GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures
2018 Requirements
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GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Ethical Principles of the IRB
Section Number: 1.1
Effective Date: January 1, 2005
Last Revision: May 21, 2012
Replaced SOP Revised On:

In the United States, regulations protecting human subjects first became effective on May 30, 1974. Promulgated by the Department of Health, Education and Welfare (DHEW), those regulations raised to regulatory status policies for the protection of human subjects. The regulations established the Institutional Review Board (IRB) as one mechanism through which human subjects would be protected.

GBMC encourages the conduct of research in and among its facilities, and in collaboration with other educational institutions, agencies, and organizations. While respecting the right of the researcher to full academic freedom in research, GBMC is firmly committed to adhering to the basic ethical principles underlying the acceptable conduct of research involving human subjects, as set forth in *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*.

The Belmont report sets forth the basic ethical principles underlying the acceptable conduct of research involving human subjects. These principles are now accepted as the three quintessential requirements for the ethical conduct of research involving human subjects:

Respect for persons involves recognition of the personal dignity and autonomy of individuals, and special protection of persons with diminished autonomy.

Beneficence entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks.

Justice requires that the benefits and burdens of research be distributed fairly.

The report also describes how these principles apply to the conduct of research. Specifically, the principle of *respect for persons* underlies the need to obtain informed consent; the principle of *beneficence* underlies the need to engage in a risk/benefit analysis and to minimize risks; and the principle of *justice* requires that subjects be fairly selected.

GBMC has set standards for the conduct of research which mandate well-conceived and well-conducted research. Research must also be in keeping with the GBMC Mission. The IRB is charged with assisting in maintaining both these standards, and the GBMC mission.

The mission of GBMC is to provide medical care and service of the highest quality to each patient leading to health, healing and hope with a vision phrase of "To every patient, every time, we will provide the care that we would want for our own loved ones" and dedicated to the Greater Values of Respect, Excellence, Accountability, Teamwork, Ethical Behavior and Results.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Authority of the IRB
Section Number: 1.2
Effective Date: January 1, 2005
Last Revision: July 1, 2024
Replaced SOP Revised On: November 20, 2017

The IRB is an independent administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of GBMC. Ultimate oversight of the IRB belongs to GBMC's Executive Vice President and Chief Medical Officer who serves as the GBMC IRB Signatory and Institutional Official.

The IRB has the authority to "approve, require modifications in (to secure approval), or disapprove all research activities" as stated in 45 CFR 46.109(a) and 21 CFR 56.109(a). Research that has been reviewed and approved by the IRB may be subject to further review and approval or disapproval by GBMC officials. However, those officials may not approve research if it has been disapproved by the IRB (45 CFR 46.112 and 21 CFR 56.112).

The IRB has the authority to "suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects" as stated in 45 CFR 46.113 and 21 CFR 56.113.

The GBMC IRB is a local IRB serving the employees of GBMC and its subsidiaries; however, as a courtesy, GBMC will extend the services of the IRB to the following individuals who wish to have their research reviewed by an expert body:

1. Non-employed GBMC medical staff affiliates.
2. Non-GBMC affiliated individuals in cooperation with a GBMC employed liaison.

Research submitted to the GBMC IRB by a non-GBMC employed/affiliated individual shall be reviewed on a case-by-case basis.

Research submitted to the GBMC IRB by a non-GBMC employed/affiliated individual and approved by the IRB can be suspended or terminated at any time at the discretion of the IRB.

Standard Operating Policies and Procedures (SOP)

Name of SOP: Federalwide Assurance and IRB Registration Process
Section Number: 1.3
Effective Date: August 18, 2014
Last Revision:
Replaced SOP Revised On:

The review of research at GBMC is conducted in accordance with its Federalwide Assurance (FWA). All organizations engaged in human subjects research that are federally-funded or subject to federal regulatory oversight must have a FWA. An FWA is an agreement between the organization and the Office for Human Research Protections (OHRP) in which the organization commits itself to the Health and Human Services (HHS) requirements set forth in 45 CFR 46 as well as Food and Drug Administration (FDA) requirements set forth in 21 CFR 50 and 56 to protect human subjects participating in research. Additionally, the organization commits to the ethical principles outlined in the Belmont Report and to the "Terms of Assurance" of the FWA.

Each organization's FWA is identified by a number that is assigned by the OHRP. GBMC's FWA number is FWA00003849. GBMC must renew its FWA at least every five years in order to maintain an active FWA. GBMC must update its FWA within 90 days after changes occur regarding the legal name of the institution, the designated Human Protections Administrator, or the designated Signatory Official.

Each FWA must list at least one designated IRB. All IRBs designated in a FWA must be registered with the OHRP. GBMC's IRB is registered with the OHRP, and its registration number is IRB00002961. GBMC must renew its IRB registration at least every three years. GBMC must update its IRB registration within 90 days after changes occur regarding the contact person who provided the IRB registration information or the IRB chairperson.

The FWA and IRB registration numbers and expiration dates are posted for public view on the GBMC IRB webpage.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Applicability of the Revised 2018 Common Rule (2018 Requirements)
Section Number: 1.4
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

On January 19, 2017 the U.S. Department of Health and Human Services along with fifteen other federal departments and agencies published in the Federal Register a final rule revising the Federal Policy for the Protection of Human Subjects, otherwise known as the Common Rule.

The revised 2018 Common Rule (hereinafter referred to as the "2018 Requirements") is effective as of January 21, 2019, except for cooperative research requirements which do not go into effect until January 20, 2020.

This policy outlines GBMC's procedural response to the 2018 Requirements in relation to its applicability to human subjects research activities conducted at GBMC HealthCare, Inc. or its subsidiaries.

45 CFR 46.101(a) states that the 2018 Requirements apply "to all research involving human subjects conducted, supported, or otherwise subject to regulations by any Federal department or agency that takes appropriate action to make the policy applicable to such research". However, institutions are given the flexibility to voluntarily extend the 2018 Requirements to all research activities, regardless of funding.

To assure that all research subjects are equally protected and to maintain continuity for the review and oversight of research, GBMC applies the 2018 Requirements to all research, regardless of funding; therefore, all proposed research, regardless of funding, to be conducted at GBMC HealthCare, Inc. or its subsidiaries, shall be submitted to and undergo GBMC IRB review prior to initiation.

All research projects initially approved or determined to be exempt by the GBMC IRB on or after January 21, 2019 shall be subject to and comply with the 2018 Requirements in accordance with 45 CFR 46.101(l)(4).

All research projects initially approved or determined to be exempt by the GBMC IRB prior to January 21, 2019 shall continue to be subject to and comply with the pre-2018 Requirements in accordance with 45 CFR 46.101(l)(3).

45 CFR 46.101(l)(3) permits an institution to decide, on a study-by-study basis, whether or not to apply the 2018 Requirements to a research project initially approved or determined to be exempt prior to January 21, 2019. GBMC recognizes the IRB Chairperson as the only individual having

the authority to make this decision. Should this determination be made, it shall remain permanent and be formally documented in correspondence to the project's principal investigator, other key project personnel as appropriate and IRB meeting minutes.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Membership Requirements
Section Number: 2.1
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

In accordance with Federal regulations 45 CFR 46.107 and 21 CFR 56.107 regarding IRB membership, the GBMC IRB shall:

1. Have a minimum of five members

2. Consist of persons who are "sufficiently qualified through experience and expertise"

3. Have a diverse membership in regards to "race, gender, cultural backgrounds, and sensitivity to such issues as community attitudes"

4. Include persons who are knowledgeable and can "ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice"

5. When reviewing research involving vulnerable populations (e.g. children, individuals with impaired decision-making capacity), consider including "one or more individuals" who are "knowledgeable about and experienced in working with" these types of subjects

6. "Include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas"

7. Include at least two members who are not affiliated with GBMC nor have any immediate family members who are affiliated with GBMC

8. Not have any member participate in the review of research projects in which the member has a conflicting interest, "except to provide information requested by the IRB" (See also SOP Section 2.7—Conflicts of Interest)

9. When deemed necessary, consult with and invite to meetings persons "with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB" (See also SOP Section 2.4--Consultants)

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Appointment of Members
Section Number: 2.2
Effective Date: January 1, 2005
Last Revision: April 17, 2017
Replaced SOP Revised On: September 15, 2014

Individuals expressing an interest in serving on the IRB shall be invited to attend at least one convened meeting to see firsthand how the meetings are conducted and meet the IRB members. Once an individual firmly decides to pursue membership, he/she shall be presented to the convened IRB and approved for membership by a majority vote.

The IRB shall have a Chairperson and up to two Vice Chairpersons.

The Chairperson shall be appointed by the GBMC Executive Vice President/Chief Medical Officer. The duties of the Chairperson shall include but not be limited to the following:

- Presiding over the IRB meetings
- Reviewing all IRB submissions
- Conducting expedited, facilitated and administrative reviews
- Making exempt and not research determinations
- Being available for consult as needed

Vice Chairpersons shall be selected by the Chairperson and approved as Vice Chairperson by a majority vote of the convened IRB. In the event that two Vice Chairpersons are appointed, one shall be the designated Primary Vice Chairperson and the other shall be the designated Secondary Vice Chairperson.

The Primary Vice Chairperson shall assume the duties of the Chairperson in the absence of the Chairperson and in the event the Chairperson is unable to perform his duties due to a conflict of interest.

The Secondary Vice Chairperson shall assume the duties of the Chairperson in the absence of both the Chairperson and the Primary Vice Chairperson.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Alternate Members
Section Number: 2.3
Effective Date: January 1, 2005
Last Revision: September 15, 2014
Replaced SOP Revised On:

The IRB may approve alternate members for any of its primary members, limited in number to no more than one alternate per member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unable to attend a convened meeting. The alternate members shall have similar qualifications to the members that they are representing and comply with the same training requirements as described in Section 2.6. Alternate members shall be given the same IRBNet access as primary members. Alternate members shall have the same voting rights as primary members and shall be counted when determining the existence of a quorum at a meeting. The alternate member shall not be counted as a voting member unless the primary member is absent. The IRB minutes shall document when an alternate member replaces a primary member.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Consultants
Section Number: 2.4
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

In accordance with Federal regulations, 45 CFR 46.107(e) and 21 CFR 56.107(f); an IRB may use consultants and seek out persons who have "competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB."

Whenever possible the IRB shall identify consultants from within GBMC Healthcare, Inc., or GBMC-related health systems. Consultants shall be appointed by the IRB Chairperson (or designee). Consultants may be asked to provide their expertise regarding a specific issue or provide general comments regarding a protocol. Consultants shall not be given access to IRBNet. If the consultant requires documents that are contained in the project's electronic file, they shall be supplied to the consultant in hard copy. As needed, a consultant may be asked to provide his/her comments in writing. Written consultant comments shall be retained in the project's electronic file in the form of a posted board document. Consultants may be asked to attend a convened IRB meeting but shall be excused prior to any voting. Consultants are not considered to be members of the IRB and are not included in determining or establishing a quorum at a convened meeting. However, consultants shall be subject to the conflicting interest rules applicable to IRB members and be required to disclose and document any conflicts of interest by signing a conflict of interest statement as described in SOP Section 2.7—Conflicts of Interest.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Length of Service, Attendance and Removal
Section Number: 2.5
Effective Date: January 1, 2005
Last Revision: September 15, 2014
Replaced SOP Revised On:

Members shall serve on the IRB for an indefinite period of time but no less than two years. Members are expected to attend two thirds of the IRB meetings per year.

Members may resign by providing written notice to the IRB Chairperson. If the resigned member has an alternate, the alternate shall be given the option of becoming a primary member. The alternate may attend meetings and have full voting rights until a new primary member is found.

Members may be removed for good cause, including failure to meet the above stated attendance requirements. Members are removed by a majority vote of the convened IRB and shall be notified in writing of the cause for removal and termination date.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Member Training Requirements
Section Number: 2.6
Effective Date: January 1, 2005
Last Revision: March 18, 2019
Replaced SOP Revised On: November 19, 2012

All new appointees to the IRB shall be obligated to receive basic training in human subjects research. This training shall consist of the "Biomedical Research – Basic/Refresher" course made available on the Collaborative Institutional Training Initiative's (CITI) on-line training website. This course is made up of nine modules plus two elective modules. New IRB members shall select the following two elective modules: 1) Records-Based Research and 2) Research Involving Children. New members must complete the training within 90 days of appointment. It is the responsibility of the new IRB member to submit a copy of their completion certificate to the IRB Office. Members who have not completed the training within the 90 day period can no longer vote until the training requirements are fulfilled and a copy of their completion certificate has been received by the IRB Office.

If the new appointee has completed comparable training within the past three years, this may be accepted in lieu of the above-mentioned GMBC specific CITI course. A letter or certificate of completion as proof must be turned in to the IRB Office within 90 days of appointment.

New IRB members shall be supplied with the following documents in electronic format (PDF) within five working days of their appointment to the IRB:

- GBMC IRB Standard Operating Policies and Procedures (SOPs) Pre-2018 Requirements
- GBMC IRB Standard Operating Policies and Procedures (SOPs) 2018 Requirements
- GBMC IRB Bylaws with SOP Cross References
- *Belmont Report*
- 45 CFR 46 Pre-2018 Requirements (HHS)
- 45 CFR 46 2018 Requirements (HHS)
- 21 CFR 50 (FDA)
- 21 CFR 56 (FDA)

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Conflicts of Interest
Section Number: 2.7
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

Federal regulations require IRB members to abstain from participating in the review of research projects in which the member has a conflicting interest, except to provide information requested by the IRB [45 CFR 46.107(d) and 21 CFR 56.107(e)]. A conflicting interest is defined as any interest in a research project that would make it difficult for the member to objectively review the project in relation to the protection of human research subjects according to federal regulations. Conflicting interests can be financial or non-financial.

Each year, the IRB office staff shall prepare and distribute to each member a personalized conflict of interest statement. New IRB members shall be presented with a personalized conflict of interest statement within five working days of their appointment to the IRB. Each member shall complete and return their conflict of interest statement to the IRB office within 30 days of receipt. Completed conflict of interest statements shall be maintained in each member's file located in the IRB office. Members who fail to complete their conflict of interest statement by the designated deadline shall be brought to the attention of the IRB chairperson who shall determine what disciplinary action shall be taken (e.g. suspension or termination of membership).

When an IRB member abstains from participating in a project review being conducted by the convened IRB, quorum as defined in SOP Section 3.3--Quorum Requirements must be maintained. If quorum fails, no further action or voting may take place. If the abstaining member has an alternate and the alternate is present, the alternate may participate in the review and vote in their stead. Any abstentions, alternate voting and quorum failures shall be documented in the meeting minutes.

The IRB Coordinator shall identify members with conflicting interests prior to assigning expedited reviews. The IRB Coordinator shall assign expedited reviews to a designated reviewer who does not have a conflict with the project involved.

In addition to expedited reviews, the IRB Coordinator shall not assign to any designated reviewer with a conflicting interest any reviews for exempt determination, not human subjects

research determinations, requests for a waiver of IRB jurisdiction or any type of administrative review.

The above-mentioned requirements apply to all initial reviews, continuing reviews, enrollment status changes, and reviews of amendments/revisions.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Compensation of Members
Section Number: 2.8
Effective Date: January 1, 2005
Last Revision: September 15, 2014
Replaced SOP Revised On:

While it is acknowledged that service on the IRB requires a significant investment of time, IRB members do not receive financial compensation. IRB members who are not affiliated with GBMC shall receive compensation for parking in the form of one GBMC complimentary parking ticket for each meeting they attend to be distributed to them at the time of the meeting.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Membership Roster
Section Number: 2.9
Effective Date: January 1, 2005
Last Revision: September 15, 2014
Replaced SOP Revised On:

The IRB shall maintain a roster of IRB members that includes the following information with respect to each member:

- Name
- Gender
- Earned degrees
- Representative capacity (scientific or non-scientific)
- Title and/or area of expertise
- Affiliation with GBMC (affiliated or non-affiliated)
- Membership status (primary or alternate)
- If alternate, who they substitute for

The roster is available from the IRB office upon request.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Meeting Schedule
Section Number: 3.1
Effective Date: January 1, 2005
Last Revision: October 20, 2014
Replaced SOP Revised On:

The IRB shall have up to twelve scheduled meetings per year, or as needed to adequately review initial and ongoing project submissions. The IRB meets on the third Monday of the month. A meeting schedule shall be posted for view on the GBMC IRB webpage.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Agenda and Meeting Materials
Section Number: 3.2
Effective Date: January 1, 2005
Last Revision: November 19, 2018
Replaced SOP Revised On: October 20, 2014

Convened meetings of the IRB shall have an agenda which clearly shows the topics and items that the members will review at the meeting. The agenda is constructed by the IRB office staff and posted on IRBNet prior to each scheduled meeting. The agenda shall also be printed out and distributed to the members in hard copy at the time of the meeting. The agenda is routinely divided into fourteen sections:

- Welcome and General Announcements
- Review of Previous Minutes
- New Project Presentations
- Continuing Reviews for Renewal
- Project Closures
- Enrollment Status Changes
- Amendments and Revisions
- Adverse Events
- Deviations
- Reports—Updates—Follow-up
- NCI-CIRB and Other Ceded Project Reviews
- Reviews Performed by the Chairman
- Review Board Business
- Adjournment and Next Meeting Date

Meeting materials are received via IRBNet in the form of electronic submission "packages". Submission packages are electronically "shared" with the members over the course of several weeks prior to the scheduled meeting date. It is the responsibility of each member to access IRBNet and review the shared submission packages. IRB members shall review the submission materials in advance of the meeting in enough depth to be familiar with the materials and prepared to discuss them at the meeting.

GREATER BALTIMORE MEDICAL CENTER
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Standard Operating Policies and Procedures (SOP)

Name of SOP: Quorum Requirements
Section Number: 3.3
Effective Date: January 1, 2005
Last Revision: November 19, 2018
Replaced SOP Revised On: October 20, 2014

The IRB shall, except when an expedited review procedure is used, review proposed research at convened meetings at which a majority of the IRB members are present, including at least one member whose primary concerns are in nonscientific areas [45 CFR 46.108(b) and 21 CFR 56.108(c)]. When the IRB reviews FDA regulated research, there shall be at least one member present who is a licensed physician. The IRB Chairperson and Vice Chairperson shall be voting members and count toward quorum. Quorum is defined as being fifty percent of the primary voting membership (including alternate members who may replace primary voting members) plus one.

