MOUNT SINAI HOSPITAL
Research Ethics Board (REB)
Operating Procedures

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What Activity Requires Review by the REB

All research involving human subjects within Mount Sinai Hospital (MSH) requires approval of the MSH REB prior to the initiation of a research project. The MSH REB has similar authority over investigators from other institutions who may wish to carry out research on Mount Sinai Hospital premises or with Mount Sinai Hospital patients.

The definition of research is outlined in the Tri-Council Policy 2. In summary, human research is considered to include any of the following: if the researcher

- will administer a drug, take a blood sample, do a test or perform any procedure, clinical, therapeutic, or otherwise, upon the person of himself/herself or someone else, for research rather than treatment
- will ask people information whether by telephone, letter, survey, questionnaire or interview
- will review information from patient charts (even their own patients' charts) for research rather than clinical purposes
- will use material derived from people (tissue samples, blood, DNA)
- will be using non-public records (e.g. not the telephone book) which contain identifying information about anyone either directly or indirectly
- will use information previously gathered about anyone, even if anonymized (secondary data analysis)
- will be observing anyone's responses or behaviour, either directly or indirectly

In the event that an investigator cannot determine whether an intended investigation constitutes research (for instance, quality assurance studies do not constitute research), the investigator should approach the Chair of the Research Ethics Board or the Ethics Coordinator for such a determination. Providing such consultation on ethics matters is part of the responsibility of the REB.

Type of Reviews

In accordance with the Tri-Council Policy Statement 2, the MSH REB conducts a proportionate review of research protocols. The default review process is the full REB review process where the REB considers the science and ethics associated with a research protocol in a face-to-face meeting. The discussion of such REB meetings are minuted and the consensus of the REB is forwarded in writing to the principal investigator.

Some research protocols will qualify, based on a decision made by the REB Chair, for an expedited review as is outlined in the proportionate review process of the Tri-Council Policy. Several types of research protocols usually qualify for expedited review:

- protocols involving of minimal risk or protocols where there are minimal incremental risks over standard procedures
- minimal risk protocols where data are collected non-invasively such as questionnaires or direct/indirect observation
- protocols primarily using previously collected data such as chart reviews, data base information such as that used in epidemiological studies (forms are available for retrospective Chart reviews)
- protocols primarily using previously collected tissue or other samples
- protocols that may be involve greater than minimal risk but have previously been reviewed by acceptable peer-review panels or other appropriately constituted (in compliance with Tri-Council Policy) and acceptable REBs

In the case of previously reviewed and approved protocols, the protocol can only be expedited if all relevant documentation accompanies the application. Documentation regarding the correspondence between the investigator and the REB must be submitted with the application so that the review process can be adequately adjudicated. It is insufficient simply to submit a letter of approval. Without such supporting material, protocols will be reviewed by the full REB.

Protocol Review Process

I. Initiating the Review Process

Completed application forms should be directed to the Research Ethics Board Office at Mount Sinai Hospital, Room 1003A, phone (416) 586-4726. Meetings are held bi-monthly depending on the volume of protocols that require full review by the REB. In general the investigator will receive an initial response from the REB within 2 weeks of the REB meeting for a full review. Application forms and guidelines on writing proposals and consent forms are available.

Applications will not be considered until all relevant information for the review is complete. A complete application includes the application form, protocol, consent form(s) (as necessary), all supplemental material (e.g., questionnaires and other assessment tools), the most recent investigator's brochure for clinical trials, the allocated budget and any other relevant correspondence. In addition, other supplemental material necessary for the decision process should be provided before the review. Such supplemental material may include advertisements for recruitment, preclinical information from animal studies depending on the Phase of the clinical trial, and any correspondence from other sources that might be pertinent to the review (such as the details from any other scientific or ethical reviews that have been carried out by other review committees or Boards). The primary cause of delay in ethics approval is incomplete information.

II. The Review Process

a) Full Review Process by the REB

REB reviews will generally involve a detailed assessment from both internal and external reviewers (details for internal/external review forms). If either the Chair of the REB, the internal appraisers of the submitted protocol, or member of the REB at large feel that the protocol cannot be adequately reviewed by the REB, external reviewers are sought.

The REB internal reviewers will present the protocol to the REB at the regularly scheduled REB meetings where all members can meet face-to-face. If REB members are unable to attend the REB face-to-face meeting, REB members should provide relevant comments to the REB office for incorporation into the communication to the investigator. All REB members are routinely provided with the application form and the Consent Form for all studies but have access to the entire protocol for the discussion. On rare occasions the investigator may be invited to attend. Alternatively, the investigator may request attendance at an REB meeting though the investigator will be asked to withdraw during deliberations. Following the Board meeting, any requested modifications are communicated in writing to the investigator as official REB correspondence. All official communication with investigators comes through the Research Ethics Board Office who coordinates the activities of the REB.

