide a reasonable basis for authorizing an individual to consent on behalf of a prospective subject to their participation in the research procedure(s), OHRP would consider such an individual to be an LAR as defined by HHS regulations at 45 CFR 46.102(c). IRBs may wish to consult with legal counsel when deciding who can serve as an LAR for subjects of proposed research.

L. OHRP FAQs: When may a legally authorized representative provide consent on behalf of an adult with diminished decision-making capacity?

In answering this question, the HHS regulations at 45 CFR part 46 should be consulted in addition to the laws of the jurisdiction in which the research is conducted. As a general matter, if an adult lacks capacity to consent, for example, as a result of trauma, mental retardation, some forms of mental illness, or dementia - whether temporary, progressive, or permanent - only a legally authorized representative for that adult can give consent for participation in the research, unless the requirement to obtain informed consent is waived by the IRB in accordance with the requirements at 45 CFR 46.116(c)(d), or in accordance with the provisions for emergency waiver, which are permitted under the authority of the HHS Secretary at 45 CFR 46.101(i).

(See the Federal Register notice of this waiver at: http://www.hhs.gov/ohrp/documents/100296.pdf.) Should the subject regain or develop the capacity to consent, then his or her consent must be obtained for any further research, as the consent of the legally authorized representative is no longer valid.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852
Telephone: 301-435-0062
FAX: 301-402-2071

June 26, 2002

Lee E. Limbird, Ph.D.
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RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1363

Research Protocol: Prospective, Randomized, Multicenter Trial of 12ml/kg vs. 6 ml/kg Tidal Volume Positive Pressure Ventilation and Ketoconazole vs. Placebo for Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome
IRB Protocol #: 7942
Principal Investigator: Dr. Arthur Wheeler
HHS Project Number: N01-HR46054

Research Publication: Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome (N.Engl. J Med 2000;342:1302-8)

Dear Dr. Limbird and Mr. Mountcastle:

The Office for Human Research Protections (OHRP) has reviewed Vanderbilt University's (VU's) March 7, 2002 report responding to OHRP's February 4, 2002 letter regarding the above- referenced research.

Based upon its review, OHRP makes the following determinations regarding the above-referenced research:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.116(a)(2) require investigators to provide research subjects with a description of any reasonably foreseeable risks or discomforts to the research. In its February 4, 2002 letter to VU, OHRP found that the informed consent documents for the above research reviewed and approved by the VU IRB failed to adequately describe all reasonably foreseeable risks and discomforts of receiving non-traditional, 6 ml/kg tidal volume mechanical ventilation, and required VU to take corrective action.

Corrective Action: OHRP finds that VU has adequately addressed the above OHRP finding in its March 7, 2002 corrective action plan. Specifically, OHRP notes that the VU IRB adopted several policies effective September 15, 2000, including a policy providing guidance to ensure that research subjects are provided with an adequate description of the reasonably foreseeable risks and discomforts of research. OHRP acknowledges VU's concern that the HHS regulations protecting human research subjects do not expressly state whether risks of standard care treatments are included within the requirements of 45 CFR 46.116(a)(2). OHRP notes that the regulatory requirement to inform subjects of *any reasonably foreseeable risks or discomforts* includes the risks of standard care treatments that are part of the research protocol.

(2) HHS regulations at 45 CFR 46.116 stipulate that, except as provided elsewhere under the HHS regulations, no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. HHS regulations at 45 CFR 102(c) 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. VU's September 26, 2000 report indicated that 78 subjects enrolled in the above-referenced research at VU were unable to provide legally effective informed consent and consent for these subjects instead was obtained from another individual (spouse, parent, adult sibling, adult child, uncle, or cousin). OHRP expressed several concerns regarding the legal basis for such individuals serving as legally authorized representatives for the subjects under Tennessee law.

Based upon its review of VU's September 26, 2000 and March 7, 2002 reports, OHRP finds that:

(a) VU has not cited to OHRP any Tennessee statute or other applicable law which permits a family member or other close relative not appointed under a durable power of attorney for health care (Tenn. Code Ann. section 34-6-201 *et seq.)* to consent to medical procedures involved in research.

(b) Tennessee law apparently does not authorize surrogate consent for medical procedures or for research in the absence of judicial intervention or the appointment of a durable power of attorney for health care under Tenn. Code Ann. section 34-6-201 *et. seq*.

(c) VU has not indicated that any of the 78 subjects for whom surrogate consent was obtained in the above-referenced research had, under applicable Tennessee law, either a durable power of attorney for health care or a judicially authorized guardian for medical treatment and/or research decisions. As a result, OHRP finds that VU failed to demonstrate that legally effective informed consent was obtained in accordance with 45 CFR 46.116 and 46.102(c) for these 78 subjects.

Required Corrective Action: OHRP acknowledges that the above-described research has been completed. OHRP requests that VU submit a response that adequately addresses this finding.

(3) OHRP finds that VU has adequately addressed the additional concerns raised in OHRP's February 4, 2002 letter.

Please submit VU's response to the above request so that OHRP receives it no later than August 2, 2002. OHRP appreciates the commitment of VU to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Carol J. Weil, J.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Mark Magnuson, Assistant Vice Chancellor for Research, VU
Dr. Margaret Rush, Chairperson, IRB-01, VU
Dr. William Cooper, Chairperson, IRB-02, VU
Dr. Arthur Wheeler, VU
Mr. Barry Bowman, OHRP
Dr. Michael Carome, OHRP
Dr. Jeffrey Cohen, OHRP
Mr. George Gasparis, OHRP
Dr. Greg Koski, OHRP

Dr. Melody H. Lin, OHRP
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Commissioner, FDA
Dr. David Lepay, FDA
Dr. John Mather, Director, Office of Research Compliance and Assurance, Veterans Health Administration

Section 3.4

Appendix 15: SACHRP recommendations

Secretary's Advisory Committee on Human Research Protections (SACHRP)
Recommendations from the Subcommittee for the Inclusion of Individuals with Impaired Decision Making in Research (SIIIDR)

The following SIIIDR recommendations and preamble were approved by SACHRP at its March 27th, 2008, and March 4th, 2009 meetings:

Preamble to SIIIDR Recommendations

The Secretary's Advisory Committee on Human Research Protections (SACHRP) convened the Subcommittee on Inclusion of Individuals with Impaired Decision-making in Research (SIIIDR "*…to develop recommendations for consideration by SACHRP about whether guidance and/or additional regulations are needed for research involving individuals with impaired decision-making capacity*."

Impaired decision-making capacity or impaired consent capacity,[1] occurs in a wide range of disorders and conditions that affect large numbers of Americans, causing suffering, morbidity, and mortality on a large scale. For example, 5 million Americans are currently diagnosed with Alzheimer's disease, nearly 800,000 strokes occur in the U.S. each year, and 50,000 patients are admitted to intensive care units each day. As the U.S. population ages, these three conditions associated with impaired consent capacity will be even more prevalent. Traumatic brain injury, developmental disorders, intellectual disabilities, and serious mental illness are other common and devastating problems in which impaired consent capacity occurs. Current approaches to early detection, diagnosis, and treatment are inadequate, and there is a pressing need to advance therapeutics and understand basic mechanisms of disease and disease progression. Progress requires the inclusion of individuals with impaired consent capacity in research. A viable human protections oversight process must be equipped to meet the demands of research with the most impaired populations and must apply the highest ethical standards to research and research oversight.

It is noteworthy that despite over thirty years of federal oversight of human subject research in the United States, an understanding that these individuals are uniquely susceptible to exploitation and research related harm, and several high profile attempts to regulate in this area, research regulations and related guidance remain all but silent with regard to individuals who have impaired consent capacity. Without question, the field of human subject protections as a whole is better informed and has become increasingly professionalized over the last decade. However, is it equipped to oversee vitally important research involving some of the most impaired and vulnerable research participants? The core of the problem is the fact that the protections provided by free and informed consent are not available to individuals with impaired decision-making capacity, and consent provided by the LAR may not be ethically equivalent[2].

[1] Regarding terminology: We defined the term *consent capacity* in our Recommendation 1. We refer to individuals as having impaired consent capacity and at times as lacking consent capacity. The use of these and other terms, such as impaired decision-making, is not intended to describe different phenomena. The term research *participant* is used instead of the regulatory *subject* throughout the document, except where referring to regulatory language or specific terms of art. Research participant conveys a more equal and active role and was strongly favored by patient advocates.

[2] Further, approaches to surrogate-based consent reflected in state law often describe hierarchies of decision-makers, reflecting an understanding that some individuals may be better able to make decisions on behalf of the impaired individual.