The IRB meeting shall not convene until quorum is established. It is the responsibility of the IRB Coordinator to inform the IRB Chairperson when quorum has been established. It shall also be the responsibility of the IRB Coordinator to inform the membership if quorum is lost during a meeting (e.g. a member who abstains from voting due to a conflict of interest). If quorum fails, no further action or voting may take place unless quorum is re-established.

Every effort shall be made to convene meetings at which all members are physically present; however, members who are not able to be physically present during a convened meeting may participate by telephone conference call. Members participating via teleconferencing shall be counted as part of the quorum, as long as they have had opportunity to review all of the meeting materials.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Voting, Decisions and Actions
Section Number: 3.4
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

The IRB shall review and have authority to "approve, require modifications in (to secure approval), or disapprove all research activities" [45 CFR 46.109(a) and 21 CFR 56.109(a)].

Voting shall take place during a convened meeting where quorum as defined in SOP Section 3.3—Quorum Requirements has been established. The only individuals who may vote shall be primary IRB members and alternates in the absence of their designated primary member. The IRB Chairperson and Vice Chairperson(s) shall be voting members. Members participating via teleconferencing may vote, as long as they have had opportunity to review all of the meeting materials.

The following submission types, when reviewed by the convened IRB, must undergo a formal voting and/or approval process:

1. New Projects,
2. Continuing Review/Progress Reports,
3. Independent Annual Reviews
4. Enrollment Status Changes,
5. Amendment/Modifications, and
6. Response/Follow-ups when in response to an approval with conditions

In order for research to be approved by the convened IRB, "it shall receive the approval of a majority of those members present at the meeting" [45 CFR 46.108(b) and 21 CFR 56.108(c)]. Majority is defined as being fifty percent of the members present plus one.

All research proposals are submitted and reviewed via IRBNet in the form of electronic submission "packages". In accordance with 45 CFR 46.109(a) and 21 CFR 56.109(a) cited above and the choices available in IRBNet, the IRB shall take one of the following fourteen actions in response to each submission "package" received:

1. Acknowledged -- signifies that the IRB has acknowledged the submission and corresponding documents as received. No further action is required.

[This determination applies only to submissions that do not undergo a formal voting and/or approval process.]

2. Approved -- signifies that the IRB has approved the submission and corresponding documents as received. No further action is required.

3. Approved with conditions -- signifies that the IRB has approved the submission and corresponding documents but specific conditions must be satisfactorily met to secure full approval.

   [This determination applies only to submissions that undergo a formal voting and/or approval process.]

   When a submission is approved with conditions, the principal investigator shall be notified as to the pending approval and the conditions that must be met to secure full approval.

   The IRB shall designate a member who will be responsible for reviewing responsive material and determining whether or not the conditions of the approval have been satisfactorily met. This designation is not necessary if it is determined that the matter will go back to a meeting of the convened IRB.

   Upon the determination that the approval conditions have been satisfactorily met, the designated reviewer of the responsive material shall notify the IRB Coordinator of the effective date of the decision, indicating that the research activities may be initiated. The principal investigator shall be notified regarding the determination, and the action taken shall be reported back to the convened IRB at the next scheduled meeting.

   Research activities may not proceed as set forth in the submission until the specified conditions have been satisfactorily met and full approval from the IRB has been granted, unless dictated otherwise by the IRB.

   If no responsive action is taken by the principal investigator within 90 days of being notified of the approved with conditions decision, the submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety to be reconsidered.

4. Closed -- signifies that a project has been permanently closed and all research activities have ceased.

5. Exempt -- signifies that the IRB Chairperson or Vice Chairperson has determined that the submission and/or proposed research activity qualifies for an exemption from IRB review under 45 CFR 46.104.

6. Information Required -- signifies that the IRB has accepted the submission and corresponding documents but additional information is being requested.

   The principal investigator shall be notified as to the additional information being requested.

   If no responsive action is taken by the principal investigator within 90 days of being notified, the submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety.

7. Modifications Required -- signifies that the IRB has accepted the submission and corresponding documents but specific modifications are being requested.

   The principal investigator shall be notified as to the modifications being requested.

   If no responsive action is taken by the principal investigator within 90 days of being notified, the submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety.

8. Not Approved -- signifies that the IRB has found significant and sufficient fault with a submission to warrant its disapproval.

   In the event that this occurs, the principal investigator shall be notified as to the reason for the disapproval and the corrective action, if any, that could be taken to secure approval. No further action will be taken by the IRB. Any decision to appeal in accordance with SOP Section 4.7—Appeal of Review Actions and Determinations or resubmit rests with the principal investigator.

   [This determination applies only to submissions that undergo a formal voting and/or approval process by the convened IRB.]

9. Not Research -- signifies that the IRB Chairperson or Vice Chairperson has determined that the submission and/or proposed research activity does not meet the definition of human subjects research as stated in 45 CFR 46.102.

10. Referred to Full Board -- signifies that the IRB Chairperson or Vice Chairperson has determined through an expedited review procedure that the submission and/or proposed research activity is more appropriately suited for review by the convened IRB.

11. Suspended -- signifies that IRB approval has been suspended and a temporary cessation of some or all research activities has taken place.

12. Tabled Without Action -- signifies that the IRB was unable to initiate voting. This most commonly takes place when quorum is lost but may also take place under other circumstances.

    In the event that quorum is lost, the principal investigator shall be notified that the submission was tabled without action. If the submission and/or proposed research activity meets the criteria for an expedited review, it shall be presented to the IRB Chairperson or Vice Chairperson for review. If the submission does not meet the criteria for an expedited review, it shall be placed on the agenda for the next scheduled meeting of the convened IRB.

    In the event that a submission is tabled without action with a directive from the IRB, the principal investigator shall be notified of the directive. If no responsive action is taken by the principal investigator within 90 days of being notified, the submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety.

13. Terminated -- signifies that IRB approval has been terminated and a permanent cessation of all research activities has taken place.

14. Withdrawn -- signifies that the IRB office staff has withdrawn the submission "package". No further action will be taken on the submission.

All voting, decisions and actions shall be documented in the IRB meeting minutes as described in SOP Section 3.5—Minutes of the Meeting.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Minutes of the Meeting
Section Number: 3.5
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

In accordance with Federal regulations; the IRB meeting minutes "shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on the actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution" [45 CFR 46.115(a)(2) and 21 CFR 56.115(a)(2)].

The IRB Coordinator and IRB Assistant shall attend the IRB meetings and take sufficiently detailed notes to document IRB discussions and determinations. A draft version of the minutes shall be prepared by the IRB Assistant. The IRB Coordinator shall then review, edit and finalize the meeting minutes.

Prior to the next scheduled IRB meeting the finalized minutes shall be posted electronically on IRBNet for review by the IRB members. The minutes shall then be presented for consideration and acceptance at the next scheduled IRB meeting. If any corrections are warranted, the minutes shall be edited by the IRB Coordinator and brought back to the convened IRB at the next scheduled meeting. Once the minutes are formally accepted by the convened IRB, they shall not be altered by anyone.

The IRB shall, in accordance with 45 CFR 46.108(a)(3)(i) and 21 CFR 56.109(e), report back to "the institution" (GBMC) its "findings and actions" by submitting a copy of all IRB meeting minutes on a monthly basis to the Chief Medical Officer and Signatory Official on GBMC's Federalwide Assurance.

The IRB meeting minutes shall be kept both in hard copy and electronically in IRBNet indefinitely.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Confidentiality
Section Number: 3.6
Effective Date: November 17, 2014
Last Revision:
Replaced SOP Revised On:

Proceedings of IRB meetings and all shared materials relating to the meetings are considered confidential. IRB members shall not discuss, disclose, or reproduce any confidential IRB information, except as necessary to perform legitimate duties as an IRB member.

Each IRB member shall agree to and sign an Institutional Review Board Member Confidentiality Agreement. Signed confidentiality agreements shall be maintained in each member's file located in the IRB office.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Criteria for Human Subjects Research Approval
Section Number: 4.1
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

The GBMC Institutional Review Board reviews and approves research in accordance with 45 CFR 46 (Federal Policy for the Protection of Human Subjects--Common Rule), 21 CFR 56 (Food and Drug Administration) and other regulations and laws as applicable.

In order for a project to be reviewed by the IRB, the proposed activity shall first meet the following two federal definitions for human subjects research:

1. Research
2. Human subject

Research is defined in the Common Rule at 45 CFR 46.102(l) as meaning "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." The Food and Drug Administration list of definitions at 21 CFR 56.102 does not include "research".

A human subject is defined in the Common Rule at 45 CFR 46.102(e) as meaning "a living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens."

The Food and Drug Administration at 21 CFR 56.102(e) defines a human subject as meaning "an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient."

All activities meeting the above-mentioned federal definitions for human subjects research shall be reviewed by the IRB. Activities that fail to meet the federal definition of research or do not involve human subjects are excluded from IRB review (See SOP Section 5.4—Not Human Subjects Research).

In order to approve research involving human subjects, the IRB shall determine that all of the following regulatory criteria taken from 45 CFR 46.111(a)(1-7) and 21 CFR 56.111(a)(1-7) 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 will 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 (e.g., 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. The IRB should be particularly cognizant of the special problems of research that involves a category of *subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons*."

   [Italics: The list of vulnerable populations in the Food and Drug Administration regulations at 21 CFR 56.111(a)(3) reads as follows: "children, prisoners, pregnant women, handicapped, or 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 and/or part 50 of title 21.

5. "Informed consent will be appropriately documented or appropriately waived in accordance with" 46.117 and/or "IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects" dated July 2017.

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."

All IRB members shall review enough information so they will be able to determine whether the research meets the above regulatory criteria for approval.

[CFR Title 21 Parts 50 and 56 only apply to research projects that are FDA regulated]

[For IRB review and approval of research using the "limited IRB review" process as described in 45 CFR 46.104 and 46.111 see SOP Section 5.2—Expedited Reviews and SOP Section 5.3—Exempt Determinations].

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Submission Deadlines and Requirements
Section Number: 4.2
Effective Date: January 1, 2005
Last Revision: November 19, 2018
Replaced SOP Revised On: December 30, 2014

GBMC uses IRBNet for the electronic administration and management of its IRB. All submissions for review by the IRB must be sent electronically via IRBNet. Paper submissions are not accepted.

Submissions are due the first Monday of every month unless otherwise indicated. A schedule of IRB meeting dates with corresponding submission deadlines shall be posted on the GBMC IRB webpage. Posted submission deadlines apply to submissions requiring full board review only. All other submission types (e.g. expedited reviews, exempt determinations) are handled on an ongoing basis and not subject to submission deadlines.

All submission forms and templates shall be made available and maintained by the IRB Coordinator within IRBNet under "Forms and Templates" located on the "Submission Manager" page. Submissions are sent to the IRB Office via IRBNet in the form of electronic submission "packages."

The IRB office staff shall perform preliminary reviews of all submission packages for determination of completeness and accuracy. A submission package shall not be assigned for final review by the IRB until it is determined to be complete by the IRB office staff. In the event that a package is incomplete and/or requires revisions, the individual who submitted the package shall be notified via email and/or an internal IRBNet communication by the IRB office staff, and the package shall be "unlocked" so the required revisions can be completed. If no responsive action is taken within 90 days of being notified, the submission package shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety.

All submission packages must be electronically signed by the principal investigator of the project. The IRB office staff shall not process any package that has not been signed by the principal investigator. Signatures made on behalf of the principal investigator are not acceptable.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Review Fees
Section Number: 4.3
Effective Date: January 21, 2019
Last Revision: July 1, 2024
Replaced SOP Revised On:

A review fee shall be charged for all initial project reviews, continuing reviews and independent annual reviews performed by the GBMC IRB, and reviews for projects ceded to an external IRB.

The fees collected vary according to the type of review (e.g. full board, expedited, ceded) as follows:

Projects Approved After July 1, 2024

FULL BOARD REVIEWS	INITIAL REVIEW	CONTINUING AND INDEPENDENT ANNUAL REVIEWS
Sponsored	$2,000	$1,000
Non-funded	$100	$50
EXPEDITED REVIEWS		
Sponsored	$500	$250
Non-funded	$100	$50
CEDED REVIEWS		
External IRB Oversight	$500	$250

Projects Approved Prior to July 1, 2024

FULL BOARD REVIEWS	CONTINUING REVIEWS AND INDEPENDENT ANNUAL REVIEWS
Sponsored	$500
Non-funded	$25

EXPEDITED REVIEWS	
Sponsored	$100
Non-funded	$25
CEDED REVIEWS	
External IRB Oversight	$100

No review fees shall be charged for the following:

- Permanent project closures
- Enrollment status change notifications
- Amendments/revisions
- Adverse and other reportable events
- Deviation reports
- General reporting/information only submissions
- Exempt determinations
- Not research determinations
- Humanitarian use device protocols
- Single patient (compassionate) use protocols

Review fees shall apply to the following individuals who use the GBMC IRB to evaluate their research (See SOP Section 1.2—Authority of the IRB):

3. Non-GBMC employed medical staff affiliates
4. Non-GBMC affiliated individuals in cooperation with a GBMC employed liaison

The IRB shall waive the review fees for all employees of GBMC and its subsidiaries conducting research as part of their employment. A department, as a whole, shall not be charged review fees.

The IRB shall waive the review fees for residents, fellows and other graduate students affiliated with GBMC.

All fees collected must be in the form of a check (payable to GBMC IRB). No cash or charge payments will be accepted. Payment is due upon receipt of invoice. IRB review fees are not refundable.

The fee schedule shall be subject to change without advance notice by a majority vote of the convened IRB.

The fee schedule shall be posted on the GBMC IRB webpage.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Investigator Conflicts of Interest
Section Number: 4.4
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

Individuals directly involved in the conduct, design or reporting of research involving human subjects should not have more than a minimal personal or financial interest in the company that sponsors the research or owns the product(s) being used as a part of the research.

Relationships with research sponsors can create, or appear to create, conflicts of interest. While having a conflict of interest does not imply wrongdoing or inappropriate activity, conflicts do require review and management to ensure that the conflict does not improperly influence, or appear to improperly influence, the research. It is, therefore, critical that all conflicts be disclosed promptly and thoroughly. It is the responsibility of the IRB, under the guidance of the GBMC Corporate Compliance Officer, to determine if a disclosed conflict of interest is significant enough to affect the design, conduct or reporting of the research.

All principal investigators, co-investigators and sub-investigators shall complete a project-specific conflict of interest statement:

1. At time of initial application,
2. Annually at time of continuing review or independent annual review until the project is permanently closed, and
3. Within 30 days of discovering and/or acquiring a new conflict of interest.

Only GBMC IRB conflict of interest statement forms will be accepted.

If the research is funded, either directly or indirectly, by the public health service, the directives as set forth in the GBMC compliance policy "Policy on Financial Conflicts of Interest in Public Health Service Funded Research" shall be followed in compliance with 42 CFR 50, subpart F.

If the research is a non-funded retrospective chart review, the requirement for submitting a formal conflict of interest statement is waived.

All completed conflict of interest statements shall be submitted to the IRB for review via IRBNet. If the IRB determines that a significant conflict of interest has been disclosed, a formal management plan shall be developed and implemented in cooperation with the GBMC compliance and legal departments. The plan shall specify the actions that have been, and shall be, taken to manage the disclosed significant conflict of interest. The conditions or restrictions that may be applied include, but are not limited to:

1. Disclosure of the conflict of interest to research participants (e.g. declaration statement incorporated into the informed consent document);

2. Change in responsibilities (e.g. removal as principal investigator) or disqualification from participating in all or a portion of the research (e.g. no involvement with recruiting and/or consenting participants);

3. Modification of the research plan;

4. Appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of the research against bias resulting from the conflict of interest;

5. Reduction or elimination of the conflict of interest (e.g. sale of an equity interest);

6. Severance of relationships that create the conflict of interest; or

7. Public disclosure of the conflict of interest (e.g. when presenting or publishing the research)

Whenever the IRB implements a management plan, the IRB shall monitor investigator compliance on an ongoing basis until the completion of the research project.

If the investigator believes that a determination made by the IRB is not appropriate or is based on erroneous information, the investigator may request an appeal by submitting a written request to the IRB Chairperson.

Failure to comply with the IRB's recommendations as set forth in the formal management plan may result in suspension of the involved research project and other applicable sanctions.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Investigator Qualifications, Responsibilities and Training Requirements
Section Number: 4.5
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

Principal investigators are obligated to design and conduct human subjects research in accordance with the ethical principles of the Belmont Report, federal regulations, state and local laws, and GBMC institutional policies, including those policies specific to the IRB. Principal investigators should not undertake responsibility for human subjects research unless they understand these requirements and are willing to uphold them.

An IRB approved principal investigator can be any of the following:

- employees of GBMC and its affiliates
- physicians who are a member of GBMC's medical staff
- residents or fellows affiliated with GBMC
- non-affiliated individuals who have a designated GBMC liaison

Principal investigators shall have the appropriate education, training, and experience to assume full responsibility for the conduct of their human subjects research. Although the principal investigator may delegate study-related tasks to appropriately qualified and trained study personnel, the principal investigator shall maintain oversight of and retain ultimate responsibility for the conduct of those who perform delegated functions.

Principal investigators are responsible for but are not limited to:

- Designing and conducting research in a manner that minimizes risk and maximizes benefit, using sound research design and generally accepted scientific and/or scholarly standards.
- Ensuring that adequate resources and facilities are available to carry out the proposed research project.
- Submitting and obtaining IRB approval prior to the initiation of any research-related activities.
- Ensuring that all members of the research staff, and all others directly involved in the conduct of the research project, are qualified by education, training, and experience to perform their research responsibilities.
- Recruiting subjects in a fair and equitable manner, weighing the potential benefits of the research to the participants against their vulnerability and the risks to them.
- Not enrolling subjects prior to IRB approval of the research project or after expiration of IRB approval.

- Ensuring that legally effective and approved informed consent has been obtained, using an adequate and appropriate consent process, and ensuring the consent process is documented appropriately unless the IRB has granted a waiver of informed consent or documentation of informed consent.
- Ensuring that the informed consent process is led only by individuals who have appropriate training and knowledge of the research, including any investigational product involved, in order to discuss the risks and benefits of the research with prospective subjects.
- Conducting the research project in strict accordance with the current IRB-approved research protocol except where a change may be necessary to eliminate an apparent immediate hazard to a given human research subject.
- Reporting promptly to the IRB proposed changes in the research.
- Implementing no changes in the approved protocol, informed consent or other IRB approved research related documents without prior IRB approval, except in an emergency when it is necessary to safeguard the well-being or human subjects.
- Obtaining continuing review and approval of ongoing research at the interval determined by the IRB (at least annually) to avoid expiration of IRB approval and cessation of all research activities.
- Promptly reporting to the IRB any serious & unexpected adverse events, unanticipated problems involving risks to subjects and/or others, or any changes made to eliminate apparent immediate hazards to subjects.
- Reporting promptly to the IRB any deviations from the currently approved research protocol.
- Complying with all IRB policies, decisions, conditions, and requirements.

