Organization:
University of Minnesota
Minneapolis, Minnesota

Final Site Visit Report

Dates:

June 1, 2015 – June 3, 2015

Final Accreditation Status:
Reaccreditation Pending
General Overview

University of Minnesota initially received Full Accreditation on April 20, 2004 and is applying for reaccreditation.

University of Minnesota follows the Department of Health and Human Services (DHHS), the Food and Drug Administration (FDA), the Department of Defense, the Department of Education, the Department of Energy, the Department of Justice regulations, and the ICH-GCP (E6) guideline as adopted by the U.S. FDA.

University of Minnesota conducts International Research. University of Minnesota has four IRBs. University of Minnesota applies equivalent protections to all research not funded by the DHHS.

University of Minnesota’s HRPP had the following strengths:

- The HRPP had dedicated, available, and knowledgeable HRPP staff and leadership.
- The Faculty Social IRB and the Student Social IRB have highly qualified and engaged IRB members and IRB chairs.
- The process for the review of contracts is well organized and thorough.
- Researchers were knowledgeable and committed to the protection of human participants.
- University of Minnesota leadership’s commitment to providing additional resources and improving the protections of human participants is commendable.

Domain I: Organization

**Standard I-2: The Organization ensures that the Human Research Protection Program has resources sufficient to protect the rights and welfare of research participants for the research activities that the Organization conducts or oversees.**

**Draft Site Visit Report**

**Observations:**

The Institutional Official and the Executive Director of the Human Research Protection Program periodically reviewed the resources allocated to the HRPP and adjusted resources as needed.

University of Minnesota had four IRBs. The HRPP Executive Committee and Institutional Official annually evaluated whether the number of IRBs was appropriate to the volume and types of research reviewed.

For each study, the IRB determined whether the resources necessary to protect participants were provided.

**Areas of Concern:**

The HRPP was not allocated the financial and personnel resources necessary to carry out policies and procedures.

Researchers and IRB staff described the IRB review of research as not being timely. Although the number of the IRBs were evaluated in relation to the volume and types or research, adjustments were not made as needed. (Standard I-2)

**Response to Draft Site Visit Report**

**Observations:**

In response to an Independent Inquiry Panel report, University of Minnesota developed a Work Plan to address the recommendations of the Panel’s report, including a plan to address the financial and personnel resources allocated to the HRPP. The Work Plan also describes a planned process to evaluate the number of IRBs in relation to the volume and types of research and make adjustments as needed.

**Areas of Concern:**

University of Minnesota Work Plan that will address the financial and personnel resources allocated to the HRPP and includes education and monitoring has not been implemented and will not be until fiscal year 2016. (Standard I-2)

**Council Determination:**

Standard is not met.
Standard I-4: The Organization responds to the concerns of research participants.

**Draft Site Visit Report**

**Observations:**
Consent documents provided current and past participants with contact information for an individual who was unaffiliated with a specific research study to discuss problems, concerns, and questions; obtain information; and offer input. The consent form and HRPP website made available to prospective participants contact information for an individual who was unaffiliated with a specific research study to discuss problems, concerns, and questions; obtain information; and offer input. The Research Compliance Supervisors responded to contacts from participants or others. IRBs members and researchers could describe the characteristics and culture of the communities in which they conducted research.

University of Minnesota promoted the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results, when appropriate. The convened IRBs and reviewers using the expedited procedures were aware of additional considerations for reviewing research that involved community members in the research process, including the design and implementation of research and the dissemination of results.

**Areas of Concern:**
Some components of the HRPP provided prospective participants and the community with information designed to enhance their understanding of research; there was, however, no process to evaluate and make improvements, as needed, to University of Minnesota’s outreach activities. (Element I.4.B.)

**Response to Draft Site Visit Report**

**Observations:**
The HRPP plans to conduct an evaluation of the existing HRPP outreach activities and to make improvements as needed by September 1, 2015. The review will engage other components of the organization to assess whether improvements to the HRPP outreach activities are needed. In response to an Independent Inquiry Panel report, University of Minnesota developed a Work Plan to address the recommendations of the Panel’s report, including a plan to enhance community engagement and participant outreach.