During the review process and discussion, the following issues are considered:

<u>Scientific</u>

- background and study rationale
- objectives
- importance of study
- research design
- methodology
- appropriate inclusion/exclusion criteria
- sample size justification
- statistical analysis
- overall scientific merit and validity

<u>Ethical Considerations</u>

- risk-benefit assessment
- the treatment of research subjects with dignity and respect
- method of recruitment (to assess perceived coercion, conflict of interest, privacy)
- method of obtaining consent
- justification for substitute consent if necessary
- funding, budget and sponsor insurance
- consent form and patient information

Decisions will be made by consensus; only in exceptional circumstances will decisions be made by majority vote. A decision can take the form of a final REB approval, a request for minor or major points of clarification or modification, or rejection (as submitted). Typically, a request for modification is made to the investigator. The REB usually delegates the responsibility for reviewing the responses to such requests for modification to the Chair of the REB and directs the Chair to issue approval for the protocol if the investigator has satisfactorily responded to the concerns of the REB. If the response from the investigator is not satisfactory, the Chair will request further modifications or information to ensure that the concerns of the REB have been adequately addressed. Alternatively, the REB may request that the response from the investigator be considered by the full REB. Typically such a request would be required if significant modification to the protocol were deemed necessary. Approval is not granted until the investigator satisfies the REB.

On behalf of the full REB, the Chair of the REB is delegated the authority to review and approve amendments and monitor reports of serious adverse events for all approved protocols. All actions of the Chair of the REB will be reported to the full REB at the next available opportunity.

b) Expedited Review Process

Consistent with the Tri-Council Policy Statement, research protocols receive a proportionate review. While the default remains a full REB review, some research protocols involving minimal incremental risk or those that have had previous ethical review may qualify for an expedited review process. The Chair of the REB is mandated on behalf of the full REB to determine which research protocols qualify for expedited review and to review, modify and approve such expedited protocols. An expedited review will result in either:

- approval
- request for modification
- a full review by the committee (with the attendant requirement for documentation)
- rejection

Protocols that are likely to qualify for an expedited review include:

- protocols previously approved by the University Health Network or another fully affiliated teaching hospital of the University of Toronto
- protocols that involve only minimal risk or minimal incremental risk over standard procedures
- chart reviews, use of secondary data sources, and use of tissue or other samples

Expedited reviews will be carried out by the Chair or delegate, will be reported at the next REB meeting and will be reflected in the minutes of that meeting. Any REB member may request that an expedited protocol receive consideration from the full REB with appropriate discussion. By reporting to the full REB expedited protocols and allowing these protocols to be challenged by any member, the full REB fulfills its obligation to maintain surveillance over all research at Mount Sinai Hospital.

In addition to submitted protocols that qualify for expedited review, on behalf of the full REB, the Chair of the REB is delegated the authority to review and approve amendments and monitor reports of serious adverse events. All such actions of the Chair of the REB will be reported to the full REB at the next available opportunity.

III. The Decision Process

Decisions will be made by consensus; only in exceptional circumstances will decisions be made by majority vote. All documentation and communication will be through the REB Chair and REB Office to investigators. Decisions by the REB will be communicated to the investigator by the REB based on the documentation and deliberations at the REB meeting.

Submissions to the REB may receive approval, approval pending revision and clarification, deferral in order to obtain further information or consultation, or rejection (as submitted). If a submission is rejected, the REB will provide the investigator with a detailed list of the deficiencies so that any resubmission will meet the standards needed to achieve REB approval.

As the REB has an obligation to monitor studies that have been approved, the approval of any study will remain in force for a 12-month period (unless otherwise stipulated). The investigator must seek a renewed approval for a further 12 months prior to the expiration of the current approval. The investigator cannot continue with the study after the 12-month (or stipulated) period without applying for a renewal of the REB approval. Prior to the end of the 12-month period, the REB will send an Annual Renewal Form (application form available) to the principal investigator to be completed before approval can be extended for another 12 months.

IV. Conflict of Interest

Investigators must disclose any real or apparent conflict of interest with regard to the proposal. In addition, REB members of Mount Sinai Hospital must disclose any real or apparent conflict of interest regarding a proposal under review. Members may not be present for any REB discussion regarding a proposal in which they have any vested interest and may not participate in the decision process regarding such a proposal.