As mentioned above, principal investigators are responsible for ensuring that all members of the research staff, and all others directly involved in the conduct of the research, are qualified by education, training, and experience to perform their research responsibilities. This includes human subjects research training.

Federal regulations for the protection of human subjects do not require investigators and research staff to obtain training in the protection of human subjects in research. However, the OHRP strongly recommends that an institution holding an OHRP-approved Federalwide Assurance (FWA) and their designated IRB establish training oversight mechanisms appropriate to the nature and volume of their research.

In response to this federal recommendation, the IRB has made it policy that all principal investigators, co-investigators and designated research project coordinators receive and maintain certification in human subjects research and comply with the following by:

1. Including evidence of human subjects research training in all new project submission packages (exempt studies excluded).
2. Including evidence of human subjects research training in all continuing review and independent annual review submission packages.

3. Including evidence of human subjects research training in all amendment submission packages requesting a study team change and/or addition involving the principal investigator, co-investigator or project coordinator.
4. The evidence of human subjects research training submitted shall be current with a completion date within the past three years.
5. The evidence of human subjects research training shall consist of the appropriate GBMC IRB approved training course(s) or documented equivalent training obtained elsewhere.

Submission packages that do not contain the above-mentioned, required evidence of human subjects research training shall not be processed until such evidence is included.

The IRB has approved three training courses in human subjects research. These courses are made available on the Collaborative Institutional Training Initiative's (CITI) on-line training website. The web address and instructions for accessing the training courses are available on the GBMC IRB webpage.

The IRB approved training courses and modules are as follows:

Basic Course in Biomedical Research
History and Ethics of Human Subjects Research
Basic Institutional Review Board (IRB) Regulations and Review Process
Informed Consent
Research and HIPAA Privacy Protections
Populations in Research Requiring Additional Considerations and/or Protections
Genetic Research in Human Populations
FDA-Regulated Research
Recognizing and Reporting Unanticipated Problems Involving Risks to Subjects or Others in Biomedical Research
Conflicts of Interest in Research Involving Human Subjects

Elective Modules
Records-Based Research
Social and Behavioral Research (SBR) for Biomedical Researchers

Research Involving Children
Research Involving Pregnant Women, Human Fetuses, and Neonates
Research with Older Adults
Stem Cell Research Oversight (Part 1)
Stem Cell Research Oversight (Part 2)
Avoiding Group Harms—U.S. Research Perspectives

All nine of the "Basic Course in Biomedical Research" modules plus two "Elective Modules" must be completed with a score of at least 80% on all quizzes to pass the entire course.

Investigators who limit their activities to records-based research may limit their human subjects research training to the following course and modules:

Basic Course in Records-Based Research
All modules must be completed with a score of at least 80% on all quizzes to pass the entire course.
History and Ethics of Human Subjects Research
Basic Institutional Review Board (IRB) Registration and Review Process
Records-Based Research
Research and HIPAA Privacy Protections

Investigators who limit their research activities to the use of surveys and/or questionnaires may limit their human subjects research training to the following course and modules:

Basic Course in Survey/Questionnaire Research
All modules must be completed with a score of at least 80% on all quizzes to pass the entire course.
History and Ethics of Human Subjects Research
Basic Institutional Review Board (IRB) Registration and Review Process
Social and Behavioral Research (SBR) for Biomedical Researchers
Informed Consent

Research and HIPAA Privacy Protections

The following modules are available for general interest and do not count toward the completion of the above-mentioned required courses:

Supplemental Modules
Consent and Subject Recruitment Challenges: Remuneration
Consent with Subjects Who Do Not Speak English
Cultural Competence in Research
Gender and Sexuality Diversity (GSD) in Human Research
Humanitarian Use Devices (HUDs)
I Have Agreed to be an IRB Community Member. Now What?
International Studies
The IRB Administrator's Responsibilities
The IRB Member Module – What Every New IRB Member Needs to Know
Phase 1 Research: Understanding Phase 1 Research
Phase 1 Research: Protecting Phase 1 Subjects
Research and Decisionally Impaired Subjects
Research Involving Subjects at the End of Life
Research with Critically Ill Subjects
Research with Persons who are Socially and Economically Disadvantaged
Single Institutional Review Board (sIRB) Use & Administration: Authorization Agreements
Single Institutional Review Board (sIRB) Use & Administration: When Relying on a sIRB
Single Institutional Review Board (sIRB) Use & Administration: When Serving as a sIRB of Record
Students in Research
Vulnerable Subjects—Research Involving Workers/Employees

The IRB will accept evidence of comparable human subjects research training from an outside source provided the completion date is within the current three years; however, the IRB prefers that the above-mentioned GBMC IRB approved course(s) and modules be taken.

The IRB can, at its discretion, require an investigator or other research staff member to take any combination of the above-mentioned courses and/or individual modules regardless of the human subjects research training evidence provided.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Notification and Documentation of Review Actions and Determinations
Section Number: 4.6
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

The IRB is obligated to report "its findings and actions to the investigator and the institution" as stated in 45 CFR 46.108(a)(3)(i) and comparably stated in 21 CFR 56.109(e). Therefore, the GBMC IRB shall notify in writing the principal investigator and institutional officials of its actions and determinations relative to approval, disapproval, required modifications, suspensions, terminations and other information and matters for which such disclosure is required.

All research proposals are submitted and reviewed via IRBNet in the form of electronic submission "packages". In accordance with 45 CFR 46.109(a) and 21 CFR 56.109(a) which states that the IRB "shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities" and in line with the choices available in IRBNet, the IRB shall take one of the following 14 actions in response to each submission "package" received:

1. Acknowledged
2. Approved
3. Approved with Conditions
4. Closed
5. Exempt
6. Information Required
7. Modifications Required
8. Not Approved
9. Not Research
10. Referred to Full Board
11. Suspended
12. Tabled without Action
13. Terminated
14. Withdrawn

For definitions and more complete details regarding these 14 actions, see SOP Section 3.4—Voting, Decisions and Actions.

All IRB actions and determinations are conveyed by IRB office staff to the principal investigator and other key project personnel as soon as possible after a convened meeting of the IRB or any review performed by the IRB Chairperson or his designee. Each action is recorded within the appropriate electronic submission "package" and triggers a brief (action only) auto-generated

email notification via IRBNet. Each action notification is then followed by a detailed letter addressed to the principal investigator. Follow-up letters are drafted by the IRB Assistant and include, at a minimum, the following information:

1. Project title
2. Submission type (e.g. new project, continuing review)
3. Action
4. Approval/Effective date
5. Review type (e.g. Full Board, Expedited)
6. New expiration date (for continuing reviews)

If a determination is made by the IRB requiring a response from the principal investigator, it shall be stated within the body of the letter.

All draft letters are reviewed, edited as appropriate, electronically signed and published in IRBNet as a board document by the IRB Coordinator. The act of publishing a board document triggers an auto-generated email to key project personnel alerting them that there is a document available for review. It is the responsibility of the appropriate study personnel to access IRBNet and review published board documents.

IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer and Signatory Official on GBMC's Federalwide Assurance. (See also SOP Section 3.5—Minutes of the Meeting)

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Appeal of Review Actions and Determinations
Section Number: 4.7
Effective Date: January 1, 2005
Last Revision: January 15, 2018
Replaced SOP Revised On: November 21, 2016

IRB review actions and determinations are conveyed by IRB office staff to the principal investigator and other key project personnel as soon as possible after a convened meeting of the IRB or any review performed by the IRB Chairperson or his designee (See SOP Section 4.6—Notification and Documentation of Review Actions and Determinations).

If the principal investigator disagrees with an action taken by the IRB, he/she may make an appeal to the IRB. The appeal must be submitted within 30 days from the date of the decision letter. The appeal must be made via IRBNet as a "subsequent package" and contain the rationale for the appeal and any supporting information and/or documents. If no appeal is made within the 30 day timeframe, the IRB's original decision shall be considered final.

The IRB office staff shall place submitted appeal "packages" on the agenda for the next scheduled meeting of the convened IRB. The principal investigator may be required to attend the meeting to present his/her appeal to the IRB and be available to answer questions.

The IRB shall take one of the following three actions after considering the appeal:

1. Approve the appeal as presented
2. Approve the appeal as presented with conditions
3. Disapprove/not approve the appeal

The IRB's action in response to the appeal shall be conveyed by the IRB office staff to the principal investigator as soon as possible after the convened meeting of the IRB. The action shall be recorded within the appeal submission "package" and trigger a brief (action only) auto-generated email notification via IRBNet. The action notification shall then be followed by a detailed letter addressed to the principal investigator. If the appeal receives an "approved with conditions" determination by the IRB requiring a response from the principal investigator, the conditions shall be stated within the body of the letter. If no responsive action is taken by the principal investigator within 30 days of being notified of the IRB's "approved with conditions" determination, the appeal package shall be administratively withdrawn and the IRB's original decision shall be considered final. Only one appeal shall be allowed on a given matter. The concluding determination made by the IRB regarding the appeal is final and not subject to further appeal.

IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer

and Signatory Official on GBMC's Federalwide Assurance. (See also SOP Section 3.5—Minutes of the Meeting)

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Initial Full Committee Reviews
Section Number: 5.1
Effective Date: January 1, 2005
Last Revision: November 19, 2018
Replaced SOP Revised On: December 18, 2017

Research projects involving greater than minimal risk to human subjects, that do not qualify for expedited review (See SOP Section 5.2—Expedited Reviews) or an exempt determination (See SOP Section 5.3—Exempt Determinations) must be reviewed by the convened IRB at a regularly scheduled meeting. Research activities cannot be initiated until the project has been reviewed and approved by the IRB.

In order to approve research, the IRB must receive project information in sufficient detail to determine that all regulatory criteria for the approval of research cited at 45 CFR 46.111(a)(1-7) and/or 21 CFR 56.111(a)(1-7) are satisfied (See also SOP Section 4.1—Criteria for Human Subjects Research Approval)

All project information must be sent electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The electronic submission "package" for an initial full committee review shall contain but not be limited to the following documents:

1. Application for New Research Project
2. Research Plan/Protocol
3. Informed Consent Form
4. HIPAA Research Authorization (unless combined with informed consent form)
5. Conflict of Interest Statements
6. Evidence of Human Subjects Research Training
7. Curriculum Vitae of Principal Investigator (unless already on file)

All research projects shall have one designated principal investigator who will have full responsibility for the conduct of the research and the research personnel.

The principal investigator or a qualified substitute must attend the initial convened IRB meeting in person to present a brief overview of the research. The IRB shall use this time to ask the principal investigator questions to clarify or explain any issues that are unclear or about which they may have concern. At the conclusion of the presentation and question and answer period, the principal investigator shall be excused while the IRB further discusses the proposed research, votes and makes a formal decision as described in SOP Section 3.4—Voting, Decisions and Actions. The IRB's decision shall be conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible after the convened meeting as

described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Expedited Reviews
Section Number: 5.2
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

In accordance with federal regulations 45 CFR 46.110 and 21 CFR 56.110, expedited review procedures may be used for certain kinds of research involving no more than minimal risk. "Minimal risk means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests" [45 CFR 46.102(j) and 21 CFR 56.102(i)].

In order to be eligible for expedited review, the proposed research activity must fall within one or more of the following expedited review categories:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

    a. research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

    b. research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

    a. from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

    b. from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means.

   Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

   Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects [45 CFR 46.101(b)(4)]. This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt

from the HHS regulations for the protection of human subjects [45 CFR 46.101(b)(2) and (b)(3)]. This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the convened IRB as follows:

    a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

    b. where no subjects have been enrolled and no additional risks have been identified; or

    c. where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

(Source for above list: Federal Register, November 9, 1998, Volume 63, Number 216)

Expedited review procedures may also be used for the following:

1. "Minor changes in previously approved research during the period (of one year or less) for which approval is authorized" [45 CFR 46.110(b)(ii) and 21 CFR 56.110(b)(2)]. The term "minor changes" is not defined by either the OHRP human subjects regulations (45 CFR 46) or FDA human subjects regulations (21 CFR 50); however, minor changes should have no substantive effect upon an approved protocol and should not increase risk to the subject. The following are examples of changes that may be viewed as minor by the GBMC IRB:

    - A reduction in physical and/or psychological risk/discomfort to participants
    - Minor editorial modifications that do not alter meaning or procedure
    - Removing questions from a questionnaire
    - Narrowing the range of inclusion criteria
    - Broadening the range of exclusion criteria
    - New or changed recruitment/advertising methods and/or materials (flyers, Internet, etc.)
    - New or changed patient materials (diaries, medical alert cards, etc.)
    - An increase in the number of study visits for safety purposes
    - Minor increase/decrease in the number of subjects to be enrolled
    - Minor change in remuneration amount or type
    - Additions or deletions of project team members (including principal investigator)
    - Any change that does not alter the risk/benefit ratio

2. ”Research for which limited IRB review is a condition of exemption under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8).

As stated in 45 CFR 46.110(b)(2) and 21 CFR 56.110(b)(2), expedited reviews “may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB.” The GBMC IRB recognizes the following two individuals as having the authority to perform expedited reviews:

1. IRB Chairperson
2. IRB Vice Chairperson

The above named designated reviewers shall “exercise all of the authorities of the IRB except that the reviewers may not disapprove the research” [45 CFR 46.110(b)(2) and 21 CFR 56.110(b)(2)].

All new project, continuing review, and amendment/modification submissions shall be screened by the IRB Coordinator to determine whether a submission may qualify for expedited review. If the IRB Coordinator determines that a submission meets the regulatory criteria for expedited review, the submission shall be forwarded to the IRB Chairperson for review. (Note: Continuing review and amendment/modification submissions, as a rule, are assigned to a convened IRB meeting unless circumstances are such that an expedited review is necessary.) If the IRB Chairperson has a conflict of interest with the proposed research activity, the submission shall then be forwarded to the IRB Vice Chairperson.

As with a full board review, expedited reviews are subject to the same regulatory criteria for the approval of research as set forth in 45 CFR 46.111(a)(1-7) and/or 21 CFR 56.111(a)(1-7) (See also SOP Section 4.1—Criteria for Human Subjects Research Approval). The only difference between a full board review and an expedited review is the number of IRB members who participate in the review.

Limited IRB reviews are subject to the criteria for IRB approval of research as set forth in 45 CFR 46.111(a)(7) or (a)(8) and 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8).

The expedited reviewer shall take one of the following three actions:

1. Approve
2. Approve with conditions
3. Refer to full board

If the reviewer recommends that the proposed research be disapproved, the submission shall be referred back to the full board and placed on the agenda for the next regularly scheduled meeting of the convened IRB.

In the case of a limited IRB review being performed as a condition for an exempt determination, the decision made by the reviewer/IRB shall be incorporated with the exempt determination procedures as described in SOP Section 5.3—Exempt Determinations.

The reviewer/IRB's decision shall be conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible after the expedited review as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

The reviewer shall report the expedited review decision back to the convened IRB at the next scheduled meeting in accordance with 45 CFR 46.110(2)(c) and 21 CFR 56.110(c) which requires that an IRB "adopt a method for keeping all members advised of research proposals that have been approved" under expedited procedures.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Exempt Determinations
Section Number: 5.3
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

In accordance with federal regulations 45 CFR 46.104 and 21 CFR 56.104, some human subjects research may be exempt from federal and institutional review board oversight.

In order for non-FDA regulated human subjects research to be eligible for exempt status, the proposed research activity must fall within one or more of the following categories found at 45 CFR 46.104(d):

1. "Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:
   (i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

   (ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

   (iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7).

3. (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7).

(ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 4 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 *et seq.*

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

   (i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

6. Taste and food quality evaluation and consumer acceptance studies:

   (i) If wholesome foods without additives are consumed or

   (ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

7. Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by 45 CFR 46.111(a)(8).

8. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

   (i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with 45 CFR 46.116(a)(1) through (4), (a)(6), and (d);

   (ii) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with 45 CFR 46.117;

   (iii) An IRB conducts a limited IRB review and makes the determination required by 45 CFR 46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and

   (iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results."

45 CFR 46.104(d) exempt categories 2, 3, 7 and 8 quoted above include a provision for limited IRB review. Research "for which limited IRB review is a condition of exemption" may be reviewed by using expedited review procedures [(45 CFR 46.110(b)(1) and (b)(1)(iii)]. The procedures to be followed are described in SOP Section 5.2—Expedited Reviews.

FDA regulated research does not qualify for exemption unless it falls under the FDA's emergency use provision for the use of a test article [21 CFR 56.104(c)] or taste and food quality evaluations and consumer acceptance studies [21 CFR 56.104(d)]. The only 45 CFR 46.104(d) exemption category that is applicable to FDA regulated research is number six (6) quoted above.

All new projects being submitted for possible exemption shall be screened by the IRB Coordinator. If the IRB Coordinator finds that the proposed research project meets the regulatory criteria for an exemption, the submission shall be forwarded to the IRB Chairperson for final review and determination. If a limited IRB review is required as a condition for exemption, this review shall be performed concurrently with the exempt review. If the IRB Chairperson has a conflict of interest with the proposed research, the submission shall then be forwarded to the IRB Vice Chairperson.

The GBMC IRB recognizes the following two individuals as having the authority to make an exempt determination:

1. IRB Chairperson
2. IRB Vice Chairperson

The exempt reviewer shall take one of the following two actions:

1. Exempt

2. Defer

If the reviewer determines that the proposed research does not qualify for an exemption and defers the submission, the submission shall then be reviewed by expedited review procedures or by the convened IRB, whichever is more appropriate for the research activity.

The reviewer/IRB's decision shall be conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

If the principal investigator proposes to make any changes to the project once an exemption is granted, the proposed change must be submitted to the IRB for review prior to implementation to ensure that the project still qualifies for exempt status. The IRB Coordinator shall forward the submission to the IRB Chairperson for review. If the IRB Chairperson has a conflict of interest with the research project, the submission shall then be forwarded to the IRB Vice Chairperson.

The GBMC IRB recognizes the following two individuals as having the authority to perform a review to determine whether or not a research project still qualifies for exempt status:

1. IRB Chairperson
2. IRB Vice Chairperson

The reviewer shall take one of the following two actions:

1. Exempt (meaning that the project still qualifies for exempt status)
2. Defer (meaning that the project no longer qualifies for exempt status)

If the reviewer determines that the research project no longer qualifies for exempt status and defers the submission, the principal investigator shall be informed of the decision as soon as possible, and the principal investigator must resubmit the revised research project in its entirety. The resubmitted, revised project shall then be reviewed by expedited review procedures or by the convened IRB, whichever is more appropriate for the research activity.