**Areas of Concern:**
In response to the site visit report the organization has developed a plan to conduct an evaluation of the existing HRPP outreach activities and to make improvements as needed by September 1, 2015. The University of Minnesota Work Plan includes a plan to enhance community engagement and participant outreach but it will not be implemented until fiscal year 2016 and does not include education, and monitoring. (Elements I.4.B.)

**Council Determination:**
Standard is not met.

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.

**Draft Site Visit Report**

**Observations:**
The Post Approval Review staff conducted quality assurance activities that periodically assessed compliance of the HRPP. The plan included at least one goal and at least one measure of compliance and described the process to make improvements.

The HRPP followed policies and procedures to invite researchers and research staff to contact individuals who could answer their questions, address their concerns, and respond to their suggestions regarding the HRPP.

The IRB and IRB staff followed policies and procedures to identify, manage, and report findings of non-compliance. Investigators and research staff reported non-compliance to the IRBs. The Executive Director of the Human Research Protection Program or other senior IRB staff who are also IRB members decided whether each allegation of non-compliance had a basis in fact. The convened IRBs decided whether each incident of non-compliance was serious or continuing. The convened IRBs managed serious or continuing non-compliance. The Executive Director of the HRPP or other senior staff who are also IRB members managed non-compliance determined to be neither serious nor continuing. The IRB staff reported serious and continuing non-compliance to regulatory agencies and appropriate organizational officials within thirty days.

Areas of Concern:

The HRPP did not conduct quality improvement activities that periodically assessed the quality, efficiency, and effectiveness of the HRPP. The HRPP did not have a plan that included at least one goal and at least one measure of quality, efficiency, and effectiveness and described the process to make improvements. (Element I.5.B.)

Response to Draft Site Visit Report

Observations:

Although not provided to the site visitors at the time of the site visit, the HRPP identified two quality improvement activities that assessed the quality, efficiency, and effectiveness of the HRPP: Monthly evaluation of performance metrics and an evaluation of the average number days from submission to approval.

Council Determination:

Standard is met.

Standard I-7: The Organization has and follows written policies and procedures to ensure that the use of any investigational or unlicensed test article complies with all applicable legal and regulatory requirements.

Draft Site Visit Report

Observations:

The Manager of the Investigational Drug Service followed policies and procedures to control investigational drugs so that they were used only in approved research protocols and under the direction of approved researchers. The researchers followed policies and procedures to control investigational devices so that they were used only in approved research protocols and under the direction of approved researchers.

The senior IRB staff followed policies and procedures to ensure that the emergency use of a test article followed regulations.

Areas of Concern:

When research involved the use of a drug other than the use of a marketed drug in the course of medical practice, there was no process to confirm that the drug had a valid IND or met one of the FDA exemptions from the requirement to have an IND. (Element I.7.A.)

When research was conducted to determine the safety or effectiveness of a device, there was no process to confirm that the device had an IDE issued by the FDA, the device fulfilled the requirements for an abbreviated IDE or the device was exempt from the requirements for an IDE. (Element I.7.B.)
There was no process to ensure that research did not commence until a valid IND or IDE was secured.
(Elements I.7.A. and I.7.B.)

Response to Draft Site Visit Report

Observations:
The HRPP provided information to indicate that a process has been in place since February 2015 to confirm that a drug had a valid IND or met one of the FDA exemptions from the requirement to have an IND. The IRB minutes template will be revised to include the specific IND number validation to be documented in the IRB minutes. IRB members and IRB staff will be trained on the new IRB minutes template no later that September 1, 2015. After implementation of the new IRB minutes template, monitoring is planned for the next year at 3, 6, 9, and 12 months.

The HRPP provided information to indicate that a process has been in place since February 2015 to confirm that a device has an IDE issued by the FDA, the device fulfilled the requirements for an abbreviated IDE or the device was exempt from the requirements for an IDE. This process includes questions on the application form, IRB members validating via the IRB reviewer checklist, and documentation in the IRB minutes. The IRB minutes template will be revised to include the specific validation of IDE number in IRB minutes and documentation of device risk determination. IRB members and IRB staff will be educated on the new IRB minutes template no later than September 1, 2015. After implementation of the new IRB minutes template, monitoring is planned for the next year at 3, 6, 9, and 12 months.

Council Determination:

Standard is met.