V. Appeal Process

The REB will follow the appeal policy as defined in TAHSN.

VI. Rejected Protocols, Appeals, and Mount Sinai Hospital

The Board of Trustees of Mount Sinai Hospital through the Medical Advisory Committee (MAC) has delegated the authority to determine ethical acceptability of research projects to the REB. If the investigator is unable to modify a protocol to make it satisfactory to the REB, the protocol will be rejected by the REB and the research may not proceed at Mount Sinai Hospital. Neither the Board of Trustees nor the MAC may overturn a negative decision (rejection) by the REB but may disallow a project approved by the REB for other administrative, philosophical or resource-based issues.

VII. Subject Confidentiality, Privacy, Recruitment and Surrogate Consent

Some of the most common concerns of REB in regard to reviewing research protocols are the methods of subject recruitment and the methods of obtaining consent.

Regarding subject recruitment, the Board pays special attention to issues of inappropriate or perceived coercion of subjects to participate, conflict of interest for research staff enrolling subjects, and issues of patients' right to privacy. Therefore we ask that investigators to carefully consider and explicitly state in their protocols: who will be enrolling subjects; what is their relationship to the subject; and whether the recruiter holds any have real or perceived power over the intended subjects (such as a therapeutic relationship).

Ensuring confidentiality, while necessary, may not be sufficient to justify the use of patient information. Patient privacy must also be ensured. For example, the process of identifying potential research subjects may seem to violate patients' sense of privacy of privileged information regarding their health status and/or health records even if the researchers claim to keep the information confidential. As a further example, investigators often

request that the REB grant permission for the investigator and the study sponsors to obtain information by reviewing medical charts. To protect such information, the REB requests the specific information to be obtained from such charts so that only relevant and necessary information will be gathered from the patients' confidential and private medical charts.

Generally, referral to a study is best initiated by medical care personnel to whom the patient has already entrusted their private and confidential medical information. Recruitment and consent, on the other hand, is best obtained by persons not involved in the care and treatment of the patient.

Regarding the subject information and consent form, the REB has drafted guidelines to help investigators compose their information and consent forms (see available guidelines).

Surrogate consent is appropriate when **all** of the following criteria are met:

- the research protocol has scientific merit
- it would not be feasible to carry out the research relying only on subjects who are capable to give free and informed consent
- any imposition on the individual subject does not expose the subject to more than minimal risk without the potential for direct benefit
- the research is limited to the investigation of those conditions or aspects of behaviour which are directly related to the identifying characteristic of the group
- the researchers specifically define the process by which surrogate consent will be obtained and how the best interests of the subjects will be protected
- the researchers must demonstrate that they will ascertain the wishes of the subject if the subject becomes competent during the course of the investigation and respect the "dissent" of the incompetent subject

The REB may grant a Waiver of Consent for research carried out in Emergency Health Situations when all of the following criteria are met based on Article 3.8 of the Tri-Council Policy Statement 2:

- a serious threat to the prospective participant requires immediate intervention
- either no standard efficacious care exists or the research offers a realistic possibility of direct benefit to the participant in comparison with standard care
- either the risk is not greater than that involved it standard efficacious care, or it is clearly justified by the prospect for direct benefits to the participant
- the prospective participant is unconscious or lacks capacity to understand the risks, methods and purposes of the research project
- third party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so
- no relevant prior directive by the participant is know to exist

Ongoing Ethical and Scientific Validity and Ethical Conduct

It is a requirement that research involving human subjects be continually reevaluated with respect to ongoing ethical and scientific validity. It is the responsibility of the investigator to ensure that their research projects remain valid with respect to changes in the ethical or scientific context of the study. The REB will request that investigator report immediately on any significant deviations in the protocol or any significant new information that might alter the risk/benefit ratio. In addition, all protocols require annual review to assess any relevant changes that may affect the ongoing validity of the study. This will include a statement that all changes in the

protocol and all adverse event reports have been immediately reported to the REB and that there is no new information, in the opinion of the principal investigator, that threatens the ongoing safety of the study or requires changes in the study protocol. Further, the annual review will assess the progress of the study to ensure that the study remains sufficiently feasible and viable to warrant subject participation. The Annual Review Form will function as a reporting mechanism for investigators of the ongoing ethical conduct of their research.

Should the ethical conduct associated with any specific study be questioned, the REB will investigate any allegations. The REB has the authority to withdraw their previous approval and suspend the study if circumstances warrant.