Research that is determined to be exempt under 45 CFR 46.104 and/or 21 CFR 56.104 is not required to undergo continuing review as set forth in 45 CFR 46.109(e) and 21 CFR 56.103(a). However, to keep the GBMC IRB Office files current, exempt research shall be given a three year expiration date. If the principal investigator wishes to continue the research after the three year period, the principal investigator must request an extension. If the principal investigator does not request an extension within 30 days of the expiration date, the research project shall be administratively closed.

Principal investigators, co-investigators and research project coordinators on the study team of a research project that is determined to be exempt are also exempt from the GBMC IRB's human subjects research training requirements as described in SOP Section 4.5—Investigator Qualifications, Responsibilities and Training Requirements.

All determinations and actions made solely by the IRB Chairperson or IRB Vice Chairperson in regards to exemptions shall be reported back to the convened IRB at the next scheduled meeting.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Not Human Subjects Research
Section Number: 5.4
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

All activities that fall under the federal regulatory definitions of human subjects research are required to undergo Institutional Review Board review. However, activities that fail to meet the federal definition of research or do not involve human subjects are excluded from Institutional Review Board review.

Determining whether or not an activity meets the federal definition of human subjects research is a two-step process that involves answering two specific questions:

Step 1 – Is it research?

Research is defined in the Common Rule at 45 CFR 46.102(l) as meaning "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." The Food and Drug Administration's list of definitions at 21 CFR 56.102 does not include "research".

Step 2 – Does it involve human subjects?

A human subject is defined in the Common Rule at 45 CFR 46.102(e) as meaning "a living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens."

The Food and Drug Administration at 21 CFR 56.102(e) defines a human subject as meaning "an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient."

The process of determining whether or not an activity meets the federal definitions of human subjects research can be complex and involve assessing the activity's intent, design, expected outcomes and dissemination of results. The GBMC IRB recognizes the following two individuals as having the authority to make a not research determination:

1. IRB Chairperson
2. IRB Vice Chairperson

All newly proposed activities that may qualify for a not research determination shall be screened by the IRB Coordinator. If the IRB Coordinator finds that there is sufficient evidence to qualify the activity for a not research determination, the information provided shall be forwarded to the IRB Chairperson for final review and determination. If the IRB Chairperson is not available to perform the final review and determination, the information provided shall then be forwarded to the IRB Vice Chairperson. A formal IRBNet submission is not routinely required, and a final determination of not research is not reported back to the convened IRB as the proposed activity is not research and IRB review and oversight is not required.

If it is determined that the proposed activity does meet the federal definitions of human subjects research, then the information provided must be formally submitted to the IRB via IRBNet. The submission shall then be reviewed for a possible exempt determination, by expedited review procedures or by the convened IRB, whichever is more appropriate for the proposed activity.

The following are examples of activities that typically would not need GBMC IRB review and would be considered not human subjects research:

- QI/QA activities that are systematic, data-guided and designed to implement promising ways to improve clinical care, patient safety and health care operations. The activity is designed to bring about immediate positive changes in the delivery of health care, programs, services or business practices in the local (GBMC) setting.
- Surveys issued or completed by GBMC personnel with the intent and purpose of improving GBMC services and programs or for developing new GBMC services or programs, as long as the privacy of the individuals is protected, the confidentiality of individual responses is maintained and survey participation is voluntary.
- Evidence based practice activities designed to utilize existing generalizable knowledge to implement local (GBMC) practice changes and/or answer a local (GBMC) practice question. These activities may include implementing practice changes on a pilot unit and evaluating processes and outcomes.
- Coded private information or biological specimens that were not collected for the currently proposed activity as long as the investigator cannot link the coded data/specimens back to individual subjects.
- Research involving cadavers, autopsy material or bio-specimens from now deceased individuals.
- Case history reports involving less than three individual medical records which are published and/or presented at national or regional meetings if there is no intent to form a research hypothesis, draw conclusions or generalize findings.
- Oral histories—Interviews that collect, preserve and interpret the voices and memories of people, communities, and participants in past events as a method of historical documentation.
- Information-gathering interviews of individuals where questions focus on things, products, or policies, rather than on people or their opinions or experiences.
- Innovative or novel procedures or treatments designed solely to enhance the well being of an individual patient or client.
- Activities involving the use of publicly available data.
- Data collection for GBMC internal departmental and/or administrative purposes only.

The above list contains only examples of activities that may not need to undergo GBMC IRB review. This list is not comprehensive. Only the GBMC IRB Chairperson or Vice Chairperson can make a final not research determination.

A not research determination is not the same as an exemption from IRB review and oversight. A determination of not research means that the activity does not meet the federal human subjects or research definitions and, therefore, does not require IRB review and oversight. An exempt determination means that the activity does meet the federal human subjects and research definitions but does not require IRB review and oversight as the activity falls under one or more of the federal regulatory exemption categories (See SOP Section 5.3—Exempt Determinations).

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Continuing Reviews
Section Number: 5.5a
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

The IRB conducts continuing review of research in accordance with 45 CFR 46, 21 CFR 56 and SOP Section 1.4—Applicability of the Revised 2018 Common Rule (2018 Requirements).

This policy puts into writing, as required by 45 CFR 46.108(3)(i) and 21 CFR 56.108(a)(1), the procedures followed for continuing review.

The IRB shall conduct continuing review of research "at intervals appropriate to the degree of risk, but not less than once per year" [45 CFR 46.109(e) and 21 CFR 56.109(f)]. However, the 2018 Requirements [45 CFR 46] do not require continuing review under the following circumstances, unless an IRB determines otherwise:

"(i) Research eligible for expedited review in accordance with 45 CFR 46.110;

(ii) Research reviewed by the IRB in accordance with the limited IRB review described in 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8);

(iii) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

(A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

(B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care." [45 CFR 46.109(i-iii)]

The above exceptions from the 2018 Requirements do not apply to FDA regulated research, and the GBMC IRB has determined that research qualifying for exceptions (i) and (iii) shall be subject to an "independent annual review" (See SOP Section 5.5b—Independent Annual Reviews). Should the IRB determine that continuing review is required for research qualifying for exceptions (i) and (iii) above, the IRB shall notify the principal investigator and other key project personnel in the determination letter and document the rationale for requiring continuing review in the IRB meeting minutes in accordance with 45 CFR 46.115(a)(3). Factors the IRB may take into consideration when determining the need for continuing review shall include but not be limited to:

1. Continuing review is required by other applicable regulations (e.g., FDA)

2. The research involves topics, procedures, or data that may be considered sensitive or controversial

3. The research involves particularly vulnerable subjects or circumstances that increase subject's vulnerability

4. An investigator has minimal experience in research or the research type, topic, or procedures

Federal regulations have established criteria for IRB approval of human subjects research, and the IRB shall apply the same regulatory approval criteria to continuing reviews as it does to initial reviews (See SOP Section 4.1—Criteria for Human Subjects Research Approval).

Except when an expedited review procedure is used, the IRB shall conduct continuing reviews "at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for research to be approved, it shall receive the approval of a majority of those members present at the meeting." [45 CFR 46.108(b) and 21 CFR 56.108(c)]

The IRB shall have no member participate in a continuing review who has a conflicting interest in the project undergoing review, except to provide information requested by the IRB [45 CFR 46.107(d) and 21 CFR 56.107(e)]. This applies to continuing reviews conducted by the convened IRB and continuing reviews where expedited review procedures are used.

The GBMC IRB uses expedited review procedures for continuing reviews on only the rarest of occasions when a continuing review cannot be conducted in a timely fashion in relation to when a meeting of the convened IRB is scheduled. On the occasion when a continuing review is conducted using expedited review procedures, the review is conducted as set forth in SOP Section 5.2—Expedited Reviews.

At the time of initial review, whether it be by the convened IRB or expedited review procedures, all projects are given an approval expiration date indicating when the project must undergo a continuing review. Typically, the IRB initially approves a research project or continuation request for a period of one year. However, approval may be granted for less than one year (e.g. six months) in some circumstances. The IRB determines the frequency of continuing review by considering the following factors recommended by the OHRP:

- The nature of any risks posed by the research project
- The degree of uncertainty regarding the risks involved
- The vulnerability of the subject population
- The experience of the investigators in conducting research
- The IRB's previous experience with the investigators (e.g., compliance history, previous problems with the investigator obtaining informed consent, or prior complaints from subjects about the investigator)
- The projected rate of enrollment; and

- Whether the research project involves novel interventions

(Source for the above list: Guidance on IRB Continuing Review of Research dated 11/10/10)

The actual date of approval expiration necessitating continuing review shall be calculated as follows and applies to both initial and continuing reviews:

- For research projects reviewed and approved without conditions by the convened IRB, the approval expiration date shall be calculated from the date of the convened meeting.
- For research projects reviewed via expedited review procedures without conditions, the approval expiration date shall be calculated from the date approval is granted by the person (IRB Chairperson or Vice Chairperson) authorized to perform the review.
- For research projects approved with conditions, whether it be by the convened IRB or expedited review procedures, the approval expiration date shall be calculated from the date the project was approved with conditions, not the effective date when full approval was ultimately granted.

It is the responsibility of the principal investigator to submit for a continuing review prior to the approval expiration date with sufficient time for the continuing review to be performed by the IRB. Federal regulations (45 CFR 46 and 21 CFR 56) make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval.

As a courtesy, continuing review reminder emails shall be sent out automatically via IRBNet 60 and 30 days prior to a project's approval expiration date. If the project does not undergo a continuing review prior to the approval expiration date, IRBNet will send a final notice on the date of approval expiration. In conjunction with this final notice of expiration, the IRB Coordinator shall inform the principal investigator and any other key project personnel that the project's approval has expired and all research activities must cease. Research activities that must cease include but are not limited to contact with currently enrolled subjects, data collection and data analysis. Currently enrolled subjects may continue participating in the research if it is determined that the research interventions hold out the prospect of direct benefit to the subjects or when withholding those interventions poses increased risks to the subjects. The principal investigator shall request in writing special consideration from the IRB Chairperson to continue to follow currently enrolled subjects in the event that the approval expires. The IRB Chairperson shall consider such requests on a case-by-case basis. No new subjects may be enrolled.

Once a project's approval expires, the principal investigator shall have 30 days to submit for a continuing review. If the project is not submitted for a continuing review within this 30 day period, the project shall be administratively closed at the next scheduled meeting of the convened IRB, and the project must be resubmitted in its entirety to be reconsidered.

In the event that a continuing review submission is received by the IRB office staff after the project's approval has expired, it shall be screened by the IRB Coordinator to determine if the submission qualifies for an expedited review. If the submission qualifies for an expedited review, the procedures as described in SOP Section 5.2—Expedited Reviews shall be followed. If the submission does not qualify for an expedited review, the submission shall be placed on the agenda for the next regularly scheduled meeting of the convened IRB. Regardless of the

circumstances, the new approval expiration date for an expired project shall be calculated from the current approval expiration date, not from the effective date when the continuing review was performed and approval was granted to continue the research.

All continuing review submissions must be sent electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The IRB recommends that continuing review requests be submitted for review at the convened IRB meeting scheduled in the month prior to the project's approval expiration date. The electronic submission "package" for a continuing review shall contain but not be limited to the following documents:

1. Continuing review submission form
2. Conflict of interest statements from the principal investigator and all co-investigators on the study team
3. Evidence of current human subjects research training from the principal investigator, co-investigators and study coordinator

The continuing review submission form shall contain but not be limited to the following information:

1. Project status
2. Enrollment data
3. Summary of any subject withdrawals
4. Summary of any subject complaints
5. Description of any adverse and other reportable events that have not been reported to the IRB since the last review.

The project's complete IRBNet file can be accessed at any time by the IRB members to aid in conducting the continuing review. The IRBNet file includes but is not limited to the following as applicable:

- Current protocol and any previously submitted versions
- Current informed consent form and any previously submitted versions
- Current investigator brochure and any previously submitted versions
- Previously submitted revisions/amendments and corresponding documents
- Adverse event and/or unanticipated problem reports
- Deviation reports
- All previous continuing reviews and corresponding documents

As part of the continuing review process, federal regulations require an IRB to determine "which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review" [45 CFR 46.108.(3)(ii) and 21 CFR 56.108(a)(2)]. The need for verification shall be determined by the IRB on a case-by-case basis. Source verification shall be required when the:

- Investigator is providing inconsistent information that cannot be resolved
- IRB doubts the investigator's veracity

- IRB doubts the investigator has sufficient relevant knowledge
- IRB perceives that the investigator is intentionally not providing necessary information

If the IRB determines that a need for source verification exists, the IRB may request an independent assessment. The scope and extent of the assessment shall be determined by the IRB on a case-by-case basis. Sources for information could include but not be limited to site visits conducted by authorized personnel, literature searches, or a directed audit. The IRB has the "authority to observe or have a third party observe the consent process and the research" [45 CFR 46.109(e) and 21 CFR 56.109(g)].

Once a continuing review has been completed, the IRB's decision shall be conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations. Continuing review follow-up letters shall clearly state the period of time for which the project is approved and the new approval expiration date.

IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer and Signatory Official on GBMC's Federalwide Assurance. (See also SOP section 3.5—Minutes of the Meeting)

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Independent Annual Reviews
Section Number: 5.5b
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

The IRB conducts continuing review of research in accordance with 45 CFR 46, 21 CFR 56 and SOP Section 1.4—Applicability of the Revised 2018 Common Rule. However, the revised 2018 Common Rule [45 CFR 46] does not require continuing review under the following circumstances, unless an IRB determines otherwise:

"(i) Research eligible for expedited review in accordance with 45 CFR 46.110;

(ii) Research reviewed by the IRB in accordance with the limited IRB review described in 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8);

(iii) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

(A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

(B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care." [45 CFR 46.109(i-iii)]

The GBMC IRB has determined that research qualifying for exception (i) and (iii) above shall be subject to an "independent annual review".

[Exception (ii) applies to exempt research—See SOP Section 5.3—Exempt Determinations]

Independent annual review dates are calculated as follows:

- For research approved using expedited review procedures in accordance with 45 CFR 46.110, the initial independent annual review date shall be calculated as one year from the date approval is granted by the person (IRB Chairperson or Vice Chairperson) authorized to perform the expedited review and on an annual basis thereafter until permanent closure of the project.
- For research that has progressed to the point that it involves only data analysis or accessing follow-up clinical data as stated in (iii) above, the independent annual review date shall be calculated as one year from the date of the last continuing review and on an annual basis thereafter until permanent closure of the project.

It is the responsibility of the principal investigator to submit for an independent annual review prior to the IRB determined annual review due date.

As a courtesy, independent annual review reminder emails in the form of a "Project Expiration Reminder" shall be sent out automatically via IRBNet 60 and 30 days prior to a project's annual review due date. If the project does not undergo an independent annual review prior to the IRB determined annual review due date, IRBNet will send a final notice on the due date of the annual review. In conjunction with this final notice, the IRB Coordinator shall inform the principal investigator and any other key project personnel that the project is now out of compliance with SOP Section 5.5b—Independent Annual Reviews, SOP Section 4.4—Investigator Conflicts of Interest and SOP Section 4.5—Investigator Training Requirements, and the project must be submitted for the required independent annual review within 30 days. If the project is not submitted for independent annual review within this 30 day period, the project shall be administratively closed at the next scheduled meeting of the convened IRB, and the project must be resubmitted in its entirety to be reconsidered.

Independent annual reviews are performed by the convened IRB.

All independent annual review submissions must be sent electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The IRB recommends that independent annual review requests be submitted for review at the convened IRB meeting scheduled in the month prior to the annual review due date. The electronic submission "package" for an independent annual review shall contain but not be limited to the following documents:

4. Independent annual review submission form (same as continuing review submission form)
5. Conflict of interest statements from the principal investigator and all co-investigators on the study team
6. Evidence of current human subjects research training from the principal investigator, co-investigators and study coordinator

Once an independent annual review has been completed, the IRB's action shall be conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations. Independent annual review follow-up letters shall clearly state the due date for the next annual review.

IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer and Signatory Official on GBMC's Federalwide Assurance. (See also SOP Section 3.5—Minutes of the Meeting)

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Permanent Project Closures
Section Number: 5.6
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

Principal investigators have the responsibility of informing the IRB when a project has been completed. The GBMC IRB requests that, upon the completion of a project, a "Closure of Project (Permanent) Reporting Form" be submitted as a final report.

A project may be closed if any of the following conditions apply:

- All research-related interventions or interactions with human subjects have been completed and/or all data collection and analysis of identifiable private information have been finished
- All that remains is the analysis of aggregate data sets without individual subject identifiers or identifiable private information and with no identifying links or codes to the data
- The project sponsor agrees to or recommends closure
- The project has been open for one or more years, no subjects have been enrolled, and the principal investigator sees no likelihood of doing so
- The project was never initiated
- The principal investigator plans to terminate employment/affiliation with GBMC and/or be removed from the project team without transferring the research to another investigator

If the project does not meet any of the above criteria for closure, the project must remain open and undergo continuing review or independent annual review as determined by the IRB.

Regardless of initial review type (full or expedited), all closure of project submissions shall be reviewed by the convened IRB and acknowledged. The IRB's acknowledgement shall be formally conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible after the convened meeting as described in SOP Section 4.6—Notification and Documentation of Review Actions and Decisions. IRB office records shall be coded to indicate that the project is now permanently closed.

In the event that the principal investigator seeks to resume research activities for a project that has been permanently closed, the project can be reactivated by one of the following two ways:

1. If the project has been closed for six months or less, the principal investigator may request that the project be reopened by submitting a "Revisions and Amendments Submission Form"
2. If the project has been closed for more than six months, the project must be resubmitted in its entirety to be reconsidered and will be reviewed as a new project as described in SOP 5.1—Initial Full Committee Reviews

The GBMC IRB may administratively close a project without the approval of the principal investigator in the following three instances:

1. A project's approval has expired and no continuing review submission is made within 30 days of the approval expiration date as set forth in SOP Section 5.5a—Continuing Reviews
2. A project's independent annual review date has past and no independent annual review submission is made within 30 days of the IRB determined annual review due date as set forth in SOP Section 5.5b—Independent Annual Reviews
3. It is determined that the principal investigator has terminated employment and/or affiliation with GBMC without notifying the IRB and requesting the research be transferred to another investigator

Projects that are administratively closed by the IRB cannot be reopened. To resume research activities, the project must be resubmitted in its entirety.