Status Report (Elements I.7.A. and I.7.B.): Provide the results of monitoring of the IRB reviewer checklist, and IRB minutes to ensure there is a valid IND and IDE for four months and describe any actions that took place as a result of the monitoring.

Domain II: Institutional Review Board or Ethics Committee

Standard II-1: The structure and composition of the IRB or EC are appropriate to the amount and nature of the research reviewed and in accordance with requirements of applicable laws, regulations, codes, and guidance.

Draft Site Visit Report

Observations:
The Vice President for Research appointed IRB members, the IRB chairs, and alternate members. The IRBs were sufficiently qualified. The IRBs were appropriately constituted. IRB meetings were appropriately convened.

The IRB chairs, IRB members, and IRB staff were knowledgeable. The IRB chairs and the Executive Director of the Human Research Protection Program annually evaluated, and if necessary, adjusted the membership and composition of the IRBs to meet regulatory and the organization’s requirements.

The Executive Director of the Human Research Protection Program and the IRB chairs periodically evaluated the IRB chairs, the IRB vice-chairs, IRB members, and IRB staff.

The IRBs followed policies and procedures to identify and eliminate conflicts of interest of the IRB members and consultants. IRB members knew when they had a conflict of interest. IRB members with a conflict of interest were excluded from voting and discussion except to provide information requested by the IRB. IRB members with a conflict of interest left the meeting room for discussion and voting; and were not counted towards quorum.
University of Minnesota followed policies and procedures to separate competing business interests from ethics review functions.

There was a process to obtain consultants. Consultants did not vote with IRB members. When a consultant was obtained, the IRB members were made aware of the information provided by the consultant. Information provided by consultants was documented.

Areas of Concern:

The IRB rosters did not include all required information as described in policy #201. For example whether or not they had been designated by the IRB chair to be an expedited reviewer. (Element II.1.A.)

When the convened IRBs reviewed research that involved participants likely to be vulnerable to coercion or undue influence, it was not evident that at least one IRB member who was knowledgeable about or experienced in working with such participants was present at the IRB meeting. (Element II.1.A.)

IRB members reported that they did not receive feedback on their performance and there was no evidence that appropriate actions took place as needed. (Element II.1.B.)

Policies and procedures required protocols to be reviewed by individuals with appropriate expertise; however, this was not evident in practice. For example, the IRB member reviewer for a randomized parallel-group multicenter clinical trial of a device was a non-scientist with background in information systems and operations. (Element II.1.E.)

Response to Draft Site Visit Report

Observations:

The IRB policy related to membership and roster management has been revised and will be implemented by September 1, 2015. After implementation of the revised policy, monitoring is planned for the next year at 3, 6, 9, and 12 months.

In response to an Independent Inquiry Panel report, University of Minnesota developed a Work Plan to address the recommendations of the Panel’s report, including a plan for when the convened IRB reviewed research that involved participants likely to be vulnerable to coercion or undue influence, it was not evident that at least one IRB member who was knowledgeable about or experienced in working with such participants present at the IRB meeting. The Work Plan, education, and monitoring will be implemented during the fiscal year 2016.

IRB chairs and IRB members completed a self-evaluation in February 2015 and results of the evaluation were shared with IRB members in the May 2015 Member newsletter.

In response to an Independent Inquiry Panel report, University of Minnesota developed a Work Plan to address the recommendations of the Panel’s report, including a plan for having individuals with appropriate expertise review protocols. The Work Plan, education, and monitoring will be implemented during the fiscal year 2016.

Areas of Concern:

University of Minnesota Work Plan includes additional protections for research that involves participants likely to be vulnerable to coercion or undue influence. The plan has at least one IRB member who is knowledgeable about or experienced in working with such participants present at the convened IRB meeting. The Work Plan, education, and monitoring will be implemented during the fiscal year 2016. (Element II.1.A.)

Although the aggregated results of the member self evaluation were shared with members via a newsletter, IRB members were not aware that they had received feedback on their performance. This appears to be an education issue. No planned education was proposed for IRB chairs and members regarding the self-evaluations and how they will be utilized to provide feedback to members on their performance. (Element II.1.B.)

University of Minnesota Work Plan includes a plan for having individuals with appropriate expertise review protocols. The Work Plan, education, and monitoring will be implemented during the fiscal year 2016. (Element II.1.E.)