The Common Rule requires that when individuals vulnerable to coercion or undue influence take part in research, "additional safeguards are included." Questions about the nature of required safeguard and to whom they should be applied are left unanswered by the Common Rule and related guidance. Few standards have emerged with regard to the consent process in general, and fewer still with regard to standards of capacity to consent, and the use of surrogate-based consent. Whether and in what fashion thresholds defining acceptable risk should be adapted for participants who are unable to consent for themselves has not been formally or uniformly addressed. At best, the field is characterized by a patchwork of IRB policies and research practices. Without a framework of regulations or guidance within which to conduct IRB review, it is evident that individuals may be unjustifiably called upon to take part in research, important ethical consideration may be missed, and valuable research may be hindered.

Another substantial shortcoming in the current federal oversight structure derives from the fact that federal rules point to state and local law to define who may provide consent for research on behalf of individuals with impaired consent capacity. Very few states specifically define legally authorized representatives (LARs) for research, and most state's laws are silent on the topic. Virtually no state laws address the many ethical issues that arise when LARs are involved in research decision-making, leaving it to IRBs and institutions to invent solutions. This shortcoming creates a legal and regulatory void and place investigators, institutions, and IRBs at risk for regulatory and/or state law violations. The resulting inconsistency and incompatibility among local rules does not serve the interest of contemporary scientific inquiry—inquiry that is commonly multi-institutional and multi-state. The field is left on its own to interpret "legally authorized representative" or to define LARs' responsibilities. This does not serve the interests of research participants or of science.

In fulfilling its charge, SIIIDR examined current practice and reviewed relevant empirical research on impaired decision-making, consent, and surrogate-based consent. Experts involved in the conduct and oversight of research with affected populations and those who advocate on behalf of such populations shared valuable data and perspectives with us at subcommittee and SACHRP meetings. SIIIDR studied the public comments provided to OHRP and the FDA pursuant to a Request for Information published in the Federal Register in September, 2007. We conducted a town hall meeting and workshops at a major national conference. Our membership itself reflected expertise in neurology, psychiatry, critical care medicine, research ethics, patient advocacy, law, and human subject protection. We encouraged and benefited from the active involvement of the ex-officio members of our subcommittee who represent the federal agencies that are signatory to the Common Rule. OHRP leadership and DHHS counsel educated SIIIDR on the regulatory and legal landscape and provided invaluable assistance. SACHRP provided ongoing input as we crafted and shared our approach and preliminary recommendations. Finally, SIIIDR carefully examined the body of work produced by predecessor committees; we aimed to learn from this history of failed efforts to regulate research involving individuals with impaired decision-making capacity.

SIIIDR's response to the question at the core of our charge is in the affirmative: new guidance and/or additional regulations are necessary to provide appropriate research protections for individuals who have impaired consent capacity. To this end, we have crafted a series of ten interdependent recommendations describing our priorities and best advice.

Recommendations 1 through 8 call for new guidance at this time rather than regulation. There are several reasons for this. First, guidance can be developed, disseminated, and influence practice in the field on a relatively short time frame. Second, guidance can promote the introduction of necessary safeguards with great flexibility, deferring when necessary to local

(IRB and institutional) considerations and expertise. In a clinical landscape as broad and varied as research with individuals who lack consent capacity, a less flexible approach might have the unwanted effect of limiting ethically sound and scientifically appropriate research. Finally, guidance can provide a potentially rich format within which to convey ethical priorities and capture clinical subtleties. By educating the field, guidance can drive good institutional policy and IRB practice. Guidance alone is not sufficient to address problems related to the regulation's reliance on local definitions of who may serve as a legally authorized representative. Therefore, recommendations 9 and 10 present options for a federal regulatory solution and consideration of model state legislation, respectively.

Current regulatory guidance is often regarded by the field as insufficiently educational, overly-fragmented, and difficult to access. It is SIIIDR's intent that guidance on this topic be developed and disseminated as a single, comprehensive resource document or pamphlet. The quality of IRB review and the conduct of research with individuals with impaired consent capacity can be improved with the development of clear, ethically and clinically informed and user-friendly guidance.

Throughout its work, SIIIDR acknowledged the extent to which the academic community feels over-regulated: a clear and consistent theme in responses to the OHRP/FDA Request for Information. We attempted to avoid being overly proscriptive when by allowing greater latitude for investigators, IRBs and institutions we could better serve the interests of research protections. Similarly, we sought to recognize the strength of our current, re-invigorated, better resourced, and better trained IRBs.

Individuals who have impaired consent capacity are uniquely vulnerable to exploitation and susceptible to harm, and SIIIDR's primary obligation was to enhance protections for those who are unable to protect themselves through the process of consent. This is an obligation we share with the community of researchers and professionals involved in research oversight. We believe our recommendations will move the field in the necessary direction.

Recommendation 1. Guidance should adopt the term "consent capacity" (following the working document developed by NIH) to denote the specific abilities necessary for a prospective research participant to understand and use information relevant to consent.

Recommendation 2. Guidance should provide information for institutions, IRBs and investigators on the nature of consent capacity and its impairment as it relates to research participation.

Specifically:

a**.** An individual's consent capacity is not simply present or absent; capacity is best understood as occurring along a continuum.

b. Impaired consent capacity occurs in a wide range of conditions and disease states. To respect the rights and welfare of all research participants, guidance should encourage the development of policies that acknowledge the many manifestations of impaired consent capacity and are not limited to consideration of specific disorders.

c. Consent capacity is task-specific and depends on the nature and complexity of the relevant decision-making process. Therefore, a judgment regarding an individual's capacity to consent may not be the same for all research studies.

d**.** In many individuals, impairment in capacity to consent is not a static phenomenon. During the course of a research study, a research participant's consent capacity may improve, fluctuate over time, or worsen with changes in the individual's underlying condition. Guidance should encourage policies on consent, the assessment of capacity, and the use of surrogate-based consent procedures to reflect this fact.

Recommendation 3. Guidance should address the implementation of appropriate safeguards related to the identification of individuals who may have impaired consent capacity. Such safeguards can be applied prior to participant enrollment, and as appropriate, throughout the course of research participation.

a. For all studies, investigators and research staff who obtain consent should consider each participant's capacity to consent to the research. In studies where the recruitment of individuals with impaired consent capacity is not anticipated, the judgment that prospective participants have the capacity to consent to the research can ordinarily be made informally during routine interactions with the participant during the consent process.

b. The method used to assess capacity, and when appropriate, the documentation of this assessment, should be tailored to the study population, the level of study risk, and the likelihood of the involvement of participants with impaired consent capacity.

(i) When it is anticipated that the research will include individuals who have impaired consent capacity, researchers should assess prospective participants' consent capacity and determine whether it is adequate to permit informed consent. This determination should be documented, when appropriate.

(ii) Formal methods such as questionnaires, structured instruments, or independent evaluators can be used to support or supplement the assessment of consent capacity by the researcher.

(iii) The likelihood of impaired consent capacity and the manifestations of that impairment will vary depending on the proposed study population and the setting in which the research is conducted. The choice of the method used to assess capacity must be informed by these clinical considerations.

(iv) The level of capacity required for consent will depend on the anticipated benefits from participation in the study, the degree to which the study protocol departs from ordinary practice or clinical care, and the magnitude of foreseeable risks associated with participation. These factors should be carefully considered in policy and practice.

(v) Investigators and research staff responsible for the consent process and consent capacity determinations should be appropriately qualified and trained.

c. Specific enhancements to the consent form and process may serve to improve a prospective participant's understanding and enable some individuals who otherwise lack consent capacity to make capable decisions. (Note: guidance may benefit from examples.) Consent enhancements should be adapted to the needs of the specific study and study population.

d. In making the determination as to methods to be used to ascertain consent capacity, it is important to note that more intensive approaches involve burdens for participants and researchers alike. Therefore, these should be reserved for those situations in which impairment is more likely to be present, anticipated benefits are fewer, and foreseeable risks are greater.

e. When changes in participants' consent capacity are anticipated or discovered during the course of a study, requirements for redisclosure of relevant information, reconsent, and reassessment of consent capacity should be considered. The frequency of any necessary reconsent procedures should be appropriate to the circumstances.

Recommendation 4. The inclusion of individuals who lack consent capacity presents unique ethical and procedural challenges to the IRB and to investigators. Consent to research by the legally authorized representative (LAR) stands in for the consent by the prospective research participant, but it is not fully equivalent to consent by the participant him or herself. Therefore, when the participant is unable to protect his or her interests through the process of consent, additional protections or safeguards at the level of IRB review are required. The following is intended to provide guidance to IRBs, institutions and investigators on additional considerations related to the approval of research under 45CFR46.111 when individuals who lack consent capacity are included in research.