Once a project is permanently closed, the IRB shall retain individual project files for six years in accordance with federal regulations which state that an IRB shall maintain "copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects" [45 CFR 46.115(a)(1) and 21 CFR 56.115(2)] and that these records "shall be retained for at least 3 years after completion of the research." [45 CFR 46.115(a)(7) and 21 CFR 56.115(7)(b)]

Once the six year retention time frames has elapsed, the project files (both hard copy and those maintained electronically in IRBNet) shall be permanently deleted and/or destroyed.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Enrollment Status Changes
Section Number: 5.7
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

Principal investigators have the responsibility of informing the IRB when a project's enrollment status changes. An enrollment status change is considered a change in research activity that must be reported to the IRB in accordance with federal regulations at 45 CFR 46.108(3)(iii) and 21 CFR 56.108(a)(3-4).

The GBMC IRB considers the following enrollment status changes to be reportable:

- Permanent closure to enrollment
- Temporary closure to enrollment
- Reactivation of enrollment to entire project
- Permanent closure of a project arm to enrollment
- Temporary closure of a project arm to enrollment
- Reactivation of enrollment to project arm

Enrollment status changes should be submitted to the IRB for review and approval prior to implementation; however, the IRB acknowledges that sponsors of multi-site studies may announce enrollment status changes before IRB review and approval can be obtained. When this is the case, it is the responsibility of the principal investigator to notify the IRB as soon as possible after the enrollment status change is announced.

Enrollment status change submissions shall be handled as set forth in SOP Section 5.8—Changes in Research Activity: Revisions and Amendments.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Changes in Research Activity: Revisions and Amendments
Section Number: 5.8
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

In accordance with federal regulations 45 CFR 46.108 and 21 CFR 56.108, the IRB shall have written procedures for "ensuring prompt reporting to the IRB of proposed changes in a research activity."

This policy outlines the procedures followed for the prompt reporting to the IRB of proposed changes in research activity.

A proposed change in research activity can be as simple as a slight wording change to a consent document or as complex as the addition of a new arm to a project.

A change in research activity can be referred to as a modification, revision or amendment. Typically, a revision refers to a change in something that already exists (e.g. increase in number of subjects to be enrolled) while an amendment refers to something that is added (e.g. new person on the project team).

Proposed changes in research activity can be broken down into two categories:

- Major changes
- Minor changes

Major changes are changes that may have a substantive effect on the conduct of the research, increase the research population's risk or are of questionable risk. Examples of major changes include but are not limited to the following:

- An increase in physical and/or psychological risk/discomfort to subjects
- A major change in research design or methodology
- Substantive changes to the protocol, consent and/or other documents
- Adding a new consent form, questionnaire or other instrument
- Significant new findings that may affect subjects' willingness to participate
- Addition of serious unexpected adverse events to the informed consent
- Broadening the range of inclusion criteria
- Narrowing the range of exclusion criteria
- Alterations in the use and/or administration of study drugs, devices or biologics
- Additions or deletions of laboratory tests, monitoring procedures, etc.
- Project team changes involving the principal investigator

- Enrollment status changes (e.g. closure to enrollment) (See also SOP Section 5.7)
- Any change that may alter the risk/benefit ratio

All major changes shall be reviewed by the convened IRB.

Minor changes are changes that have no substantive effect upon an approved protocol or reduce the risk to the subject. Examples of minor changes include but are not limited to the following:

- A reduction in physical and/or psychological risk/discomfort to participants
- Minor editorial modifications to documents that do not alter meaning or procedure
- Removing questions from a questionnaire
- Narrowing the range of inclusion criteria
- Broadening the range of exclusion criteria
- New or changed recruitment/advertising methods and/or materials (flyers, Internet, etc.)
- New or changed patient materials (diaries, medical alert cards, etc.)
- An increase in the number of study visits for safety purposes
- Minor increase/decrease in the number of subjects to be enrolled
- Minor change in remuneration amount or type
- Additions or deletions of project team members (not including principal investigator)
- Any change that does not alter the risk/benefit ratio

Federal regulations at 45 CFR 46.110(b)(1)(ii) and 21 CFR 56.110(b)(2) permit IRBs to use expedited review procedures to review "minor changes in previously approved research during the period (of 1 year or less) for which approval is authorized"; however, the GBMC IRB has opted to review all proposed changes in previously approved research regardless of how minor at convened meetings.

The GBMC IRB will use expedited review procedures in urgent cases when time is of the essence. On the occasion that a review of minor changes in previously approved research is conducted using expedited review procedures, the review shall be conducted as set forth in SOP Section 5.2—Expedited Reviews.

The GBMC IRB recognizes the following two individuals as having the authority to review minor changes in previously approved research using expedited review procedures:

1. IRB Chairperson
2. IRB Vice Chairperson

Regardless of whether changes in previously approved research are reviewed by the convened IRB or expedited review procedures, the criteria for approval of changes to previously approved research are the same as those for initial review. The IRB must determine that, in light of the proposed changes, research continues to satisfy 45 CFR 46.111 and/or 21 CFR 56.111, as applicable.

When proposed changes to previously approved research are reviewed by the convened IRB, a primary reviewer shall be appointed. The IRB Assistant shall assign each change in research

activity submission to a qualified IRB member for review. The IRB member shall summarize and present the nature of the proposed changes to the convened IRB. The IRB Assistant shall not assign a change in research activity submission to any IRB member who has a conflict of interest with the proposed research activity.

As appropriate, the convened IRB shall determine whether re-consenting of currently enrolled subjects is necessary. This determination shall be based on any new information provided that could possibly affect a subject's decision to continue with the research activities. The convened IRB shall also decide whether subjects who have concluded active treatment, are in long-term follow-up or have completed all study requirements should be contacted and provided with additional information.

All decisions made by the IRB regarding a submission for a proposed change to previously approved research, regardless of whether the review was performed by the convened IRB or expedited review procedures, shall be conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

Principal investigators shall not implement any change in research activity without prior IRB review and approval. The only exception to this requirement is in instances when the change is "necessary to eliminate apparent immediate hazards to the subject" [45 CFR 46.108(a)(3)(iii) and 21 CFR 56.108(a)(4)].

If a principal investigator implements a non-IRB approved change to previously approved research to eliminate apparent hazards to a subject, the change shall be reported to the IRB within 48 hours of implementation as a protocol deviation/violation as described in SOP Section 5.10—Protocol Deviations/Violations.

If the principal investigator of a project previously determined to be exempt by the IRB proposes to make a change in research activity to the project, the proposed change in research activity must be submitted to the IRB prior to implementation to ensure that the project still qualifies for exempt status in accordance with federal regulations 45 CFR 46.104 and 21 CFR 56.104 and as set forth in SOP Section 5.3—Exempt Determinations.

IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer and Signatory Official on GBMC's Federalwide Assurance. (See also SOP Section 3.5—Minutes of the Meeting)

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Adverse Events and Unanticipated Problems
Section Number: 5.9
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

Federal regulations 45 CFR 46.108(a)(4) and 21 CFR 56.108(b)(1-3) require the IRB to follow written procedures for ensuring the prompt reporting to the IRB, appropriate institutional officials, and governmental departments and/or agency heads of any:

1. unanticipated problems involving risks to subjects or others
2. serious or continuing noncompliance with Federal regulations
3. serious or continuing noncompliance with requirements or determinations of the IRB
4. suspension or termination of IRB approval

This policy outlines the procedures for prompt reporting.

Definitions

Adverse Event (AE): An AE is defined as "any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse Events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research."

Serious Adverse Event (SAE): A SAE is defined as "any adverse event temporally associated with the subject's participation in research that meets any of the following criteria:

1. results in death;
2. is life-threatening (places the subject at immediate risk of death from the event as it occurred);
3. requires inpatient hospitalization or prolongation of existing hospitalization;
4. results in a persistent or significant disability/incapacity;
5. results in a congenital anomaly/birth defect; or
6. any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition"

Unanticipated Problem (UP): An unanticipated problem is defined as "any incident, experience, or outcome that meets all of the following criteria:

1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. related or possibly related to participation in the research; and
3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized."

Possibly related to the research means that "there is a reasonable possibility that the adverse event, incident, experience or outcome may have been caused by the procedures involved in the research".

Internal Adverse Event: An adverse event that occurs in study participants who were enrolled through GBMC or a GBMC affiliated study site.

External Adverse Event: An adverse event that occurs in study participants who were not enrolled through GBMC or a GBMC affiliated study site.

Reporting Requirements for Internal Adverse Events

All internal adverse events that meet the above-definition of a serious adverse event or an unanticipated problem shall be reported to the IRB within 5 business days of the investigator becoming aware of the event.

All internal events that meet the above-definition of an adverse event but do not meet the above-definition of a serious adverse event or unanticipated problem shall be reported to the IRB within 10 business days of the investigator becoming aware of the event.

All internal adverse events that are reported to an outside entity (e.g. sponsor, FDA) with study oversight shall be reported to the IRB within 10 business days of the investigator becoming aware of the event.

All subject deaths that occur while on study shall be reported to the IRB within 48 hours of the investigator becoming aware of the event unless the event is clearly unrelated to the study procedures or related to natural progression of a disease process.

Reporting Requirements for External Adverse Events

The "OHRP advises that it is neither useful nor necessary under the HHS regulations at 45 CFR part 46 for reports of individual adverse events occurring in subjects in multicenter studies to be distributed routinely to investigators or IRBs at all institutions conducting the research."

Only external adverse events that meet the following criteria need to be reported to the GBMC IRB:

1. events that are determined by the sponsor to be an unanticipated problem involving risks to subjects or others
2. events that result in a modification to the protocol, informed consent document and/or investigator brochure
3. events that result in suspension of all or parts of the research
4. events that result in early termination of the research

External adverse events shall be reported to the GBMC IRB within 10 business days of the investigator becoming aware of the event.

Other Reportable Events

In addition to the above-mentioned adverse events, serious adverse events, and unanticipated problems, the IRB considers the following to be reportable events:

1. new or updated safety information relating to the study or study product
2. DSMB/DMC or other independent safety monitoring group report
3. any sponsor imposed suspension or termination of the research due to new or increased risks
4. a breach of confidentiality or violation of HIPAA
5. unresolved participant complaints
6. adverse audit results or enforcement actions
7. any other problem indicating that the research places subjects or others at an increased risk of harm or otherwise adversely affects the rights, welfare or safety of subjects or others

The above mentioned other reportable events shall be reported to the IRB within 10 business days of the investigator becoming aware of the event.

For reasons of confidentiality, subject names must not be included in any reportable event submission. Subject identifiers such as enrollment numbers should be used instead.

IRB Review Process for Reported Events

All reported events shall be screened by the IRB office staff. The IRB office staff shall either place the submitted item on the agenda for the next scheduled meeting of the convened IRB or forward it to the IRB Chairperson or his designee for review.

The following internal events shall be promptly forwarded to the IRB Chairperson or his designee for immediate review:

1. Death of a subject or life-threatening circumstances
2. Serious adverse events that are unresolved
3. Unanticipated problems resulting in risks to subjects or others
4. Serious or continuing noncompliance with Federal regulations
5. Serious or continuing noncompliance with requirements or determinations of the IRB
6. Any other event involving risks to subjects or others

The IRB Chairperson or designee shall report the review findings back to the convened IRB at the next scheduled meeting. The principal investigator shall be notified of all review findings and if any corrective action is required or additional information is needed.

If the IRB determines that corrective action is necessary, the required action may include:

1. Changes to the research protocol
2. Modification of informed consent documents
3. Notification of previously enrolled subjects of new information
4. Notification of currently enrolled subjects of new information
5. Frequent progress or status reports to the IRB
6. More frequent intervals of continuing review
7. Suspension of all or parts of the research
8. Termination of the research
9. Other actions as determined by the IRB

If the IRB determines that the event is of a magnitude that it must be reported to other appropriate authorities, those authorities may include:

1. GBMC institutional officials
2. The Office for Human Research Protection (OHRP)
3. The Food and Drug Administration (FDA)
4. Other governmental departments or agency heads as appropriate

[Numbers 2, 3 and 4 above shall not be applied to non-Federally funded, non-FDA regulated research initially approved by the GBMC IRB on or after January 21, 2019]

The IRB Coordinator shall be responsible for notifying the following GBMC officials regarding the reportable event within 5 business days of the IRB's determination:

1. Chief Medical Officer
2. Vice President for Legal Affairs and General Counsel
3. Vice President for Quality and Patient Safety

The IRB Chairperson shall be responsible for notifying all appropriate governmental departments and/or agencies within 15 business days of GBMC officials being notified of the reportable event. A copy of all correspondence and/or reports shall be forwarded to the above-mentioned GBMC officials.

[All quoted passages within this policy have been taken from the OHRP "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" dated 1/15/07]

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Protocol Deviations/Violations
Section Number: 5.10
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

As previously stated in Section 5.9, Federal regulations 45 CFR 46.108(a)(4) and 21 CFR 56.108(b)(1-3) require the IRB to follow written procedures for ensuring the prompt reporting to the IRB, appropriate institutional officials, and governmental departments and/or agency heads of any:

1. unanticipated problems involving risks to subjects or others
2. serious or continuing noncompliance with Federal regulations
3. serious or continuing noncompliance with Federal regulations
4. serious or continuing noncompliance with requirements or determinations of the IRB
5. suspension or termination of IRB approval

This policy outlines the procedures for prompt reporting.

The term "protocol deviation" is not defined by either OHRP human subjects regulations (45 CFR 46) or FDA human subjects regulations (21 CFR 50). For GBMC IRB purposes, a protocol deviation is any modification or departure from the defined procedures and treatment plans set forth in the IRB-approved protocol. All planned protocol deviations require IRB approval prior to implementation except in emergency situations where changes are deemed "necessary to eliminate apparent immediate hazards to the subject" [45 CFR 46.108(a)(3)(iii) and 21 CFR 56.108(a)(4)] (See also SOP Section 5.8—Changes in Research Activity: Revisions and Amendments).

Protocol deviations/violations range in seriousness according to how the changes may impact subject safety. The GBMC IRB has divided protocol deviations/violations into two categories—major and minor.

A major protocol deviation/violation is defined as any change that may impact subject safety or alter the risk/benefit ratio, compromise the integrity of the study data, and/or affect a subject's willingness to participate in the study. Major protocol deviations/violations include but are not limited to the following:

- Enrollment of a subject before IRB approval of study
- Enrollment of a subject after IRB approval of study has expired
- Enrollment of a subject who did not meet inclusion/exclusion criteria
- Failure to obtain informed consent prior to initiating study procedures

- Inappropriate documentation of informed consent (e.g. missing subject signature)
- Use of a non-IRB approved informed consent (e.g. consent missing IRB approval stamp)
- Use of an invalid informed consent (e.g. outdated version)
- Failure to perform a study specific procedure (impacting subject safety)
- Out of window visit and/or procedure (impacting subject safety)
- Performing study procedures not approved by the IRB
- Drug/study medication dispensing or dosing error
- Incorrect storage/handling of study drug/medication, biological samples, etc.
- Loss or destruction of samples or data
- Failure to follow protocol safety and monitoring requirements
- Any lapse in study approval where there is a continuation of research activities
- Any event requiring prompt reporting according to the protocol or study sponsor
- Any other deviation impacting subject safety

A minor protocol deviation/violation is defined as a one-time change that does not significantly affect the safety of the subject. Minor protocol deviations/violations include but are not limited to the following:

- Use of recruitment method and/or material not approved by the IRB
- Missing original signed and dated informed consent (copy available)
- Copy of signed informed consent not given to subject
- Missing pages of executed informed consent
- Failure to perform a study specific procedure (not impacting subject safety)
- Out of window visit and/or procedure (not impacting subject safety)
- Failure of subject to return unused study drug/medication
- Improper investigational product accountability
- Failure to follow Federal regulations
- Failure to follow requirements or determinations of the IRB

Minor protocol deviations/violations that occur repetitively may be determined to be a major deviation by the IRB and require corrective action.

All major protocol deviations/violations shall be reported to the IRB within 5 business days of the investigator becoming aware of the event.

All major protocol deviations/violations resulting in the death of a subject shall be reported to the IRB within 48 hours of the investigator becoming aware of the event.

All minor protocol deviations/violations shall be submitted to the IRB on an individual basis or no less than every quarter (every 90 days) in the form of a summary report.

All emergency situations involving the implementation of a non-IRB approved protocol deviation to eliminate apparent immediate hazards to a subject shall be reported to the IRB within 48 hours of the event taking place.

Protocol deviations/violations that occur at a non-GBMC affiliated site in a multi-center research study do not need to the reported to the IRB.

All protocol deviations/violations shall be screened by the IRB office staff. The IRB office staff shall either place the submitted item on the agenda for the next scheduled meeting of the convened IRB or forward it to the IRB Chairperson or his designee for review.

The following protocol deviations/violations shall be promptly forwarded to the IRB Chairperson or his designee for immediate review:

1. All major deviations/violations that could possibly be classed as a:
   a. serious noncompliance,
   b. continuing noncompliance, or
   c. unanticipated problem involving risks to subjects or others

2. All major deviations/violations resulting in the death of a subject

3. All deviations/violations being conducted under an emergency situation

The IRB Chairperson or his designee shall report the review findings back to the convened IRB at the next scheduled meeting. The principal investigator shall be notified of all review findings and if any corrective action is required or additional information is needed.

If the IRB determines that corrective action is necessary, the required action may include:

1. Changes to the research protocol
2. Monitoring of the informed consent process
3. Re-consenting of currently enrolled subjects
4. Monitoring of research activities
5. More frequent intervals of continuing review
6. Suspension of all or parts of the research
7. Termination of the research
8. Other actions as determined by the IRB

If the IRB determines that the event is of a magnitude that it must be reported to other appropriate authorities, those authorities may include:

1. GBMC institutional officials
2. The Office for Human Research Protection (OHRP)
3. The Food and Drug Administration (FDA)
4. Other governmental departments or agency heads as appropriate

[Numbers 2, 3 and 4 above shall not be applied to non-Federally funded, non-FDA regulated research initially approved by the GBMC IRB on or after January 21, 2019]

The IRB Coordinator shall be responsible for notifying the following GBMC officials regarding the reportable event within 5 business days of the IRB's determination:

1. Chief Medical Officer
2. Vice President for Legal Affairs and General Counsel
3. Vice President for Quality and Patient Safety

The IRB Chairperson shall be responsible for notifying all appropriate governmental departments and/or agencies within 15 business days of GBMC officials being notified of the reportable event. A copy of all correspondence and/or reports shall be forwarded to the above-mentioned GBMC officials.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: General Reports
Section Number: 5.11
Effective Date: June 19, 2017
Last Revision: January 15, 2018
Replaced SOP Revised On:

Federal regulations make no reference to "general reports". This is terminology that has been adopted solely by the GBMC IRB.