Council Determination:
Standard is not met.

**Standard II-2: The IRB or EC evaluates each research protocol or plan to ensure the protection of participants.**

**Draft Site Visit Report**

**Observations:**

The IRB staff followed policies and procedures to determine when research involving human participants was exempt and provided accurate determinations. Investigators knew whom to ask for an authoritative decision about whether research involving human participants was exempt from regulation and what information to submit. Where appropriate, the IRB staff followed policies and procedures to provide additional protections for participants enrolled in exempt research.

The IRB Correspondence Administrators provided documents to IRB members seven days before convened IRB meetings. When conducting business at an IRB meeting, the majority of IRB members were present, and at least one IRB member whose primary concerns are in the non-scientific areas was present. The unaffiliated IRB member and the IRB member representing the general perspectives of participants were generally present at IRB meetings.

The convened IRBs followed policies and procedures to review research for initial review and review of modifications to previously approved research. IRB members evaluated each protocol undergoing initial or continuing review to determine which protocols needed review more often than annually. The calculation of the approval period for research was based on the date of the convened IRB meeting at which the IRBs approved the protocol or approved the protocol with modifications. The HRPP had a process to review responses from researchers.

IRB reviewers using the expedited procedure followed policies and procedures to review research for initial review, continuing review, and review of modifications to previously approved research. IRB reviewers evaluated each protocol undergoing initial or continuing review to determine which protocols needed review more often than annually. The IRB chairs or designated IRB members approved contingent revisions required by the convened IRBs, when appropriate.

The IRBs had policies and procedures to identify, manage, and report unanticipated problems involving risks to research participants or others. The IRB staff determined whether each reported problem was an unanticipated problem involving risks to participants or others. The IRB staff reported unanticipated problems involving risks to participants or others to regulatory agencies and appropriate organizational officials within thirty days.

The convened IRBs followed policies and procedures to suspend or terminate IRB approval of research that was not being conducted in accordance with the federal regulations or the IRB’s requirements or that has been associated with unexpected serious harm to participants. The IRB staff had the authority to suspend or terminate IRB approval of research in addition to the convened IRBs. Suspensions and terminations by someone other than the convened IRBs were reported to and reviewed by the convened IRBs. When study approval was suspended or terminated, the IRBs or the person ordering the suspension or termination protected the rights and welfare of currently enrolled participants. The IRB staff reported suspensions and terminations of IRB approval to regulatory agencies and appropriate organizational officials within thirty days.

When the researcher was the lead researcher of a multi-site study, applications included information about the management of information that was relevant to the protection of participants. The IRBs evaluated whether the management of information that was relevant to the protection of participants was adequate.

**Areas of Concern:**

Researchers and IRB staff reported the exempt determinations were not timely. (Element II.2.A.)
IRB members indicated that they do not receive materials in enough time prior to the IRB meeting to review them. (Element II.2.C.)

The convened IRBs did not follow policies and procedures to review research for continuing review. There was no documentation to indicate that the continuing reviews were substantive. (Element II.2.D.)

The actions documented in the IRB minutes were not consistent with those described in Policy 408 Managing Allegations of Non-Compliance with IRB Policies and Procedures. (Element II.2.D.)

Written notifications to researchers of IRB findings and actions did not provide complete information. For example letters did not contain information for researchers regarding determinations of parental signature(s), regulatory categories, or the expiration date. (Element II.2.D.)

When the convened IRBs requested substantive clarifications or modifications that were directly relevant to the determinations required by the IRBs, the protocols were not returned to the convened IRBs and were approved by the expedited procedure. (Element II.2.D.)

**Response to Draft Site Visit Report**

**Observations:**

A new SOP (HRP-142) for required monthly tasks has been developed. Based on this new SOP, the HRPP plans to track exemption turnaround times on a monthly basis and make adjustments to published review periods. SOP (HRP-141) will establish an annual evaluation process to review metrics associated with exemptions and make adjustments as needed. They will also evaluate the need for additional staff to ensure consistency in turnaround times. These revisions are planned for implementation no later than September 1, 2015.

In response to an Independent Inquiry Panel report, University of Minnesota developed a Work Plan to address the recommendations of the Panel’s report, including a plan for committee review and preparation. The Work Plan, education, and monitoring will be implemented during the fiscal year 2016.