Note: In some states and localities, applicable law defining the LAR further delineates the roles and responsibilities of the LAR and/or otherwise regulates IRB activities with regard to the inclusion of individuals who lack consent capacity. Institutions, IRBs, and investigators should familiarize themselves with applicable law. No recommendations presented are intended to preempt state or local authority.

a. **IRB Review Procedures:** IRBs should review and provide approval for the inclusion of individuals who lack consent capacity and for consent procedures to be followed by the LAR, as specified below:

(i) In determining level of review, IRBs should be especially mindful of any unique circumstances and susceptibilities of the proposed research participants. The serious medical, neurological, and psychiatric illnesses that give rise to impaired consent capacity may place participants at increased risk of harm and discomfort from research participation. Further, for participants who are unable to express discomfort, describe untoward effects or otherwise communicate their wishes once enrolled, research participation may involve added risk.

(ii) An IRB may determine that research that includes individuals who lack consent capacity may fulfill criteria for minimal risk and/or expedited review; the fact that a study includes individuals who lack consent capacity should not, in and of itself, mean that review by the convened IRB is required.

(iii) However, the expedited review of research involving such participants should be conducted by reviewers with appropriate expertise, as described below in point b. Membership and Reviewer Qualifications, and in accordance with well-defined, written policies and procedures for expedited review. These policies should describe requirements for consent by the LAR, and provide examples of additional safeguards required in the recruitment, identification, and approval of research with such individuals.

(iv) Minimal risk research that fulfills the requirement for waiver of informed consent[3] but will include individuals with impaired consent capacity may be reviewed by expedited review procedures without the additional requirements outlined in item a(iii), above.

b. **IRB Membership and Reviewer Qualifications:** 45 CFR46 requires that "**the IRB shall be sufficiently qualified** through the experience and expertise of its members." When an IRB reviews research involving research participants who lack consent capacity and consent will be provided by an LAR, convened review should involve at least one member or consultant knowledgeable about and experienced in working with the population. Information, experience, and expertise may be available to the IRB through its membership, consultants, and, as appropriate, requests for this information from the investigator. IRBs should give special consideration, as appropriate, to the involvement of the following types of individuals in the review process:

(i) Patients, former patients, patient advocates or family members or others who can represent the views and perspectives of the research participants;

(ii) Individuals with specific professional expertise related to the nature and consequences of impaired consent capacity in the study population;

(iii) Other individuals who can provide information relevant to the circumstances and context in which the participant and LAR will be recruited (e.g. the long term care facility, critical care unit, or mental health center);

[3] To fulfill criteria for waiver of consent, an IRB must demonstrate that "the research could not practicably be carried out without the waiver or alteration" (116(d)(3)). The fact that prospective participants are unable to provide consent, or that a legally authorized representative is not readily available, or that applicable law does not define an LAR for research purposes should not, in and of itself, serve to satisfy this criterion for lack of practicability. When a waiver of consent is not justifiable under 45CFR46.116(d) for research involving those with capacity to consent, a waiver would ordinarily not be applicable to research with individuals who lack consent capacity.

(iv) Individuals with expertise regarding applicable legal and regulatory requirements for consent to research by an LAR.

c. **Subject Selection: the Decision to Include Individuals who Lack Consent Capacity:** The decision to enroll individuals who lack consent capacity raises unique ethical challenges. Such individuals and their caregivers commonly experience substantial burdens related to the individual's illness and life circumstances. The individual's ability to consent to research is compromised or absent, and consent, when provided by the LAR, typically only approximates the prospective particpant's wishes or best interests. The Common Rule underscores the importance of equitable selection of subjects, recognizing the long history of incompetent adults in institutional settings who were exploited in research for reasons of convenience rather than either benefit to the population recruited or scientific necessity. The protection of prospective research participants who are unable to protect themselves through the consent process demands careful attention to both the rights and interests of the individual and the need to advance science and therapeutics for the most seriously ill. IRBs and investigators should carefully consider whether the inclusion of individuals who lack consent capacity in research is ethically appropriate and scientifically necessary. When research proposes to include individuals who lack consent capacity, each of the following should be considered:

(i) Investigators and IRBs should carefully consider the extent to which the research aims to improve the understanding, diagnosis, prevention or treatment of the disorders or conditions that are the cause of the incapacity.[4]
(ii) The study of related conditions, phenomena, or circumstances that commonly or uniquely affect the research participants may contribute in important ways to the current or future welfare of the study population[5] and therefore may also serve to justify their inclusion in research.
(iii) Review should consider the extent to which the scientific questions posed by the research are answerable in those who have capacity to consent. In general, "less burdened" groups should be studied first.
(iv) Factors such as participant availability, ease of recruitment or study cost should never alone justify the inclusion of individuals who lack consent capacity.
(v) The inclusion of individuals who lack capacity may be appropriate in research that offers therapeutic or other benefits to the individual participant when standard approaches are ineffective, unproven, or unsatisfactory.[6]

[4] It is important to note that multiple disorders or conditions may simultaneously contribute to impairment in consent capacity in particular participants or settings.

[5] Studies of problems that commonly complicate treatment in the critical care setting, for example, or are unique to this setting and cannot be studied in those with capacity may be appropriate. Similarly, studies of cognitive function and functional impairment in patients with developmental disabilities or post-traumatic brain injury may directly or indirectly contribute to the understanding of these conditions. Studies of family, social, educational or institutional processes involving individuals with impaired consent capacity may benefit these populations. Investigators should offer a scientific rationale to explain why such research questions could not be answered, or addressed first, in those with capacity, and IRBs should explicitly consider the adequacy of the rationale to justify research with this population.

[6] A clinical trial or other medical or socio-behavioral intervention may provide treatment for a disorder or benefits to participants that are unrelated to the causes or circumstances of impaired consent capacity. When standard approaches are ineffective, unproven or otherwise unsatisfactory to address the problem in

(vi) When individuals who lack consent capacity will be incidentally included in research because they are members of a larger group of prospective research participants, such as a cohort of clinic patients or a sample of the general population, the IRB should give careful consideration to the anticipated risks and potential benefits of the research as they might specifically affect those who lack consent capacity. Inclusion of those who lack consent capacity may be appropriate if the risk/benefit ratio is determined to be acceptable for these participants.

Recommendation 5. The approval of research under Subpart A requires an IRB to determine "that risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result." This regulatory language gives IRBs wide latitude in deciding when research offers a reasonable balance of risks to benefits, including circumstances when the benefits are in the form of scientific knowledge alone. Currently, no formal guidance addresses how IRBs are to interpret this criterion either for prospective research participants who have the capacity to consent, or those who do not. When a prospective participant has capacity, the process of informed consent respects the individual's autonomy and affords him or her additional protection.

Individuals who lack consent capacity, in contrast, are limited in expressing or unable to express their wishes. Consent provided on their behalf by a legally authorized representative (LAR) will only, and to a varying degree, approximate consent by the subject and may not provide equivalent protections. The criterion of reasonable risk is one that must reflect the non-equivalence of consent by the LAR, more so when the risks of research are greater and for research which does not offer a significant prospect of direct benefit.

When reviewing research with individuals with impaired consent capacity and with those who lack consent capacity, the IRB should consider the following:

a. The determination that the relationship of risks to benefits is reasonable requires a careful analysis by the IRB of several continuous variables, including the degree to which the research: introduces risk, presents a risk/benefit profile which departs from standard care, offers a prospect of benefit available only in the research, will yield knowledge that will benefit others, and the extent to which informed consent by an LAR can be considered equivalent to that of the research participants.
b. In weighing risks and benefits, IRBs and investigators should be especially mindful of the nature of the decision that the LAR will be asked to make. When a research participant is not providing informed consent, an important consideration relates to the degree to which the participant will be exposed to risks when the research provides him or her with no direct benefit but could serve to benefit others.
c. IRBs and investigators should recognize that different categories of LARs will stand in different relationships to the research participant and may not equally well fulfill the ethical requirements of informed consent.
d. Therefore, compared to research with individuals with consent capacity, it may be appropriate for an IRB to establish a lower threshold for allowable risk and require a more favorable risk/benefit ratio as a requirement for approval. This will serve to

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general or for individual participants, research that provides access to such benefits should be acceptable. A trial of an investigational anti-convulsant, for example, may reasonably include patients who lack capacity who have failed to respond to, or been unable to tolerate, existing therapies.

provide necessary additional protections.[7] It may be appropriate for an IRB to employ its standard risk-benefit considerations for studies that offer little or no prospect of direct benefit when the assessed risk of harm, discomfort or inconvenience is low.

e. IRBs should undertake a careful analysis of the anticipated direct benefits of research participation. The following should be considered:

   (i) Participation in research can serve to benefit the participant by offering assessment, diagnosis, treatment, or other (e.g., psychological, behavioral, interpersonal, or social) interventions or enhancements.
   (ii) In terms of the prospect of direct benefit, studies will vary from one another along a number of dimensions. These include the likelihood of direct personal benefit, the value of these benefits in relation to the same or similar benefits that exist outside the research,[8] and the extent to which subgroups of participants are not expected to benefit.[9]
   (iii) Financial compensation is not ordinarily considered a benefit of participation by IRBs in their risk/benefit analysis.

f. When the research involves risk at the higher end of the spectrum, IRB review should consider who will be consenting on behalf of the participants who lack consent capacity. The relationship of the prospective participant to the LAR and the responsibilities of the LAR will vary considerably based on the category of LAR, the individuals involved, and the research decision at hand. LARs will differ in whether they otherwise have been entrusted to make decisions on behalf of the prospective participants, in the extent to which they are familiar with the their wishes and attitudes, and in their ability to make a decision in the best interest of the participants. Specifically,

[7] 45CFR46.111(2) recognizes that some research is anticipated to provide little or no direct benefit to research participants but is anticipated to yield important scientific knowledge. It respects individual autonomy in allowing, within limits, for participants to assume the risks of research participation for altruistic or other reasons, even when the research offers no, or little, personal benefit. The limits (imposed by the IRB) relate to the requirement that IRBs weigh anticipated risks to research participants against anticipated benefits to society and determine what is "reasonable." In effect, in the interest of protecting research participants from research risk, the IRB decides when the relation of risk to scientific benefit is such that even an individual who is willing to participate should not be permitted to do so. When an individual's autonomy is compromised, the IRB will ordinarily recognize a greater need to protect the individual and establish a lower threshold of reasonable risk. There are, of course, circumstances in which it may not be necessary or appropriate for an IRB to alter its risk benefit analysis, for example, when all prospective participants have indicated by way of advance directives their willingness to participate in research of the sort under consideration, or when they suffer from otherwise untreatable and serious conditions.

[8] For example, a complex set of considerations arise in treatment research when standard approaches to care or commonly employed therapies are not "of proven efficacy." Enrollment in such research may therefore mean that the participant is forgoing routine—albeit untested—care in the interest of science. Other problems are posed by studies involving therapies that offer at best transient improvement for chronic conditions. Finally, and perhaps most complex, is when effective treatments exist but are not provided in the community or are not accessible for reasons of cost.

[9] A study of an intervention may offer unique benefit to some participants, but little or less value to participants who have previously failed the same or similar interventions, have not availed themselves of existing standard interventions, or are tolerating existing approaches. An IRB may determine that it is appropriate to approve the study for some participants, but not others, thereby optimizing benefit and reducing risk.

(i) The LAR for an incapable adult may have little or no experience in the required role and will have varying degrees of kinship or familiarity with prospective participants or their wishes with regard to research participation.
(ii) Some LARs may be appointed in advance by individuals to consent to research on their behalf; the subjects may have provided varying degrees of authority for the LAR, and enumerated their wishes, interests and instructions with different degrees of specificity.
(iii) LARs appointed through legally defined hierarchies for health decision-making or by a health care proxy or equivalent, are permitted to make decisions related to healthcare and, according to OHRP interpretation and barring state law to the contrary, by extension, to certain categories of research.
(iv) In the context of an individual's acute illness or chronic disability, next-of-kin or other caregivers may themselves evidence compromised ability to make a research decision.
(v) Some prospective research participants, for example, those with severe developmental disabilities, may never have been able to express wishes or attitudes with regard to research and altruistic behavior in general.
(vi) In some instances, an institution or government body may be authorized by law to provide consent for an incapable adult.

g. A careful consideration of the LAR's role in the consent process becomes increasingly important for research assessed as falling at the upper end of a continuum of risk and at the lower end of the direct benefit spectrum. For example:

(i) For certain types of research or research risk, an IRB may specify that only certain categories of surrogates may provide consent,[10] for example, those specified by advanced directives. In other cases, approval may require that consent be provided by LARs with closer kinship, those more familiar with the participants, and those who have already been in a care-giving relationship to them.
(ii) An IRB may require investigators and/or independent monitors to assess the ability of LARs to perform necessary duties.
(iii) An IRB may require that LARs be educated as to their roles and responsibilities during consent and, where applicable, throughout the course of the study.
(iv) An IRB may choose to limit or prohibit consent for certain categories of research by government or institutional authorities, require independent review, or put in place other safeguards.

h. In addition to the guidelines for subject selection specified previously, IRBs should develop written policies and procedures that define and limit research risk:

(i) Risk assessments by the IRB and investigator should carefully address the unique susceptibilities of the research participant to risk, the environment of the research and its impact on risk, and procedures to minimize risk.

[10] For example, if allowable under local law, patients with mild cognitive impairment recruited for a longitudinal study may appoint individuals to make decisions for them—assuming they retain the capacity to do so—if or when they lose consent capacity. They may also specify their interest in taking part in a research project or category of research. An IRB may determine that research that is otherwise not approvable (higher risk research with no direct benefit) is approvable when such LARs are available and are so informed.

(ii) IRBs will ordinarily establish a lower threshold for acceptable risk in studies in which consent is provided by an LAR than in studies in which consent is provided by the participant him or herself. Standards for upper limits of allowable risk should be developed and applied. IRBs developing these standards should consider the following:
    (a) In general, when the research offers little or no prospect of direct benefit, the probability and magnitude of harm or discomfort anticipated in the research (including, but not limited to, harm to physical, psychological, social or economic well-being and harms to dignity) should involve no more than a minor increase over minimal risk.
    (b) In exceptional circumstances, an IRB may consider the approval of research which offers little or no prospect of direct benefit and in which the risk of harm or discomfort anticipated in the research is moderate in terms of probability and magnitude.11 In such cases, the research must include safeguards appropriate to this degree of risk. Furthermore, the research must be of vital importance in the understanding, prevention or alleviation of a serious problem affecting the health or welfare of the study population.

Recommendation 6. Guidance to institutions, IRBs, and investigators should emphasize the value of self-determination for the research participant, even when consent capacity is impaired. While some participants, such as those with profound cognitive impairment, will not be able contribute to the consent decision, others may be able to remain actively involved in the decision to enroll and remain enrolled in the research, appoint a legally authorized representative (LAR), or define the limits of research participation. Individuals with impaired consent capacity should be included in the process of consent to the extent possible and consistent with their desires and abilities.

The IRB should consider the following during the process of review and approval:

a. When consent capacity is impaired, efforts to foster a meaningful dialogue about research participation during the consent process will often require special consideration of the time spent and methods used.
b. Specific modifications to the form and process of consent may serve to accommodate some individuals with impaired consent capacity and enable them to consent on their own behalf.
c. Common approaches, such as engaging individuals trusted by the prospective research participant during the consent process, and allocating additional time for decision-making, may be of special value.
d. When impairments in consent capacity may be amenable to intervention which may improve or enhance decision-making, such efforts should be undertaken.

[11] **It is SIIIDR's consensus that vitally important but ethically acceptable research would be prohibited by adopting "minor increase over minimal risk" as an upper limit of risk. To accommodate the variability in populations and research at issue, greater flexibility is necessary. The committee therefore recommends a "soft cap" reflected by our use of the term "moderate." This would allow research that introduces more than a minor increment above minimal risk when an IRB determines that appropriate safeguards are in place and the importance of the research justifies its approval. The subcommittee is not necessarily advocating the use of the term "moderate" in guidance.**

e. Except in circumstances of the most severe impairment, individuals should be informed that their capacity to consent has been judged to be impaired and that consent for research by an LAR is being considered.
f. In some cases, a prospective research participant who lacks consent capacity may be able to be involved in the decision to appoint an LAR or to express opinions with regard to the nature or extent of research participation; this involvement should be encouraged, when appropriate.
g. When consent will be provided by an LAR, the assent of the research participant should be sought at the outset and, as appropriate, throughout the course of research involvement, unless the participant is incapable of providing assent. Further:

    (i) As ability to express choice regarding participation will vary considerably depending on the study population, whether to require assent, and the requirements for assent, should be carefully considered by the IRB during review and approval.
    (ii) A definition of what constitutes "dissent" or unwillingness to take part may be an important consideration during IRB review, especially when prospective participants will have limited ability to communicate. For example, non-verbal communications or actions that indicate an unwillingness to take part in a research procedure should be considered a failure to assent or as a dissent to participate in that intervention.

Recommendation 7. While applicable law will define those who may serve as a legally authorized representative (LAR) for an individual who lacks consent capacity, guidance should address IRB and investigator responsibilities related to the selection and involvement of the LAR. Further, guidance should underscore the fact that the role of the LAR will in most circumstances extend beyond consent to the research participant's enrollment (e.g., to include on-going monitoring of the individual's participation). Therefore, guidance should serve to define the roles of the LAR in initial and ongoing research decision-making. Safeguards should reflect the unique nature of the task the LAR is being called upon to perform and should be tailored to study risk and benefit.