General reports refer to submissions that do not fall into any of the other primary submission types (e.g. new project, continuing review/progress report, amendment/modification).

Examples of what would be categorized as a general report include but are not limited to the following:

- Annual status reports
- Final reports received after permanent project closure
- General sponsor correspondence with directives to submit to the IRB

All general reporting submissions shall be reviewed by the convened IRB.

All general reporting submissions shall be acknowledged as soon as possible after the convened meeting as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Records-Based Research (Chart Reviews)
Section Number: 5.12
Effective Date: January 21, 2019
Last Revision:
Replaced SOP Revised On:

Research based on the review of patient medical records is considered to be human subjects research and must undergo IRB review and approval prior to initiation. There are two types of medical record/chart reviews:

- Retrospective
- Prospective

A retrospective chart review evaluates patient data that is existing at the time the project is submitted to the IRB for initial review.

A prospective chart review evaluates patient data that does not yet exist at the time the project is submitted to the IRB for initial review.

A project can involve the collection of data both retrospectively and prospectively.

Records-based research is reviewed by the GBMC IRB through one of three ways:

- Expedited Review
- Exempt Determination
- Full Board/Convened IRB Review

The above three review methods are described as follows:

1. Expedited Review

   A majority of retrospective and prospective chart reviews involving little to no risk to subjects will qualify for expedited review if the IRB finds that the following criterion [45 CFR 46.110 Category 5) is met:

   "Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis)."

   If a retrospective or prospective chart review qualifies for an expedited review, the procedures as described in SOP Section 5.2—Expedited Reviews shall be followed.

2. Exempt Determination

   A retrospective chart review involving little to no risk to subjects may qualify for an exempt determination if the IRB finds that the following criteria [45 CFR 46.104(d)(4)(ii)] are met:

   "Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects"

   If a retrospective chart review qualifies for an exempt determination, the procedures as described in SOP Section 5.3—Exempt Determinations shall be followed.

3. Full Board/Convened IRB Review

   Retrospective and prospective chart reviews that do not qualify for an expedited review or an exempt determination shall be reviewed by the convened IRB. This occurs on only rare occasions. Circumstances under which this may occur include but are not limited to the following:

   - The data to be collected is of a sufficiently sensitive nature that additional safeguards may be necessary to protect the subjects' rights
   - Research findings may result in a change to GBMC policies and/or procedures for patient care

   If a retrospective or prospective chart review does not qualify for either an expedited review or exempt determination and must be reviewed by the convened IRB, the procedures as described in SOP Section 5.1—Initial Full Committee Reviews shall be followed.

Records-based research projects that are reviewed under expedited review procedures or are reviewed by the convened IRB are subject to all applicable federal regulations, including regulations regarding informed consent. Federal regulations at 45 CFR 46.116(a)(1) state that "Before involving a human subject in research … an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative." However, in the case of records-based research, an IRB may grant a waiver of informed consent if the following regulatory criteria [45 CFR 46.116(f)(3)] are met:

"(i) The research involves no more than minimal risk to the subjects;
(ii) The research could not practicably be carried out without the requested waiver or alteration;
(iii) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;

(iv) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
(v) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation."

If the above regulatory criteria cannot be met, the IRB may determine that written consent is required. This most often occurs in the case of prospective records-based research.

The IRB also has the option of waiving the requirement to obtain a signed consent form for some or all of the subjects if the following regulatory criteria [45 CFR 46.117(c)] are met:

1. "That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;" or
2. "That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context."

If the IRB waives the requirement to obtain a signed consent form, the IRB may require the principal investigator to provide subjects with a written statement regarding the research or present the information orally in instances where subjects are contacted via telephone.

In addition to being subject to informed consent regulatory requirements, records-based research is also subject to HIPAA privacy rule requirements. A retrospective chart review typically involves the use of protected health information (PHI) for research purposes without seeking written permission from the subject. This type of access must occur under a full waiver of HIPAA research authorization. In order to qualify for a full waiver of HIPAA research authorization, the following privacy rule criteria [45 CFR 164.512(i)(2)(ii)] must be met:

1. The use or disclosure of the PHI involves no more than minimal risk to the privacy of individuals based on, at least, the presence of the following elements:
    a. An adequate plan to protect health information identifiers from improper use and disclosure.
    b. An adequate plan to destroy identifiers at the earliest opportunity consistent with conduct of research (absent a health or research justification for retaining them or a legal requirement to do so).
    c. Adequate written assurances that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

2. The research could not practicably be conducted without the waiver.

3. The research could not practicably be conducted without access to and use of the PHI.

If the above HIPAA privacy rule criteria cannot be met, the IRB may determine that HIPAA research authorization must be obtained from the project subjects. This most often occurs in the case of prospective records-based research.

All IRB decisions shall be conveyed by the IRB office staff to the principal investigator and other key personnel as soon as possible as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Expanded Access
Section Number: 5.13
Effective Date: May 18, 2020
Last Revision:
Replaced SOP Revised On:

Expanded access "is a potential pathway for a patient with an immediately life-threatening condition or serious disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available". [FDA (2019) *Expanded Access.* Retrieved from https://www.fda.gov/news-events/public-health-focus/expanded-access]

The FDA defines an immediately life-threatening condition as "a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment". [21 CFR 312.300(b)]

The FDA defines a serious disease or condition as "a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one". [21 CFR 312.300(b)]

The FDA identifies three categories of expanded access for investigational drugs:

- Individual Patients, Including for Emergency Use (21 CFR 312.310)
- Intermediate-Size Patient Populations (21 CFR 312.315)
- Treatment IND or Treatment Protocol (21 CFR 312.320)

The FDA identifies three categories of expanded access for investigational medical devices:

- Emergency Use
- Compassionate Use (or Individual Patient/Small Group Access)
- Treatment Investigational Device Exemption (IDE)

[FDA (2019) *Expanded Access for Medical Devices.* Retrieved from https://www.fda.gov/medical-devices/investigational-device-exemption-ide/explanded-access-medical-devices]

This policy will focus on the "Individual Patients, Including for Emergency Use" expanded access category for investigational drugs mentioned above. For all other expanded access

categories (including investigational medical devices), contact the GBMC IRB office for guidance.

Individual Patient INDs (Non-Emergency Use)

FDA regulations (21 CFR 312) permit an unapproved investigational drug to be used for the treatment of an individual patient by a licensed physician. These non-emergency requests are known as individual patient INDs (investigational new drug).

A physician who wants to use an unapproved investigational drug to treat an individual patient under expanded access shall complete the following steps:

1. Obtain Investigational Drug Manufacturer Cooperation

   Assurance must be obtained from the manufacturer that the company is willing to provide an adequate supply of the investigational drug for the individual patient expanded access use. This assurance is best documented in the form of a letter of authorization (LOA) from the manufacturer for submission to the FDA during the individual patient expanded access application process (See Step 2 below).

2. Submit Individual Patient Expanded Access Application to the FDA

   A licensed physician may use either Form FDA 1571 [Investigational New Drug Application (IND)] or Form FDA 3926 [Individual Patient Expanded Access Investigational New Drug Application (IND)] for submitting an individual patient expanded access request to the FDA. Form FDA 3926 is specifically designed for expanded access use and is a streamlined alternative to Form FDA 1571.

3. Obtain FDA Approval for Individual Patient Expanded Access Use

   In accordance with 21 CFR 312.305(a), the following criteria must be met to obtain FDA approval for an individual patient expanded access request:

   a. "The patient or patients to be treated have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
   b. The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated; and
   c. Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use."

   In addition to the above criteria, the following determinations must be made [21 CFR 312.310(a)]:

a. "The physician must determine that the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition; and
b. FDA must determine that the patient cannot obtain the drug under another IND or protocol."

4. Submit Individual Patient Expanded Access Use Request to the GBMC IRB

Individual patient expanded access use requires either review and approval at a convened IRB meeting at which a majority of the members are present or IRB concurrence before the treatment use begins, depending on the circumstances.

Review and approval at a convened IRB meeting is required under the following circumstances:

a. Form FDA 1571 is used as the application of choice when submitting the individual patient expanded access request to the FDA and does not include a separate request to waive the IRB review requirement, or

b. Form FDA 3926 is used as the application of choice when submitting the individual patient expanded access request to the FDA but the box in Field 10.b "Request for Authorization to Use Alternative IRB Review Procedures" is not checked

Review and approval at a convened IRB meeting is not required under the following circumstances provided the FDA waives the full board IRB requirement under 21 CFR 56.105:

a. Form FDA 1571 is used as the application of choice when submitting the individual patient expanded access request to the FDA and a separate request to waive the IRB review requirement is included, or

b. Form FDA 3926 is used as the application of choice when submitting the individual patient expanded access request to the FDA but the box in Field 10.b "Request for Authorization to Use Alternative IRB Review Procedures" is checked

The box in Field 10.b on Form FDA 3926 is a means for requesting a waiver of the requirements for IRB review and approval at a convened IRB meeting. The Field 10.b box requests "authorization to obtain concurrence by the Institutional Review Board (IRB) chairperson or by a designated IRB member, before the treatment use begins, in order to comply with FDA's requirements for IRB review and approval".

The GBMC IRB recognizes the following two individuals as having the authority to grant concurrence with individual patient expanded access requests:

- IRB Chairperson
- IRB Vice Chairperson

All individual patient expanded access requests (full board reviews and concurrences) shall be sent electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The electronic submission "package" for initial review of an individual patient expanded access request shall include but not be limited to the following:

a. Copy of manufacturer letter of authorization (LOA) or other documentation supporting manufacturer approval
b. Copy of information submitted to the FDA (e.g. FDA Form 3926 and supporting documents)
c. Copy of any correspondence received from the FDA
d. Investigational drug pharmacology and toxicology information (e.g. investigator's brochure)
e. Patient information (e.g. description of disease or condition, medical history)
f. Treatment and monitoring plan (e.g. procedures, tests, drug administration methods, duration of treatment)
g. Copy of informed consent document. Informed consent is an FDA requirement [21 CRR 312.305(c)(4)] for expanded access use, and only consent forms with a valid GBMC IRB approval stamp may be presented to the patient.
h. Conflict of interest statement
i. Curriculum vitae

All individual expanded access requests scheduled for review by the convened IRB require an in-person presentation by the treating physician.

Once the convened IRB votes and makes a formal decision regarding the individual expanded access request or the IRB Chairperson or IRB Vice Chairperson reviews the request for concurrence, the full board decision or acknowledgement of concurrence shall be conveyed by the IRB office staff to the treating physician as soon as possible as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

All individual expanded access requests reviewed for concurrence shall be reported back to the convened IRB at the next scheduled meeting.

An expanded access IND for an individual patient goes into effect 30 days after the FDA receives the individual patient expanded access IND application or earlier if the treating physician is notified by the FDA that treatment may proceed [21 CFR 312.305(c)(5)(d)]. IRB approval and informed consent must also be obtained prior to the start of patient treatment. "Treatment is generally limited to a single course of therapy for a specified duration unless FDA expressly authorizes multiple courses or chronic therapy" [21 CFR 312.310(c)(1)].

A licensed physician treating a patient under an individual patient expanded access IND is considered a sponsor-investigator and must comply with the responsibilities for sponsors and investigators as set forth in 21 CFR 312 to the extent they are applicable to the expanded access use.

Should the expanded access use of the investigational drug continue for one year or longer, the licensed physician treating the patient shall submit an annual report to the GBMC IRB.

Any serious, unexpected adverse reaction to the investigational drug must be reported to the GBMC IRB within 15 calendar days after becoming aware of the event.

Any unexpected fatal or life-threatening suspected adverse reaction to the investigational drug must be reported to the GBMC IRB within seven calendar days after becoming aware of the event.

Once the approved course of treatment is complete, the treating physician must provide the FDA "with a written summary of the results of the expanded access use, including adverse effects" [21 CFR 312.310(c)(2)]. The treating physician has the added responsibility of informing the GBMC IRB when treatment is complete. The IRB requests that a completion of treatment reporting form be submitted as a final report with a copy of the summary report submitted to the FDA.

Individual Patient INDs (Emergency Use)

FDA regulations [21 CFR 312.310(d)] permit an unapproved investigational drug to be used on an individual patient if "there is an emergency that requires the patient to be treated before a written submission can be made" and there is not sufficient time to obtain IRB review and approval.

A licensed physician who wants to use an unapproved investigational drug to treat an individual patient under expanded access for an emergency situation shall complete the following steps:

1. Obtain Investigational Drug Manufacturer Cooperation

   Assurance must be obtained from the manufacturer that the company is willing to provide an adequate supply of the investigational drug for the individual patient expanded access use. This assurance is best documented in the form of a letter of authorization (LOA) from the manufacturer.

2. Contact FDA for Emergency Expanded Access Use Authorization

   "Emergency expanded access use may be requested by telephone, facsimile, or other means of electronic communications." For investigational drugs, requests for authorization "should be directed to the Division of Drug Information, Center for Drug Evaluation and Research, 301-796-3400, e-mail: *druginfo@fda.hhs.gov*. After normal working hours (8 a.m. to 4:30 p.m.), the request should be directed to the FDA Emergency Call Center, 866-300-4374, e-mail: emergency.operations@fda.hhs.gov." [21 CFR 312.310(d)(1)]

3. Obtain FDA Authorization for Emergency Expanded Access Use

For a licensed physician to obtain FDA authorization to treat an individual patient with an investigational drug in an emergency situation, the physician must explain how the expanded access use will meet the requirements of 21 CFR 312.305 and 312.310 and agree to submit an expanded access application to the FDA within 15 working days of receiving authorization [21 CFR 312.310(d)(2)]. Authorization is normally granted by the FDA reviewing official by telephone or other rapid means of communication. Treatment of the patient may begin immediately upon receiving authorization from the FDA reviewing official [21 CFR 312.305(d)(2)(i)] and without IRB approval "provided that such emergency use is reported to the IRB within 5 working days" [21 CFR 56.104(c)] (See Step 5 below).

4. Obtain Informed Consent of Patient

Informed consent must be obtained from the patient or the patient's legally authorized representative prior to the start of treatment in accordance with 21 CFR 50. If prior consent is not possible, federal regulations do allow for an exception from the informed consent requirements provided the treating physician and a physician who is not involved in the treatment plan certify in writing to all of the following:

a. "The human subject is confronted by a life-threatening situation necessitating the use of the test article."
b. "Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject."
c. "Time is not sufficient to obtain consent from the subject's legal representative."
d. "There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject."

(21 CFR 50.23)

If time is not sufficient to obtain certification of a physician who is not involved in the treatment plan as described above, the treating physician may make the determination for exception to the informed consent requirements. However, within 5 working days from the start of treatment, the treating physician's determinations must be reviewed and evaluated by a physician who is not involved in the treatment plan [21 CFR 50.23(b)].

All documentation of exception to the informed consent requirements must be submitted to the IRB within five working days after the start of treatment [21 CFR 50.23(c)] (See Step 5 below).

5. Notify GBMC IRB of Emergency Expanded Access Use

In an emergency situation when there is not sufficient time to secure IRB review prior to beginning treatment, the emergency use of the investigational drug must be reported to the IRB within five working days of the emergency use, as required under 21 CFR 56.104(c). The report shall be sent electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The electronic submission "package" for the reporting of the emergency use of an investigational drug shall include but not be limited to the following:

a. Copy of manufacturer letter of authorization (LOA) or other documentation supporting manufacturer approval
b. Name of the investigational drug
c. Rationale for the emergency use of the drug
d. Patient information (e.g. description of disease or condition, medical history)
e. Treatment rendered
f. Copy of signed informed consent document. If informed consent was not obtained from the patient or the patient's legally authorized representative, include written certification from the treating physician and a physician who is not involved in the patient treatment that all of the following exceptions to informed consent criteria have been met as outlined in 21 CFR 50.23(a)(1-4):
    1) "The human subject is confronted by a life-threatening situation necessitating the use of the test article."
    2) "Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject."
    3) "Time is not sufficient to obtain consent from the subject's legal representative."
    4) "There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject."
g. Any adverse reactions related or possibility related to the use of the investigational drug

The GBMC IRB recognizes the following two individuals as having the authority to review a report of the emergency expanded use of an investigational drug:

- IRB Chairperson
- IRB Vice Chairperson

The reviewer shall report the emergency expanded access use back to the convened IRB at the next scheduled meeting.

Once an investigational drug is used at GBMC in an emergency situation without prior IRB approval, any subsequent use shall require prior IRB review and approval in accordance with 21 CFR 56.104(c). The procedures under "Individual Patient INDs (Non-Emergency Use)" as outlined above shall be followed.

6. Submit Expanded Access Application to FDA

For a licensed physician to obtain FDA authorization to treat an individual patient with an investigational drug in an emergency situation, the licensed physician must explain how the expanded access use will meet the requirements of 21 CFR 312.305 and 312.310 and agree to submit an expanded access application to the FDA within 15 working days of receiving authorization [21 CFR 312.310(d)(2)].

The physician may use either Form FDA 1571 [Investigational New Drug Application (IND)] or Form FDA 3926 [Individual Patient Expanded Access Investigational New Drug Application (IND)] for submitting the follow-up individual patient expanded access

application to the FDA. Form FDA 3926 is specifically designed for expanded access use and is a streamlined alternative to Form FDA 1571.

A licensed physician treating a patient under an emergency individual patient expanded access IND is considered a sponsor-investigator and must comply with the responsibilities for sponsors and investigators as set forth in 21 CFR 312 to the extent they are applicable to the expanded access use.

Should the emergency expanded access use of the investigational drug continue for one year or longer, the licensed physician treating the patient shall submit an annual report to the GBMC IRB.

Any serious, unexpected adverse reaction to the investigational drug must be reported to the GBMC IRB within 15 calendar days after becoming aware of the event.

Any unexpected fatal or life-threatening suspected adverse reaction to the investigational drug must be reported to the GBMC IRB within seven calendar days after becoming aware of the event.