In response to an Independent Inquiry Panel report, University of Minnesota developed a Work Plan to address the recommendations of the Panel’s report, including a plan to revise the continuing review process to be more substantive and establish the expectations for IRB members regarding continuing reviews. The Work Plan, which includes education and monitoring will be implemented during the fiscal year 2016.

Revisions are planned to the IRB process and a new SOP will be implemented during the 2016 fiscal year as part of the Work Plan, that will address all new information that is potentially related to unanticipated problems involving risks to subjects or others, serious or continuing noncompliance, suspensions, or terminations of IRB approval.

Revisions are planned to IRB process and documents to provide written notification to researchers of IRB findings and determinations, including revised IRB letter templates, IRB member checklists, and signature block on the consent forms to inform research staff of the IRB determinations regarding parental signature and assent requirements.

A new SOP on IRB meeting conduct (HRP-106) was developed to differentiate between “conditional approval” (i.e. approval with stipulations) and “defer.” An IRB meeting minutes template and checklist were developed to be consistent with the requirements of the new SOP (HRP-106). Implementation is planned for no later than September 1, 2015. After implementation of the new SOP (HRP-106), monitoring of the completed IRB minutes template, and checklist is planned for the next year at 3, 6, 9, and 12 months. Education is planned for IRB chairs and IRB vice-chairs but specific dates have not been identified.

**Areas of Concern:**

Two new SOPs were developed SOP (HRP-142) on tracking turnaround times for exemptions on a monthly basis and SOP (HRP-141) establishing an annual evaluation to review metrics associated with exemptions. No education or monitoring was planned on the new SOPs. (Element II.2.A.)

University of Minnesota Work Plan includes a new plan for committee review and preparation, including education, and monitoring will be implemented during the fiscal year 2016. (Element II.2.C.)
University of Minnesota Work Plan includes revisions to the IRB process and a new SOP will address all new information that is potentially related to unanticipated problems involving risks to subjects or others, serious or continuing noncompliance, suspensions, or terminations of IRB approval will be implemented during the 2016 fiscal year. The Work Plan, education, and monitoring will be implemented during the fiscal year 2016. (Element II.2.D.)

University of Minnesota Work Plan includes revisions to the continuing review process to make it more substantive and establish expectations for IRB members regarding continuing reviews. The Work Plan, education, and monitoring will be implemented during the fiscal year 2016. (Element II.2.D.)

University of Minnesota Work Plan includes revisions to the IRB process and written notifications to researchers of IRB findings and determinations. The Work Plan, education, and monitoring will be implemented during the fiscal year 2016. (Element II.2.D.)

**Council Determination:**

**Standard is not met.**

### Standard II-5: The IRB or EC maintains documentation of its activities.

#### Draft Site Visit Report

**Observations:**

- IRB records included all required information and were retained for the required time period. IRB records were accessible for inspection and copying by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner. Records were stored safely and in a way that maintained confidentiality.
- IRB minutes reflected the actions of IRB members.

**Areas of Concern:**

- IRB minutes did not document all required information. For example controverted issues were not appropriately documented in the IRB minutes. (Element II.5.B.)

#### Response to Draft Site Visit Report

**Observations:**

- A new SOP on IRB minutes (HRP-108) was developed and will be implemented no later than September 1, 2015. This SOP requires documentation of controverted issues and their resolution on all determinations. IRB chairs, IRB vice-chairs, and IRB staff will be trained on the identification of controverted issues and the new IRB minutes SOP. Initially, every set of IRB minutes will be reviewed for four weeks to ensure compliance and identify required retraining as needed. After successful implementation, random samples of previous IRB minutes will be reviewed at 3, 6, 9, and 12 months to ensure compliance and required retraining as needed.

**Council Determination:**

**Standard is met.**

**Status Report (Element II.5.B.):** Confirm SOP (HRP-108) has been implemented.

**Status Report (Element II.5.B.):** Confirm education was provided to IRB chairs, IRB vice-chairs, and IRB staff on the new IRB minutes SOP (HRP-108).

**Status Report (Element II.5.B.):** Provide the results of monitoring of the IRB minutes to ensure documentation of controverted issues and their resolution on all determinations for four months and describe any actions that took place as a result of the monitoring.