Specifically,

a. The process by which LARs will be identified and selected should be reviewed and approved by the IRB:

    (i) In some circumstances, it may be necessary for the investigator to assess the ability and willingness of the LAR to fulfill the required duties.
    (ii) IRBs and investigators should be cognizant of the potential for financial or other conflicts of interest on the part of LARs that may compromise their objectivity.
    (iii) Similarly, study compensation and other financial incentives may have unwanted effects on the objectivity of LAR decision-making and these potential effects should be carefully considered.

b. The expectations, obligations and authority of LARs should be reviewed by the IRB and communicated to the LARs by the investigator.

    (i) Where appropriate, the IRB may require an information sheet or other written material to assist LARs in understanding their roles.

(ii) LARs may benefit from guidance as to the basis (or standards) upon which their consent decisions are to be made.

c. In many studies, the role of LARs will extend beyond providing consent for study enrollment and may include observing the assent of the research participant, monitoring participant well-being, and providing re-consent.

(i) LARs should receive information about the research participant's status and well-being during the course of research participation. Investigator responsibilities in this regard should be defined.
(ii) During the course of a study, investigators should be required to provide important new information about study risks, benefits, and alternatives to LARs, as these may bear on the consent decision.
(iii) IRBs should consider when formal re-consent by LARs in a longitudinal study is a necessary safeguard.
(iv) In some instances IRBs may specify individuals other than LARs to perform monitoring or other research participant advocacy functions.

Recommendation 8. A legally authorized representative is defined at 45CFR 46.102 (c) 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 research." Guidance should provide additional information regarding the current HHS interpretation of "applicable law."

Specifically:

a. Laws defining who may provide consent to research for an individual who lacks consent capacity take many forms and vary widely among the states. Guidance should describe, with examples, those categories of laws upon which an institution or IRB may rely to determine who may serve as a legally authorized representative.
b. In states with laws or regulations that address consent to treatment but do not specifically consider consent to research, current OHRP interpretation permits consent to research by individuals authorized under laws that allow consent to the "procedures involved in the research." This interpretation should be further clarified with reference to specific examples of research that would or would not satisfy this interpretation.
c. Current OHRP interpretation is that, in the absence of applicable law, community or other standards (e.g. institutional policies, standards of care) which define hierarchies or individuals who may provide consent on behalf of someone who is unable to consent do not constitute applicable law and the individuals named are not considered legally authorized representatives. Effort should be made through guidance to insure that this interpretation is clearly disseminated to the research community.

Recommendation 9. The Subcommittee on the Inclusion of Individuals with Impaired Decision-making in Research (SIIIDR) recommends that HHS develop new regulations related to the inclusion of adults who lack consent capacity. This subpart will define a hierarchy of individuals who may provide consent on behalf of individuals who lack consent capacity when a legally authorized representative (LAR) for research is not defined in state or local law.

SIIIDR makes the following recommendations for consideration for inclusion in these regulations:

a. When an IRB approves the conduct of research under Subpart A and determines that it is appropriate for consent to research to be obtained from the LAR of adults who lack consent capacity:

    (i) Where applicable law exists to determine who is authorized to serve as an LAR to consent to an individual's participation in research, consent may only be obtained from an LAR in accordance with this law.
    (ii) In the absence of applicable law determining who is authorized to serve as an LAR to consent to a individual's participation in research, one of the persons listed below, in the following descending order of priority, shall be considered the prospective participant's LAR and may consent to participation on his or her behalf:

        (a) a person designated by the individual, while retaining the decisional capacity to do so, to make decisions for him/her regarding participation in research;
        (b) a person designated by the individual, while retaining the decisional capacity to do so, to make decisions for him/her regarding non-research health care decisions;
        (c) the individual's legal guardian with authority to make health care decisions for him or her;
        (d) the spouse, or if recognized by applicable law, the civil union partner or domestic partner;
        (e) an adult son or daughter;
        (f) a parent;
        (g) an adult brother or sister;
        (h) an adult who has exhibited special care and concern for the prospective research participant.

Recommendation 10. The Department of Health and Human Services should explore opportunities to promote the development and adoption by the states of specific and uniform legislation to enable consent by third parties for research activities involving individuals who lack consent capacity, and to ensure protection of human research participants in those circumstances.

Section 3.4

Appendix 16: University of Kentucky Impaired Consent Capacity Policy

University of Kentucky
IMPAIRED CONSENT CAPACITY POLICY
Research studies involving adult participants with impaired consent capacity

This policy applies to research with adults who may be unable to provide legally effective informed consent because of impairment in consent capacity. An individual's consent capacity is not simply present or absent, but is best understood as occurring along a continuum. It may occur in a wide range of conditions and disease states and is task-specific. This policy employs a method to determine assessment approaches that are tailored to the study population, level of study risk and nature of consent capacity impairment.. It also describes provisions for assent, dissent, process enhancements and the inclusion of legally authorized representatives for participants (subjects) with impaired consent capacity.

The following issues are considered by the IRB during its review of research involving subjects with impaired consent capacity. Any study that includes any participant who has limited or impaired consent capacity must complete Form T and address the issues as appropriate.

The IRB should obtain a review of the project by an IRB voting member or consultant, independent of the research and investigators, with appropriate professional background, knowledge and experience in working with individuals with questionable capacity.

I. Studies that are most likely to include participants with limited or impaired consent capacity:

Some studies include populations that suggest a likelihood of limited or impaired consent capacity. For example, a study of individuals with traumatic brain injury, independent of individual clinical characteristics, might be assumed to include a large number of participants with impaired capacity to understand, appreciate, freely choose, and demonstrate reasoning ability about studies. Other studies are less obviously focused on high likelihood target populations. The IRB considers the following list of study populations as likely to involve a significant number of participants with limited or impaired consent capacity. Investigators with these target populations are asked to consider the likelihood of consent capacity impairment and complete the IRB Form T-*Research Involving Adults with Impaired Consent Capacity.*

This list draws from the literature and is for the purpose of increasing awareness of the influences that chronic and acute medical and situational factors have on cognitive capacities utilized when forming consent to participate in studies.

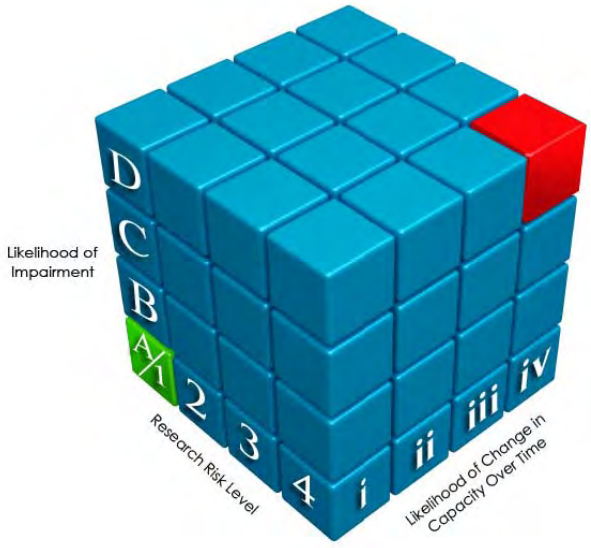
Studies with:

- Traumatic brain injury or acquired brain injury
- Severe depressive disorders or Bipolar disorders
- Schizophrenia and other severe mental disorders that involve serious cognitive disturbances
- Stroke
- Developmental disabilities
- Degenerative dementias
- CNS cancers and other cancers with possible CNS involvement
- Late stage Parkinson's Disease
- Late stage persistent substance dependence
- Ischemic heart disease
- HIV/AIDS
- COPD
- Renal insufficiency
- Diabetes
- Autoimmune or inflammatory disorders
- Chronic non-malignant pain disorders
- Drug effects
- Other acute medical crises

II. Investigator obligations and duties with participants who have limited or impaired consent capacities:

The obligations and duties of investigators vary with the level of research risk and the level of impaired consent capacity. This policy implements a multidimensional model for processing studies of individuals with impaired consent capacity. This process involves assessing three dimensions of risk: (1) Research risk; (2) Likelihood that the target population for the study has impaired consent capacity; and (3) The likelihood that consent capacity might change over time. Figure 1 shows the multidimensional model of risk in research with individuals having impaired consent capacity. This cube shows all three dimensions including the research risk level in terms of harm or benefit from participating, the potential for consent impairment, and the possibility of change in consent capacity over time. The green box shows the lowest possible risk level, a 1,1,1. The red box shows higher levels of potential risk, highest level of consent impairment and the greatest likelihood of change in capacity over time.