Once the approved course of treatment is complete, the treating physician must provide the FDA "with a written summary of the results of the expanded access use, including adverse effects" [21 CFR 312.310(c)(2)]. The treating physician has the added responsibility of informing the GBMC IRB when treatment is complete. The IRB requests that a completion of treatment reporting form be submitted as a final report with a copy of the summary report submitted to the FDA.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Humanitarian Use Devices
Section Number: 5.14
Effective Date: April 20, 2020
Last Revision:
Replaced SOP Revised On:

Introduction

A humanitarian use device (HUD) is defined by the Food and Drug Administration (FDA) at 21 CFR 814.3(n) as a "medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year." Once a device receives a HUD designation from the FDA Office of Orphan Products Development, a manufacturer may then apply for a humanitarian device exemption (HDE). When the manufacturer submits an HDE application to the FDA, sufficient information must be provided for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury to the patient and that probable benefits to health outweigh the risk of injury or illness from its use. The manufacturer is not required to provide the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose prior to marketing. The manufacturer must show that no comparable devices are available to treat or diagnose the disease or condition. Once the HDE application is approved by the FDA, the manufacturer may market the device for clinical use. The labeling for a HUD must state that the device is a humanitarian use device and, although the device is authorized by federal law, the effectiveness of the device for the specific indication has not been demonstrated. After HDE approval, a HUD may only be used after IRB review and approval has been obtained, except in certain emergency situations where prior approval is not required. Although the FDA has removed the stipulation that the reviewing IRB be local, Greater Baltimore Medical Center requires that the GBMC IRB be the IRB of record with oversight for all circumstances involving the use of a HUD at this institution.

Initial Full Board IRB Review—Clinical Use

IRBs are responsible for initial as well as continuing review of a HUD [21 CFR 814.124(a)]. Initial reviews are performed at a convened meeting of the IRB. All applications for the use of a HUD must be sent electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The electronic submission "package" for initial full review of a HUD shall include but not be limited to the following:

1. Copy of FDA HDE approval order
2. Description of the device
3. Approved indication(s) for use
4. Contraindications, warnings and precautions for use
5. Risks and benefits to the patient
6. Summary of how the device will be used

7. Clinical brochure and/or package insert
8. Device labeling information
9. Patient information materials
10. Copy of the informed consent form
11. Conflict of interest statement from all physicians who will be administering the device
12. Curriculum vitae from all physicians who will be administering the device

All applications for the use of a HUD shall identify one principal responsible physician with other physicians who will be administering the HUD listed as appropriate. IRB approval for the use of a HUD shall be limited to those physicians who are listed on the HUD application form. If additional physicians not listed on the initial application form desire to use the HUD, approval must be obtained from the IRB before such use can take place (see "Modifications to the Device or Its Use—Clinical Use" below).

The principal responsible physician must attend the initial convened IRB meeting in person to present a brief overview of the HUD. The IRB shall use this time to ask the principal responsible physician questions to clarify or explain the use of the HUD. At the conclusion of the presentation and question and answer period, the principal responsible physician shall be excused while the IRB further discusses the proposed use of the HUD.

The FDA recommends that an IRB follow the review criteria found at 21 CFR 56.111 as much as possible. The IRB's review of the HUD submission shall pay special attention to the following:

1. The risks of harm to patients,
2. Ensuring the risks are minimized, and
3. Evaluating whether the risks are reasonable in relation to the proposed use of the HUD

The IRB shall also consider the training and expertise of the physician(s) intending to use the HUD to ensure that the physician(s) is qualified to use the device.

The FDA does not require review and approval of each individual use of a HUD; however, the IRB may use its discretion in determining how to approve the use of a HUD involving high-risk procedures or serious conditions. The IRB may require additional reporting requirements, appropriate follow-up precautions and evaluations, or any other criteria it deems appropriate. Should the IRB place specific stipulations on the use of the HUD, the determination(s) shall be made known in the decision letter.

In accordance with 21 CFR 56.107(a), the IRB shall have at least one member present at the time of initial HUD review who has the appropriate experience and expertise to review the HUD in question. If there is no IRB member with the appropriate experience and expertise to perform a complete and adequate review of the use of the HUD, a consultant shall be invited to attend the convened meeting as described in SOP Section 2.4—Consultants.

Once the IRB votes and makes a formal decision regarding the use of the HUD, the decision shall be conveyed by the IRB office staff to the principal responsible physician as soon as possible after the convened meeting as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

Informed Consent Requirements—Clinical Use

Since the clinical use of a HUD does not constitute research, the FDA does not require informed consent from patients for the use of a HUD; however, an IRB may choose to require informed consent. The GBMC IRB requires that documented informed consent be obtained from the patient or the patient's legally authorized representative prior to the use of a HUD. The HUD informed consent document shall contain but not be limited to the following:

1. An explanation as to what a HUD is
2. A statement explaining why the patient is a candidate for the HUD
3. An explanation of the HUD's mechanism of action in relation to the disease or condition
4. A description of the procedures to be followed, including follow-up
5. A description of potential risks and discomforts
6. A description of potential benefits
7. What other treatment or diagnostic options are available, if any
8. A statement as to any costs to the patient
9. An explanation as to whether any compensation is available if injury occurs
10. A statement describing how the patient's identifiable information will be protected
11. Whom to contact if there are questions or concerns
12. A statement that the decision to use the HUD is voluntary

In addition to the requirement that documented informed consent be obtained prior to the use of a HUD, the GBMC IRB requires that patients receive all available consumer information accompanying the HUD.

HIPAA Requirements—Clinical Use

When a HUD is being used according to its approved labeling and indication, and not for research purposes, the HIPAA regulations requiring the use of a HIPAA research authorization are not applicable.

A HIPAA covered entity may use and disclose protected health information without the patient's authorization if the use or disclosure is for the purpose of treatment.

Modifications to the Device or Its Use—Clinical Use

All proposed changes to the HUD and/or the clinical use of the HUD must be reviewed and approved by the IRB prior to implementation. This includes the addition or removal of any physicians using the HUD.

All proposed (non-emergency) uses of the HUD outside of its approved labeling and indication(s) must be reviewed and approved by the IRB prior to implementation.

If the FDA grants approval for use of the HUD for an additional clinical indication(s), IRB review and approval must be obtained before the HUD can be used for the additional

indication(s). The documentation to be submitted to the IRB for review shall include but not be limited to:

1. A description of the modification(s) to the HUD and/or the clinical use of the HUD
2. A copy of the FDA's approval of the modification(s)
3. A copy of the HUD manufacturer's amendments to the HUD product label, clinical brochure, and/or other pertinent manufacturer information materials corresponding to the requested modification(s)
4. A copy of the revised informed consent form, if applicable

Continuing Review—Clinical Use

In addition to initial review of a HUD, the FDA requires continuing review [21 CFR 814.124(a)] to be conducted "at intervals appropriate to the degree of risk but not less than once per year" [21 CFR 56.109(f)]. The FDA recommends the use of expedited procedures (21 CFR 56.110) for continuing review; however, the FDA does allow an IRB to develop its own HUD continuing review policies and procedures and perform continuing reviews at convened meetings. The GBMC IRB uses expedited review procedures for continuing review on only the rarest of occasions when a continuing review cannot be conducted in a timely fashion in relation to when a meeting of the convened IRB is scheduled. The GBMC IRB shall apply, as appropriate, SOP Section 5.5—Continuing Reviews to all HUD continuing reviews.

All HUD continuing review submissions must be sent electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The IRB recommends that continuing review requests be submitted for review at the convened IRB meeting scheduled in the month prior to the HUD's approval expiration date. The electronic submission "package" for a HUD continuing review shall contain but not be limited to the following:

1. Total number of patients treated using the HUD
2. Total number of patients treated using the HUD in the past year
3. Total number of patients no longer using and/or had the HUD removed
4. Copies of all Medical Device Reporting (MDR) reports submitted to the FDA, if any
5. Annual conflict of interest statement(s) from all physicians administering the HUD

Adverse Event and Medical Device Reporting Requirements—Clinical Use

HUDs are subject to Medical Device Reporting (MDR) requirements in accordance with 21 CFR 803. The principal responsible physician and the user facility (GBMC) must submit reports to the FDA, the manufacturer and/or the IRB of record as described at 21 CFR 803.30 and 814.126(a) whenever a HUD may have caused or contributed to a death or serious injury. A serious injury is defined at 21 CFR 803.3(w) as "an injury or illness that: (1) Is life-threatening, (2) Results in permanent impairment of a body function or permanent damage to a body structure, or (3) Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure."

Reports of serious injury or death must be reported to the GBMC IRB within 10 working days after becoming aware of the information.

Discontinuation of HUD Use Report—Clinical Use

The principal responsible physician has the responsibility of informing the IRB when a HUD is no longer being administered at GBMC. The GBMC IRB requests that a "Discontinuation of HUD Use Report Form" be submitted as a final report.

Prompt Reporting of FDA Actions on the HUD—Clinical and Investigational Use

All FDA actions (e.g. withdrawal of HDE approval) must be reported to the GBMC IRB as soon as possible after learning of the action.

Emergency Use of a HUD for a Single Patient

"If a physician in an emergency situation determines that approval from an IRB cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be administered without prior approval by an IRB. In such an emergency situation, the physician shall, within 5 days after the use of the device, provide written notification to the chairman of the IRB of such use. Such written notification shall include the identification of the patient involved, the date on which the device was used, and the reason for the use." (21 CFR 814.124)

Should the physician use the HUD outside of its approved indication(s), the FDA recommends that the physician obtain informed consent from the patient, ensure that measures are in place to protect the patient (e.g. devising schedules to monitor the patient), and submit a follow-up report on the patient's condition to the HDE holder.

HUDs used in an emergency situation for a single patient are subject to Medical Device Reporting (MDR) requirements in accordance with 21 CFR 803 and as described above under "Adverse Event and Medical Device Reporting Requirements—Clinical Use".

Investigational Use of a HUD

IRB approval of a HUD for clinical use does not mean that the IRB has approved the HUD for investigational use. IRB approval, informed consent, HIPAA research authorization and additional safeguards for children (if applicable) are required for the investigational use of a HUD, whether the HUD is being studied for its HDE-approved indication(s) or for a different indication(s).

Applications for the investigational use of a HUD shall be submitted to the IRB as described in SOP Section 4.2—Submission Deadlines and Requirements.

The GBMC IRB shall review the investigational use of a HUD based on the same regulatory criteria (21 CFR Parts 50 and 56) as any other FDA-regulated clinical investigation (See also SOP Section 4.1—Criteria for Human Subjects Research Approval).

If the HUD is to be used in accordance with its HDE-approved indication(s), the FDA considers such an investigation exempt from the investigational device exemption (IDE) requirements at

21 CFR 812. However, if the HUD is to be used for an indication other than its HDE approved indication(s), the IDE requirements at 21 CFR 812 shall be applied, including a significant risk or non-significant risk (SR/NSR) determination. It shall be the sponsor's (or sponsor-investigator's) responsibility to make the initial SR/NSR determination for subsequent consideration by the IRB as part of its review of the HUD application. All HUD applications that involve a significant risk device must include evidence of an FDA-approved IDE application.

All applications for the investigational use of a HUD shall be reviewed at a convened IRB meeting as described in SOP Section 5.1—Initial Full Committee Reviews. The IRB's decision shall be conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible after the convened meeting as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

The principal investigator shall comply with but not be limited to the following SOPs as they relate to the investigational use of a HUD with ongoing GBMC IRB oversight:

1. Section 4.4—Investigator Conflicts of Interest
2. Section 4.5—Investigator Qualifications, Responsibilities and Training Requirements
3. Section 5.5a—Continuing Reviews
4. Section 5.8—Changes in Research Activity: Revisions and Amendments
5. Section 5.9—Adverse Events and Unanticipated Problems[1]
6. Section 5.10—Protocol Deviations/Violations

The principal investigator has the responsibility of informing the IRB when a project involving the investigational use of a HUD has been completed as described in SOP Section 5.6—Permanent Project Closures.

[1]The principal investigator shall also comply with 1) 21 CFR 812.150(1) which states that "an investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect." and 2) all applicable Medical Device Reporting (MDR) requirements at 21 CFR 803.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Significant and Nonsignificant Risk Device Determinations
Section Number: 5.15
Effective Date: August 17, 2020
Last Revision:
Replaced SOP Revised On:

All research projects involving the use of a device must be reviewed by the GBMC IRB and are subject to the FDA's Investigational Device Exemptions (IDE) regulations at 21 CFR 812. Research projects involving the use of a device cannot be initiated until the project has been reviewed and approved by the IRB.

The FDA considers a product to be a device, and subject to FDA regulations, if it meets the definition of a device as defined in the Food, Drug, and Cosmetic Act at 21 USC 321(h):

"An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

1. recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
2. intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
3. intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes".

Unless exempt from the Investigational Device Exemptions (IDE) regulations at 21 CFR 812, a device must be categorized as being either significant risk (SR) or nonsignificant risk (NSR).

The FDA, at 21 CFR 812.3(m), defines a significant risk device as "an investigational device that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject."

A nonsignificant risk device is one that does not meet the above definition for a significant risk device.

This policy outlines the procedures used by the GBMC IRB for making significant risk and nonsignificant risk device determinations.

Sponsors and/or investigators are responsible for making an initial significant or nonsignificant risk determination. It is the expectation of the IRB that all submission "packages", for research projects involving the use of an investigational device, include a device risk determination. Should there be no risk determination included in the submission "package", the sponsor and/or investigator shall be asked to submit a determination prior to IRB review.

Should the sponsor and/or investigator submit evidence that a risk determination has been made by the FDA, the GBMC IRB shall accept the FDA's determination as final. Documentation of a FDA approved IDE shall be accepted as evidence of a significant risk determination. Once the IRB is presented with satisfactory evidence of a FDA device risk determination, the IRB shall proceed with the new project review as it would with any other FDA regulated project in accordance with 21 CFR 56, using the approval criteria at 21 CFR 56.111 and as described in IRB SOP Section 4.1--Criteria for Human Subjects Research Approval.

All device risk determinations made solely by the sponsor and/or investigator shall be independently reviewed by the convened IRB for concurrence.

The IRB shall consider but not be limited to the following when making a risk determination:

--A description of the device
--How the device will be used and the type of harm that may result from use of the device
--Whether or not the device meets the definition of a significant risk device
--The rationale used by the sponsor and/or investigator in making the risk determination
--The proposed investigational plan
--Potential harm that may result from additional procedures needed as part of the device study

The IRB may also choose to consult with the FDA for guidance in making a risk determination.

The IRB may agree or disagree with the sponsor's and/or investigator's initial significant or nonsignificant risk determination:

1. <u>If the sponsor and/or investigator makes an initial nonsignificant risk determination and the IRB concurs with the determination</u>, the IRB shall proceed with the new project review as it would with any other FDA regulated project in accordance with 21 CFR 56, using the approval criteria at 21 CFR 56.111 and as described in IRB SOP Section 4.1--Criteria for Human Subjects Research Approval. The sponsor and/or investigator will not need to submit an IDE application to the FDA. The FDA considers a nonsignificant risk device study to have an approved IDE after IRB approval and when the sponsor and/or investigator meets the abbreviated requirements at 21 CFR 812.2(b). A nonsignificant risk device project may be initiated immediately following full IRB approval.

2. If the sponsor and/or investigator makes an initial nonsignificant risk determination and the IRB disagrees with the determination and determines the device to be of significant risk, the convened IRB shall terminate the new project review and take the action of "modifications required".

   The IRB action and determination shall be conveyed by the IRB office staff in writing to the sponsor and/or investigator as soon as possible after the convened meeting of the IRB. The correspondence shall include the IRB's rationale for the significant risk determination and a directive to the sponsor and/or investigator to submit an IDE application to the FDA. The sponsor and/or investigator must report the IRB's significant risk determination to the FDA within 5 working days of being notified [21 CFR 812.150(b)(9)].

   The proposed new project may not be initiated until the IRB receives documentation that the FDA has approved the IDE application and the IRB has granted full approval to the research project.

   Once the IRB receives satisfactory evidence that the IDE application has been approved by the FDA, the IRB shall proceed with the new project review as it would with any other FDA regulated project in accordance with 21 CFR 56, using the approval criteria at 21 CFR 56.111 and as described in IRB SOP Section 4.1--Criteria for Human Subjects Research Approval. The new project may be initiated immediately following full IRB approval. The sponsor and/or investigator shall meet all the requirements at 21 CFR 812.

   Should the FDA return the IDE application and make a nonsignificant risk determination, the IRB shall accept the FDA's decision as final and proceed with the new project review as it would with any other FDA regulated project in accordance with 21 CFR 56, using the approval criteria at 21 CFR 56.111 and as described in IRB SOP Section 4.1--Criteria for Human Subjects Research Approval. The new project may be initiated immediately following full IRB approval. The sponsor and/or investigator shall meet the abbreviated requirements at 21 CFR 812.2(b).

   If no responsive action is taken within 90 days of the IRB's initial "modifications required" decision, the entire new project submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety to be re-considered.

3. If the sponsor and/or investigator makes an initial significant risk determination without first consulting with the FDA and the IRB concurs with the determination, the convened IRB shall terminate the new project review and take the action of "modifications required".

   The IRB action and determination shall be conveyed by the IRB office staff in writing to the sponsor and/or investigator as soon as possible after the convened meeting of the IRB. The correspondence shall include the IRB's rationale for concurring with the significant risk determination and a directive to the sponsor and/or investigator to submit an IDE application to the FDA.

The proposed new project may not be initiated until the IRB receives documentation that the FDA has approved the IDE application and the IRB has granted full approval to the research project.

Once the IRB receives satisfactory evidence that the IDE application has been approved by the FDA, the IRB shall proceed with the new project review as it would with any other FDA regulated project in accordance with 21 CFR 56, using the approval criteria at 21 CFR 56.111 and as described in IRB SOP Section 4.1--Criteria for Human Subjects Research Approval. The new project may be initiated immediately following full IRB approval. The sponsor and/or investigator shall meet all the requirements at 21 CFR 812.

Should the FDA return the IDE application and make a nonsignificant risk determination, the IRB shall accept the FDA's decision as final and proceed with the new project review as it would with any other FDA regulated project in accordance with 21 CFR 56, using the approval criteria at 21 CFR 56.111 and as described in IRB SOP Section 4.1--Criteria for Human Subjects Research Approval. The new project may be initiated immediately following full IRB approval. The sponsor and/or investigator shall meet the abbreviated requirements at 21 CFR 812.2(b).

If no responsive action is taken within 90 days of the IRB's initial "modifications required" decision, the entire new project submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety to be re-considered.