Figure 1. Multidimensional Model of Risk Among Adult Participants with Impaired Consent Capacity



III. Specific Risk and Consent Capacity Assessment Duties:

This policy guides investigators to take a structured approach to the question of consent capacity that is protocol-specific and tailored to the study population.

The investigator selects the applicable category for each of the three dimensions as listed in **Table 1**. His/her selection results in a composite score which is associated with a set of recommended assessment options (**Appendix I**). This activity may be accomplished manually or by using the automated web-based tool found in Form T. Investigators can either use the recommended assessment or provide rationales for alternative protections.

This tailored approach reserves the most formal and validated assessments for situations in which impairment is more likely to be present, capacity fluctuations are likely, anticipated benefits are fewer, and foreseeable risks are greater.

For example, the suggested action for protocols with any research risk level 1 is to "***do an informal participant assessment during routine interview procedures to determine consent capacity and change over time if indicated***".

In this case, no other special assessment procedures must be considered. However the investigator may choose to incorporate consent enhancements as described in section IV particularly if the study requires extensive time or task commitments.

Conversely, the recommendations for a protocol receiving a composite score of 3Ciii would entail obtaining an independent assessment by a qualified mental health professional or use of a validated assessment instrument.

Sample informal discussion questions:

- *Can you tell me what will happen if you agree to be part of this study?*
- *How might this study help you?*
- *Can anything bad happen to you? Tell me about that.*
- *What will happen if you decide not to be in the study?*

Table 1 Research Dimensions and Categories

Research Risk: (This dimension is the same across all studies and is the fundamental risk level assignment)
Category 1. The study does not involve greater than minimal risk.
Category 2. The study presents greater than minimal risk *and* prospect of direct benefit to the participants.
Category 3. The study presents greater than minimal risk *and* no prospect of direct benefit to the subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition
Category 4. The study does not fall under Category 1, 2, or 3, listed above.

Likelihood of impaired consent capacity: (This is an anticipated level of consent capacity impairment that is likely for the target population)
Category A. The target population for the study has a low to no likelihood of impaired consent capacity.
Category B. The target population for the study has a minimal likelihood of impaired consent capacity.
Category C. The target population for the study has a moderate likelihood of impaired consent capacity..
Category D. The target population for the study has a high likelihood of impaired consent capacity.

Likelihood of changes in consent capacity over the duration of the study
Category i. The target population for the study has a low to no likelihood of changes in consent capacity over the duration of the study. This applies to participants who have impaired consent capacity but with conditions that are static or chronic and progressive and that show little likelihood of improving or to participants who are intact and have little likelihood of having diminished consent capacity. It is used when the consent capacity is expected to remain stable over the time period of the study duration.
Category ii. The target population for the study has a minimal likelihood of changes in consent capacity over time. This applies to participants who either have impairments that might be expected to improve over time or that might diminish over the time period of the study duration.
Category iii. The target population for the study has a moderate likelihood of changes in consent capacity over the study duration. This applies to participants who either have impairments that can be expected to improve over time or that are more likely to diminish over the time period of the study duration.
Category iv. The target population for the study has a high likelihood of changes in consent capacity over time. This applies to participants who either have impairments that most likely will improve over time or that most likely will diminish over the course of the study. Or, this level might apply to participants with waxing and waning capacities that fluctuate during the course of the study.

IV. Other safeguards:
For studies with risk level 2 and moderate or greater likelihood of impaired consent capacity (2 C i –iv), investigators describe and provide examples of safeguards or tools they intend to employ in conducting the research. Specific enhancements to the consent form and process may serve to improve a prospective participant's understanding and enable individuals who otherwise have limitations in consent capacity, to make competent decisions.

a. Use of guidance for a legally authorized representative to provide informed consent on behalf of the participant: When potential participants have been assessed as having impaired consent capacity, the investigator must engage a Legally Authorized Representative (LAR) to provide informed consent on the potential participant's behalf. Investigators should present information on how this selection will be made and how the LAR will be educated about making the consent decision. The IRB has the following pamphlets that can be provided to LARs to help them understand their special role.

- Advice to Legally Authorized Representatives of Adult Participants in Medical Research
- Advice to Legally Authorized Representatives of Adult Participants in Nonmedical Research

b. Adult assent form and procedure: When potential participants have been assessed as having limited or impaired consent capacity, the investigator should obtain assent. Failure to object should not, absent affirmative agreement, be construed as assent. Where impairment is too great even for obtaining assent, investigators may need to carefully consider attention to subject dissent.

A sample assent form is available on the ORI website. Obtaining assent may not be applicable in some cases such as where participants are physiologically incapable of responding to investigator questions. Verbal assent may be appropriate in cases where a subject is unable to sign an assent form.

c. Method for assessing dissent: The investigator must describe what methods are to be used to *assess dissent* among participants with limited or impaired consent capacity. Participants may exhibit behaviors or non-verbal cues (e.g. becoming upset, moving away, facial expressions, etc.) that indicate their desire to not want to participate. In addition, they may be asked to make a defined signal or gesture (e.g. shaking the head, using "thumbs down" sign, etc) to indicate their desire to not participate or stop participation.

d. Study overviews: Use of a study overview may enable an individual with limited consent capacity to make a decision regarding study participation. A study overview summary is written in simple language that distills the principal ideas from a consent form. Not to be used as a substitute for the full consent document, this tool provides an overview of the primary consent elements for initial consideration in the consent process. From that baseline, the process may continue with additional layers of detail.

e. If consent capacity is assessed as likely to fluctuate over time, describe intervals or conditions for re-consent. The recommended plan for participants with a higher likelihood of changes in consent capacity over the duration of the study should incorporate set timeframes for re-assessing consenting capacity. Study design implications such as timing of risky procedures, sequence of intervention and lengthy periods of no contact should be considered when determining appropriate timeframe for re-assessment and/or re-consent. The Investigator should explain why he/she does not plan to follow a specific timeframe and can describe an alternative plan.

f. Other considerations and potential safeguards. Investigators should use fair and equitable recruitment practices in research and avoid practices that place participants at risk for coercion or undue influence. The investigator should describe any other educational techniques or consent process alterations he/she plans to employ.

g. Institutionalized subjects. The impact of institutionalization may further compromise the voluntariness of an individual with impaired consent capacity. Investigators must not involve this population for convenience purposes. Investigators should justify use of institutionalized subjects and take measures to ensure decisions are voluntarily made, free of influence or potential or perceived impact on involuntary confinement.

Definitions

Minimal risk – Means that the probability and magnitude of the harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological exams or tests. (i.e., daily life of healthy persons).

Consent capacity – includes the specific abilities necessary for a prospective or current research participant to understand and use information relevant to consent. The components of consent capacity are the capacity to (1) act on one's own behalf; (2) understand the study; (3) appreciate the consequences to oneself of participation; and (4) make a free choice.

Assent - is defined as a child's [*or an impaired consent capacity individual's*] affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Dissent – is defined as an individual's verbal or non-verbal disagreement or refusal to assent to participate in research. Two general categories of non-verbal dissent are recognized: (1) Behaviors that suggest dissent such as turning away from researchers or pushing away and (2) Agreed signals of dissent such as situations where a researcher tells a subject to blink the eyes once or twice to signal dissent.

Competence – "Technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice." [OHRP Institutional Review Board Guidebook, Chapter VI, Section D]

Permission - is defined as the agreement of parent(s) or guardian to the participation of their child or ward in research or a clinical investigation. Permission includes the element of consent set forth in federal regulations and outlined in the informed consent template included in the IRB expedited and full review applications.

Qualified mental health professional – is defined by Kentucky statute (202A.011). It includes licensed physicians, psychiatrists, psychologists, mental health RNs, licensed clinical social workers, marriage and family therapists, and licensed professional counselors. See * below for the complete statutory language.

Legally authorized representative - is an individual who has the authority to make research participation decisions on behalf of another. In accord with state law and federal regulation, individuals who can serve as legally authorized representatives are as follows:

Consent and/or Authorization by a Legally Authorized Representative
Consistent with Kentucky health care decision statutes for choosing a legally authorized representative for adult subjects unable to consent, one of the following responsible parties, in the following order of priority (if no individual in a prior class is reasonably available, willing, and competent to act), is authorized to make research participation decisions on behalf of the person: (a) the judicially-appointed guardian of the person, if the guardian has been appointed and if the decisions to be made under the consent are within the scope of the guardianship; (b) the attorney-in-fact named in a durable power of attorney, if the durable power of attorney specifically includes authority for the decisions to be made under the consent; (c) the spouse of the person; (d) an adult child of the person, or if the person has more than one (1) child, the majority of the adult children who are

reasonably available for consultation; (e) the parents of the subject; (f) the nearest living relative, or if more than one of the same relation, a majority of the nearest living relatives.

Consent by a legally authorized representative should involve all the same considerations that informed consent from a competent subject involves.

***KRS 202A.011, Section (12)(a)-(12)(g)* "Qualified mental health professional" means**:
(a) A physician licensed under the laws of Kentucky to practice medicine or osteopathy, or a medical officer of the government of the United States while engaged in the performance of official duties; (b) A psychiatrist licensed under the laws of Kentucky to practice medicine or osteopathy, or a medical officer of the government of the United States while engaged in the practice of official duties, who is certified or eligible to apply for certification by the American Board of Psychiatry and Neurology, Inc.; (c) A psychologist with the health service provider designation, a psychological practitioner, a certified psychologist, or a psychological associate, licensed under the provisions of KRS Chapter 319;
(d) A licensed registered nurse with a master's degree in psychiatric nursing from an accredited institution and two (2) years of clinical experience with mentally ill persons, or a licensed registered nurse, with a bachelor's degree in nursing from an accredited institution, who is certified as a psychiatric and mental health nurse by the American Nurses Association and who has three (3) years of inpatient or outpatient clinical experience in psychiatric nursing and is currently employed by a hospital or forensic psychiatric facility licensed by the Commonwealth or a psychiatric unit of a general hospital or a private agency or company engaged in the provision of mental health services or a regional community mental health and mental retardation program; (e) A licensed clinical social worker licensed under the provisions of KRS 335.100, or a certified social worker licensed under the provisions of KRS 335.080 with three (3) years of inpatient or outpatient clinical experience in psychiatric social work and currently employed by a hospital or forensic psychiatric facility licensed by the Commonwealth or a psychiatric unit of a general hospital or a private agency or company engaged in the provision of mental health services or a regional community mental health and mental retardation program; (f) A marriage and family therapist licensed under the provisions of KRS 335.300 to 335.399 with three (3) years of inpatient or outpatient clinical experience in psychiatric mental health practice and currently employed by a hospital or forensic facility licensed by the Commonwealth, a psychiatric unit of a general hospital, a private agency or company engaged in providing mental health services, or a regional community mental health and mental retardation program; or (g) A professional counselor credentialed under the provisions of KRS Chapter 335.500 to 335.599 with three (3) years of inpatient or outpatient clinical experience in psychiatric mental health practice and currently employed by a hospital or forensic facility licensed by the Commonwealth, a psychiatric unit of a general hospital, a private agency or company engaged in providing mental health services, or a regional community mental health and mental retardation program.

Appendix I. Assessment actions and instruments by composite risk score

1	Any level	Any level	Do you plan to do an informal subject assessment during routine interview procedures?
2	A	i	Do you plan to do an informal subject assessment during routine interview procedures?
2	A	ii	
2	A	iii	
2	A	iv	Do you plan to do an informal subject assessment during routine interview procedures *and repeat as needed?*
2	B	i	Do you plan to do an informal subject assessment during routine interview procedures?
2	B	ii	Do you plan to do an informal subject assessment and document all of the following: 1) subject understanding; 2) subject understanding of the study; 3) subject choice to participate; and 4) subject's evidence of reasoning? For iv – *and repeat as needed?*
2	B	iii	
2	B	iv	
2	C	i	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study?
2	C	ii	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every year recommended?*
2	C	iii	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every 6 months recommended?*
2	C	iv	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at*

			appropriate intervals– every 6 months recommended?
2	D	i	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study?
2	D	ii	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every year recommended?*
2	D	iii	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every 6 months recommended?*
2	D	iv	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every 6 months recommended?*
3	A	i	Do you plan to do an informal subject assessment during routine interview procedures?
3	A	ii	Do you plan to do an informal subject assessment during routine interview procedures *and repeat as needed – every year recommended?*
3	A	iii	Do you plan to do an informal subject assessment during routine interview procedures *and repeat as needed – every 6 months recommended?*
3	A	iv	Do you plan to do an informal subject assessment during routine interview procedures *and repeat as needed – every 6 months recommended?*
3	B	i	Do you plan to do an informal subject assessment during routine interview procedures?
3	B	ii	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every year recommended?*
3	B	iii	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every 6 months recommended?*
3	B	iv	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every 6 months recommended?*
3	C	i	Do you plan to do an informal subject assessment during routine interview procedures?
3	C	ii	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every year recommended?*
3	C	iii	Do you plan to obtain an independent assessment by a qualified mental health professional* with experience in consent capacity assessment OR the MacArthur

			Competence Assessment Tool *and repeat at appropriate intervals – every 6 months recommended?* **See ORI Policy on assessing consent capacity or KRS 202A.011, Section (12)(a)-(12)(g). This includes: licensed physicians, licensed psychiatrists, psychologists, RNs with master's degree in psychiatric nursing or certified mental health BSN, RNs, licensed clinical social workers, marriage and family therapists, and licensed professional counselors.*
3	C	iv	Do you plan to obtain an independent assessment by a qualified mental health professional* with experience in consent capacity assessment OR the MacArthur Competence Assessment Tool *and repeat at appropriate intervals – every 6 months recommended?* **See ORI Policy on assessing consent capacity or KRS 202A.011, Section (12)(a)-(12)(g). This includes: licensed physicians, licensed psychiatrists, psychologists, RNs with master's degree in psychiatric nursing or certified mental health BSN, RNs, licensed clinical social workers, marriage and family therapists, and licensed professional counselors.*
3	D	i	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study?
3	D	ii	Do you plan to use the UBACC or comparable assessment instrument OR independent assessment by personnel not affiliated with the study *and repeat at appropriate intervals– every year recommended?*
3	D	iii	Do you plan to obtain an independent assessment by a qualified mental health professional* with experience in consent capacity assessment OR the MacArthur Competence Assessment Tool *and repeat at appropriate intervals – every 6 months recommended?* **See ORI Policy on assessing consent capacity or KRS 202A.011, Section (12)(a)-(12)(g). This includes: licensed physicians, licensed psychiatrists, psychologists, RNs with master's degree in psychiatric nursing or certified mental health BSN, RNs, licensed clinical social workers, marriage and family therapists, and licensed professional counselors.*
3	D	iv	Do you plan to obtain an independent assessment by a qualified mental health professional* with experience in consent capacity assessment OR the MacArthur Competence Assessment Tool *and repeat at appropriate intervals – every 6 months recommended?* **See ORI Policy on assessing consent capacity or KRS 202A.011, Section (12)(a)-(12)(g). This includes: licensed physicians, licensed psychiatrists, psychologists, RNs with master's degree in psychiatric nursing or certified mental health BSN, RNs, licensed clinical social workers, marriage and family therapists, and licensed professional counselors.*
4	A,B,C,D	i-iv	What methods will you use to assess consent capacity for this study?

While some investigators may choose to use adaptations of validated tools, other studies may require use of the published original tool. The following provides information regarding use and access to validated consent capacity assessment tools:

- The MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR; Appelbaum & Grisso, 2001)
  - Semi-structured interview, tailored to protocol
  - Administration takes 15-30 minutes, and substantial training is required for valid administration and interpretation
  - Available from Amazon.com
- The University of California, San Diego Brief Assessment of Capacity to Consent (UBACC; Jeste et al., 2007) is available on line
  - 10-item scale; may be tailored to protocol
  - Less than 5 minutes to administer, minimal training needed
  - AMA terms of use for the UBACC

Section 3.4

Appendix 17: Minnesota Statutes

Minnesota Statutes Cited in Policy 403c

524.5-313 POWERS AND DUTIES OF GUARDIAN.
(a) A guardian shall be subject to the control and direction of the court at all times and in all things.

(b) The court shall grant to a guardian only those powers necessary to provide for the demonstrated needs of the ward.

(c) The court may appoint a guardian if it determines that all the powers and duties listed in this section are needed to provide for the needs of the incapacitated person. The court may also appoint a guardian if it determines that a guardian is needed to provide for the needs of the incapacitated person through the exercise of some, but not all, of the powers and duties listed in this section. The duties and powers of a guardian or those which the court may grant to a guardian include, but are not limited to:

[(1)-(3) not included here]

(4)(i) the power to give any necessary consent to enable the ward to receive necessary medical or other professional care, counsel, treatment, or service, except that no guardian may give consent for psychosurgery, electroshock, sterilization, or experimental treatment of any kind unless the procedure is first approved by order of the court as provided in this clause. The guardian shall not consent to any medical care for the ward which violates the known conscientious, religious, or moral belief of the ward;

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144.291 MINNESOTA HEALTH RECORDS ACT.

Subdivision 1.Short title. Sections 144.291 to 144.298 may be cited as the "Minnesota Health Records Act."

Subd. 2.Definitions. For the purposes of sections 144.291 to 144.298, the following terms have the meanings given.

[(a)-(f) omitted]

(g) "Patient" means a natural person who has received health care services from a provider for treatment or examination of a medical, psychiatric, or mental condition, the surviving spouse and parents of a deceased patient, or a person the patient appoints in writing as a representative, including a health care agent acting according to chapter 145C, unless the authority of the agent has been limited by the principal in the principal's health care directive. Except for minors who have received health care services under sections 144.341 to 144.347, in the case of a minor, patient includes a parent or guardian, or a person acting as a parent or guardian in the absence of a parent or guardian.

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13.384 MEDICAL DATA.

Subd. 3.Classification of medical data. Unless the data is summary data or a statute specifically provides a different classification, medical data are private but are available only to the subject of the data as provided in sections 144.291 to 144.298, and shall not be disclosed to others except:

[(a)-(d) omitted]

(e) to the surviving spouse, parents, children, siblings, and health care agent of a deceased patient or client or, if there are no surviving spouse, parents, children, siblings, or health care agent to the surviving heirs of the nearest degree of kindred.

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145C.02 HEALTH CARE DIRECTIVE.
A principal with the capacity to do so may execute a health care directive. A health care directive may include one or more health care instructions to direct health care providers, others assisting with health care, family members, and a health care agent. A health care directive may include a health care power of attorney to appoint a health care agent to make health care decisions for the principal when the principal, in the judgment of the principal's attending physician, lacks decision-making capacity, unless otherwise specified in the health care directive.

145C.01 DEFINITIONS. Subd. 4.Health care. "Health care" means any care, treatment, service, or procedure to maintain, diagnose, or otherwise affect a person's physical or mental condition. "Health care" includes the provision of nutrition or hydration parenterally or through intubation but does not include any treatment, service, or procedure that violates the provisions of section 609.215 prohibiting assisted suicide. "Health care" also includes the establishment of a person's abode within or without the state and personal security safeguards for a person, to the extent decisions on these matters relate to the health care needs of the person.

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253B.095 RELEASE BEFORE COMMITMENT.

§ Subdivision 1.Court release. (a) After the hearing and before a commitment order has been issued, the court may release a proposed patient to the custody of an individual or agency upon conditions that guarantee the care and treatment of the patient.

(b) A person against whom a criminal proceeding is pending may not be released.

(c) A continuance for dismissal, with or without findings, may be granted for up to 90 days.

(d) When the court stays an order for commitment for more than 14 days beyond the date of the initially scheduled hearing, the court shall issue an order that must include:

(1) a written plan for services to which the proposed patient has agreed;

(2) a finding that the proposed treatment is available and accessible to the patient and that public or private financial resources are available to pay for the proposed treatment;

(3) conditions the patient must meet to avoid revocation of the stayed commitment order and imposition of the commitment order; and

(4) a condition that the patient is prohibited from giving consent to participate in a clinical drug trial while the court order is in effect.

(e) Notwithstanding paragraph (d), clause (4), during the period of a stay of commitment, the court may allow the patient to give consent to participate in a specific psychiatric clinical drug trial if the treating psychiatrist testifies or submits an affidavit that the patient may benefit from participating in the trial because, after providing other treatment options for a reasonable period of time, those options have been ineffective. The treating psychiatrist must not be the psychiatrist conducting the psychiatric clinical drug trial. The court must determine that, under the circumstances of the case, the patient is competent to choose to participate in the trial, that the patient is freely choosing to participate in the trial, that the compulsion of the stayed commitment is not being used to coerce the person to participate in the clinical trial, and that a reasonable person may choose to participate in the clinical trial.

Section 3.4

Appendix 18: Brochure, University of Kentucky, LAR Advice

UNIVERSITY OF KENTUCKY

An Equal Opportunity University

If you have questions about your rights as a legally authorized representative of a UK research study volunteer, you may call the University of Kentucky Office of Research Integrity at (859) 257-9428 or toll free at 1-866-400-9428.

Advice to Legally Authorized Representatives of Adult Participants

University of Kentucky
Institutional Review Board

You are what is called a "legally authorized representative" of a patient who is or might become a participant in a research study.

This means that the participant whom you represent does not have the capacity to make an independent decision about treatment or about participating in research. Therefore, you have been asked to make decisions on behalf of the patient.

Research Risk

Basically, you are being asked to weigh the risks and benefits of participating in clinical research. "Risk" means the chance of harm that might happen. There could be risks from medication side effects or risks from certain medical procedures. Sometimes doctors will tell you about these risks as "very rare" or "common" or sometimes they will give you information to help you understand the level of risk. For example, they might tell you that a side effect has happened to 10% of research subjects in the past.

Research Benefit

Likewise, you are asked to evaluate the benefits to the patient for participating. A benefit might be that the new experimental drug would actually help treat the patient's medical problem. Doctors call this kind of benefit a "direct" benefit to the individual. There is another kind of benefit that is indirect. In this case, the benefit might be that a lot can be learned about promising medications or procedures. Also, other patients might benefit from the knowledge gained from this study.

Risk and Benefit

You have to weigh the risks against the benefits. That is, "this much risk for that much benefit." The benefits should outweigh or offset the risks.

Two Approaches

When you are asked to make this risk/benefit decision, there are two ways to go about it: (1) the "substituted judgment" approach and (2) the "in the individual's best interest" approach.

The substituted judgment approach means that you are being asked to make the decision based on how you think the participant would do it. In other words, you express exactly what you think the patient would do if he or she could still make independent medical decisions.

For example, a research treatment might have a small likelihood of benefit for the patient and may have serious side effects, but you know that the patient would want to advance science and be of possible benefit to others. In this case, you might decide to agree to the patient's participation using the substituted judgment approach.

The individual's best interest approach takes a very different turn. In this situation you make the decision about a treatment or about participating in research based on what you think is best for the patient, independent of what he or she might have decided if there was no impairment in decision-making. In other words, you act almost as parent for a child where you look out for the safety and overall well-being of the patient. In using this approach, you can consider all aspects of well-being.

For example, a research treatment might hold out a promise of effectiveness, but the participant is so ill that even this improvement will make no difference in quality of life. In this case, you might decide to not agree to the research treatment if you follow the best interests of the individual approach.

Being a legally authorized representative is a serious role and the patient's research doctor takes it seriously as well.

One other thing – sometimes choosing to participate can mean that you must spend considerable time bringing the participant to appointments and waiting for procedures to be done. Be sure to ask about how much time you or other family members will need to spend waiting during these visits.

If you are having difficulty in making this decision, ask the participant's doctor or the research doctor for more information until you feel confident that you are making the best decision you can under the circumstances.

Section 3.4

Appendix 19: NIH Research Involving Individuals with Questionable Capacity to Consent- Done

Research Involving Individuals with Questionable Capacity to Consent: Points to Consider

November 2009

Use of Information/Educational Techniques

The way in which information about the study is conveyed to prospective subjects can enhance consent capacity. The following are some techniques that have been shown to be effective:

- Presentation of initial consent: Studies have shown that simplification and repetition of consent information and multi-media presentation have improved subject understanding. In addition, oral consent in combination with written consent rather than written consent only has been shown to lead to greater understanding.

- Educational techniques which can be used during consent process to improve understanding: Other techniques of presenting consent information have been shown to improve subject understanding. Designing a step-wise consent process and providing additional information as needed can improve understanding, and allow for additional education during the consent process to further enhance comprehension. Interactive questioning during the consent process has been shown to increase post-consent subject understanding, and has the added benefits of highlighting important elements for the subject to focus on, ensuring understanding of earlier material to allow understanding of subsequent information, and assessing subject understanding during the process to allow for appropriate explanation throughout the process. Two other techniques which have shown to result in enhanced understanding are additional subject education and repetition of misunderstood information.

Accessed at: http://grants1.nih.gov/grants/policy/questionablecapacity.htm

National Institutes of Health

Section 3.5

Appendix 20: “Evaluation to Consent” Form

EVALUATION TO SIGN CONSENT Date: _____

Study: _____

Subject Initials: _____ Subject Number (if applicable): _____

1. Is the subject alert and able to communicate with the examiner?

2. Ask the subject to describe the purpose of the study:

3. Ask the subject to describe one or two potential risks of participating in the study:

4. Ask the subject to describe any benefits from participating in the study:

5. Ask the subject to describe what is expected of them in the study:

6. Ask the subject what would happen if he or she no longer wants to participate in the study:

I hereby certify that the above subject is alert, able to communicate, and able to give acceptable answers to the items above.

_____
Evaluator's Printed Name

_____ _____
Evaluator Signature Date