4. <u>If the sponsor and/or investigator makes an initial significant risk determination without first consulting with the FDA and the IRB disagrees with the determination</u>, and determines the device to be of nonsignificant risk, the IRB shall proceed with the new project review as it would with any other FDA regulated project in accordance with 21 CFR 56, using the approval criteria at 21 CFR 56.111 and as described in IRB SOP Section 4.1--Criteria for Human Subjects Research Approval. The sponsor and/or investigator will not be directed by the IRB to submit an IDE application to the FDA. The FDA considers a nonsignificant device study to have an approved IDE after IRB approval and when the sponsor and/or investigator meets the abbreviated requirements at 21 CFR 812.2(b). A nonsignificant risk device project may be initiated immediately following full IRB approval.

All determinations and actions shall be documented in the IRB meeting minutes as described in SOP Section 3.5—Minutes of the Meeting.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Research Involving Children
Section Number: 5.16
Effective Date: November 16, 2020
Last Revision:
Replaced SOP Revised On:

Both the HHS (Department of Health and Human Services) and the FDA (Food and Drug Administration) consider children to be a vulnerable population requiring additional protections when they are participating as subjects in research. IRBs are obligated to ensure that the rights and welfare of children are adequately protected by complying with the following regulatory requirements, as they apply:

1. 45 CFR 46 Subpart D—Additional Protections for Children Involved as Subjects in Research (HHS) – Applied to all research projects involving children submitted to the GBMC IRB

2. 21 CFR 50 Subpart D—Additional Safeguards for Children in Clinical Investigations (FDA) – Applied to all FDA regulated research projects involving children submitted to the GBMC IRB

This policy outlines the procedures used by the GBMC IRB for approving research involving children as subjects.

The following definitions apply throughout this policy:

"*Children* are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." [45 CFR 46.402(a)] [21 CFR 50.3(o)]

"*Assent* means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent." [45 CFR 46.402(b)] [21 CFR 50.3(n)]

"*Permission* means the agreement of parent(s) or guardian to the participation of their child or ward in research." [45 CFR 46.402(c)] [21 CFR 50.3(r)]

"*Parent* means a child's biological or adoptive parent." [45 CFR 46.402(d)] [21 CFR 50.3(p)]

"*Guardian* means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care." [45 CFR 46.402(e)] [21 CFR 50.3(s)]

The above-mentioned HHS and FDA definitions are identical except that the FDA uses "clinical investigation" in place of the word "research".

Maryland law (Maryland Code Annotated Health-General §9.5-101) defines a child as meaning "an individual under the age of 18 years".

All proposed new research projects involving children shall be reviewed by the convened IRB. The IRB may request that a pediatric consultant assist in the review as described in SOP Section 2.4—Consultants.

To approve research involving children, the IRB shall first determine that all regulatory criteria at 45 CFR 46 Subpart A (HHS) and, as applicable, 21 CFR 50 Subpart A (FDA) are satisfactorily met (See also SOP Section 4.1—Criteria for Human Subjects Research Approval).

The IRB shall also consider the following as part of the review process:

1. Potential benefits to the children
2. Risks and discomforts to the children
3. Justification for the inclusion of children in the research

Once Subpart A has been taken into consideration and found to be satisfactorily met, the IRB shall continue their review by applying Subpart D of 45 CFR 46 (HHS) and, as applicable, 21 CFR 50 (FDA) to the new research project involving children.

Federal regulations at 45 CFR 46 Subpart D (HHS) and 21 CFR 50 Subpart D (FDA) identify three categories under which an IRB can approve research involving children. The GBMC IRB shall apply one of the following three categories when reviewing a new research project involving children:

1. "Research not involving greater than minimal risk." [45 CFR 46.404] [21 CFR 50.51]

   "Minimal risk means that the probability and magnitude of 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 examinations or tests" [45 CFR 46.102(j)] [21 CFR 50.3(k)]

2. "Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects."

   The IRB must also find that:

   a) "The risk is justified by the anticipated benefit to the subjects;
   b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
   c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians."

   [45 CFR 46.405] [21 CFR 50.52]

3. “Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition.”

   The IRB must also find that:

   a) “The risk represents a minor increase over minimal risk;
   b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or education situations;
   c) The intervention or procedure 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; and
   d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.”

      [45 CFR 46.406] [21 CFR 50.53]

The category choice made by the IRB, shall be documented in the meeting minutes.

There is a fourth category ("Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.” [45 CFR 46.407] [21 CFR 50.54]) for research that does not meet the requirements of any of the three above-mentioned categories. Research protocols qualifying for this fourth category require a special level of review by HHS and, as applicable, FDA review beyond what the GBMC IRB can provide. All proposed new projects involving children that fall into this fourth category shall be addressed on a case-by-case basis.

Once the IRB has selected one of the above-mentioned categories to apply to the proposed research project, the IRB shall then determine whether ‘the children are capable of providing assent” and “that adequate provisions are made for soliciting the assent of the children” in accordance with 45 CFR 46.408(a) and, as applicable, 21 CFR 50.55(a).

The IRB shall consider the following when determining whether the children are capable of providing assent, with the judgment being made for all children or for each child [45 CFR 46.408(a)] [21 CFR 50.55(b)]:

1. Age of the children
2. Maturity level
3. Psychological state

All judgments made by the IRB regarding the capability of the children to provide assent shall be documented in the meeting minutes.

Assent of the children is not necessary if the IRB determines that one of the following two conditions apply [45 CFR 46.408(a)] [21 CFR 50.55(c)(1)(2)]:

1. "The capability of some or all of the children is so limited that they cannot reasonably be consulted", or
2. "The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research"

Should the IRB determine that assent of the children is not necessary, the determination and condition applied shall be documented in the meeting minutes. Further, should the IRB determine that only some (not all) of the children are incapable of providing assent, those children shall be identified by the IRB and the determination shall be documented in the meeting minutes.

Even when the IRB determines that the children are capable of providing assent, the IRB may still waive the assent requirement if the criteria found at 45 CFR 46.116(f)(3) and, as applicable, 21 CFR 50.55(d) are met.

Federal regulations at 45 CFR 46.408(e) and 21 CFR 50.55(g) state that "When the IRB determines that assent is required, it shall also determine whether and how assent must be documented". The GBMC IRB uses the following guidelines to determine how assent shall be documented:

1. Children up to 7 years of age: Written documentation is not required; however, verbal assent should be obtained and documented when the children are capable.

2. Children 7 to 12 years of age: Written documentation is required using a simplified assent form appropriate for the age and comprehension level of the children.

3. Children 13 to 17 years of age: Written documentation is required using a form that is appropriate for the age and comprehension level of the children. Depending on the complexity of the research project, the form can be either very similar or identical to the parental permission form.

Children who reach the age of seven (7) and are still actively participating in a research project should document their willingness to continue participation by the signing of a simplified assent form appropriate for their age and comprehension level as stated above in #2.

Children who reach the age of 18 and are still actively participating in a research project should be re-approached to confirm that they are still willing to continue their participation. Their willingness to continue should be documented by the signing of an adult informed consent form that is in accordance with and to the extent required by 45 CFR 46.116 and, as applicable, 21 CFR 50 Subpart B—Informed Consent of Human Subjects.

The IRB shall also determine that adequate provisions are made for soliciting the permission of each child's parents or guardian; however, waiver of parental permission by the IRB is permitted under 45 CFR 46.408(c) (HHS) if specific criteria are met. The FDA does not have a comparable waiver of parental permission to match 45 CFR 46.408(c); however, according to the July 2017 FDA guidance "IRB Waiver or Alteration of Informed Consent for Clinical

Investigations Involving No More Than Minimal Risk to Human Subjects", the FDA will not "object to an IRB approving a consent procedure that does not include, or alters, some or all of the elements of informed consent set forth in 21 CFR 50.25" for minimal risk clinical investigations.

When parental permission is required, the parents or guardian shall provide informed consent on behalf of the child as follows and in accordance with 45 CFR 46.408(b) and, as applicable, 21 CFR 50.55(e):

1. "Research not involving greater than minimal risk" (45 CFR 46.404) (21 CFR 50.51) shall require the permission of at least one parent or guardian with the IRB determining on a case-by-case basis whether the permission of one parent is sufficient.

2. "Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects" (45 CFR 46.405) (21 CFR 50.52) shall require the permission of at least one parent or guardian with the IRB determining on a case-by-case basis whether the permission of one parent is sufficient.

3. "Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition" (45 CFR 46.406) (21 CFR 50.53) shall require the permission of both parents or guardian.

Federal regulations at 45 CFR 46.408(d) and 21 CFR 50.55(f) state that "Permission by parents or guardians shall be documented in accordance with and to the extent required by" 45 CFR 46.117 and 21 CFR 50.27 (Documentation of Informed Consent). The GBMC IRB, as a general rule, requires written documentation of parental permission; however, in certain cases, documentation of permission may be waived and an information sheet used instead [45 CFR 46.117(c)(2)] [21 CFR 56.109(d)].

The IRB shall also apply, as applicable, Maryland law (Maryland Code Annotated Health-General §20-102) which states that a minor has the same capacity as an adult to consent to medical treatment if they are (1) married, (2) the parent of a child, or (3) living separate and apart from their parent, parents, or guardian, and are self-supporting, regardless of the source of their income.

Should the IRB find that the assenting and parental permission processes as described in the submitted research protocol differ with any of the above stated GBMC IRB specific guidelines, the IRB shall address the matter on a case-by-case basis.

In addition to the requirements, guidelines and processes stated above, the IRB shall also follow all applicable parts set forth in SOP Section 5.1—Initial Full Committee Reviews.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Overview of Cooperative Research Using an External IRB
Section Number: 6.1
Effective Date: January 1, 2005
Last Revision: November 20, 2023
Replaced SOP Revised On: August 16, 2021

Cooperative research projects are those projects that involve more than one institution or site (also referred to as multi-site). Each institution or site is responsible for safeguarding the rights and welfare of human subjects. Federal regulations allow for the use of an external IRB and, under certain circumstances, mandate the use of a single IRB of record for multi-site, cooperative research projects (45 CFR 46.114 and 21 CFR 56.114).

It is the preference of GBMC that the GBMC IRB be the IRB of record and have oversight of all research conducted at GBMC; however, GBMC acknowledges that there may be instances when the use of an external or central IRB may be necessary and/or mandated to participate in proposed cooperative research. When these circumstances arise, GBMC shall consider requests to use an external IRB for cooperative research on a case-by-case basis.

All proposed cooperative research involving the use of an external IRB shall be reviewed by the convened GBMC IRB.

The review process for cooperative research using an external IRB involves ~~four~~ three steps as follows:

Step 1. Initial Request to Conduct Cooperative Research Using an External IRB

All proposed cooperative research projects involving the use of an external IRB must undergo initial review by the GBMC IRB for preliminary approval. Preliminary approval grants permission to pursue and/or execute an IRB reliance agreement, the study contract, site approval, and all other required documents necessary for initiating the proposed research at GBMC.

The proposed cooperative research activities are not approved for initiation at this stage of the review process. Final approval (See Step 3) must be obtained prior to initiating the research.

Step 2. Review and Execution of Study Related Documents

Once preliminary approval has been granted by the GBMC IRB, the appropriate personnel shall move ahead with finalizing and executing all required documents necessary for initiating the proposed research.

Once all of the necessary documents have been finalized and/or executed, final approval to conduct the proposed research shall be requested from the GBMC IRB (See Step 3).

Step 3. Final Approval of the Cooperative Research and Use of an External IRB

A request for final approval to conduct cooperative research using an external IRB must be submitted to the GBMC IRB for review by the IRB Chairperson.

The proposed cooperative research project cannot be initiated until final notification has been received from the GBMC IRB approving the cooperative research and accepting the external IRB as the IRB of record.

The approval process above (Steps 1 through ~~4~~ 3) is described in greater detail in SOP Section 6.2—Initial Review of Cooperative Research Using an External IRB.

Post-Approval Responsibilities

Once the GBMC IRB has approved the cooperative research and accepted the external IRB as the IRB of record, the GBMC principal investigator shall have the responsibility to comply with the IRB reliance agreement, study contract and any other applicable documents and/or determinations and requirements as dictated by the external IRB of record, lead principal investigator, coordinating center and/or study sponsor.

Even though GBMC does not provide IRB oversight when an external IRB is the IRB of record, the GBMC IRB shall remain responsible for all research that takes place at GBMC. The GBMC principal investigator shall have reporting obligations to the GBMC IRB as described in SOP Section 6.2—Initial Review of Cooperative Research Using an External IRB.

Cooperative Research Using the CIRB for the National Cancer Institute

GBMC is enrolled in the National Cancer Institute Central Institutional Review Board (CIRB) Adult Initiative and maintains an ongoing "Authorization Agreement/Division of Responsibilities" with the CIRB. The approval process for cooperative research using the CIRB is described in SOP Section 6.3—Initial Review of Cooperative Research Using the CIRB.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Initial Review of Cooperative Research Using an External IRB
Section Number: 6.2
Effective Date: January 20, 2020
Last Revision: November 20, 2023
Replaced SOP Revised On: August 16, 2021

Research projects involving cooperative research and the use of an external IRB must be reviewed by the GBMC IRB. Research activities cannot be initiated until the proposed project has been reviewed and approved by the GBMC IRB.

The initial review of cooperative research using an external IRB involves a three-step process. This policy outlines the process and describes the procedures to be followed for the approval of cooperative research using an external IRB.

All cooperative research projects under the oversight of an external IRB shall have one designated local principal investigator who shall have full responsibility for the conduct of the research and the study team personnel at GBMC.

Step 1. Initial Request to Conduct Cooperative Research Using an External IRB

All requests to conduct cooperative research using an external IRB shall be submitted to the GBMC IRB electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The GBMC IRB must receive project information in sufficient detail to make an informed decision. The electronic submission "package" shall contain but not be limited to the following information and/or documents:

- Name of proposed external IRB
- Complete project protocol
- Investigator brochure (if applicable)
- Informed consent form
- HIPAA research authorization (if consent is not HIPAA compliant)
- Conflict of interest statements
- Evidence of current training in human subjects research

All initial requests to conduct cooperative research using an external IRB shall be reviewed by the convened GBMC IRB.

The local principal investigator or a qualified substitute must attend the convened IRB meeting in person to present a brief overview of the research and be available to answer any questions from the committee members.

If a member of the convened IRB has a conflict of interest with the proposed cooperative research, they shall abstain from participating in the review and voting processes.

The GBMC IRB shall take one of the following three actions when reviewing requests to conduct cooperative research using an external IRB:

1. Approve – signifies that the IRB has preliminarily approved the request granting permission to pursue and execute reliance agreements, study contracts and other applicable documents (See Step 2)

2. Approve with conditions – signifies that the IRB has approved the request but specific conditions must be satisfactorily met to secure full preliminary approval.

   When a request to conduct cooperative research using an external IRB is approved with conditions, the principal investigator shall be notified as to the pending approval and the conditions that must be met to secure full preliminary approval.

   If no responsive action is taken by the principal investigator within 90 days of being notified of the approved with conditions decision, the submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety to be reconsidered.

3. Disapprove – signifies that the IRB has found significant and sufficient fault with the request/submission to warrant its disapproval.

   In the event that this occurs, the principal investigator shall be notified as to the reason for the disapproval and the corrective action, if any, that could be taken to secure preliminary approval. No further action will be taken by the IRB. Any decision to appeal, in accordance with SOP Section 4.7—Appeal of Review Actions and Determinations, or resubmit rests with the principal investigator.

Requests to conduct cooperative research using an external IRB shall be approved by a majority vote of the convened GBMC IRB. Majority is defined as being fifty percent of the members present plus one.

GBMC IRB actions and determinations shall be conveyed by the GBMC IRB office staff to the principal investigator and other key personnel as soon as possible after a decision has been made.

All GBMC IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief

Medical Officer and Signatory Official on GBMC's Federalwide Assurance. (See also SOP Section 3.5—Minutes of the Meeting)

Step 2. Review and Execution of Study Related Documents

Once preliminary approval has been granted by the GBMC IRB, the appropriate personnel shall move ahead with finalizing and executing the necessary study related documents:

- The IRB Coordinator shall contact the point person at the proposed external IRB and begin the process of entering into and executing an IRB reliance agreement. The reliance agreement will dictate the respective responsibilities of both IRBs and institutions.

  The process shall include but not be limited to the following steps:

  1. Once a copy of the reliance agreement is received from the external IRB, the agreement shall be reviewed by the IRB Coordinator. GBMC legal counsel shall be consulted and review reliance agreements as deemed necessary.
  2. Revision recommendations shall be communicated back to the external IRB point person by the IRB Coordinator.
  3. Once the content of the reliance agreement is determined to be satisfactory by both parties, the agreement shall be signed by the designated signatories and executed. The signatory for GBMC is recognized to be the Chief Medical Officer who serves as the IRB Institutional Official.
  4. When the IRB reliance agreement is fully executed, the IRB Coordinator shall notify the principal investigator and other key personnel as appropriate.

- The principal investigator and/or other key personnel, as appropriate, shall proceed with finalizing and executing the study contract and any other documents related to site approval and the conduct of the study at GBMC.

Step 3. Final Approval of the Cooperative Research and Use of an External IRB

Once all applicable study related documents have been executed, including an IRB reliance agreement, final approval to conduct the proposed cooperative research at GBMC shall be requested from the GBMC IRB.

The request for final approval shall be submitted to the GBMC IRB via IRBNet for final review as described in SOP Section 4.2—Submission Deadlines and Requirements. The GBMC IRB recognizes the following two individuals as having the authority to review requests for final approval to conduct cooperative research using an external IRB:

1. IRB Chairperson
2. IRB Vice Chairperson

If the IRB Chairperson has a conflict of interest with the proposed research activity, the submission shall be forwarded to the IRB Vice Chairperson for final review.

The reviewer/IRB shall take one of the following three actions:

1. Approve – signifies that the IRB has fully approved the cooperative research for initiation at GBMC and accepts the external IRB as the IRB of record.

2. Approve with conditions – signifies that the IRB has approved the request for final approval but specific conditions must be satisfactorily met to secure full final approval.

   When a submission is approved with conditions, the principal investigator shall be notified as to the pending approval and the conditions that must be met to secure full and final approval.

   If no responsive action is taken by the principal investigator within 90 days of being notified of the approved with conditions decision, the submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety to be reconsidered.

3. Disapprove – signifies that the IRB has found significant and sufficient fault with the submission and applicable documents to warrant its disapproval.

   The proposed cooperative research cannot be initiated at GBMC and all executed documents shall be terminated.

   In the event that disapproval occurs, the principal investigator shall be notified as to the reason for the disapproval and the corrective action, if any, that could be taken to secure final approval. No further action will be taken by the IRB. Any decision to appeal, in accordance with SOP Section 4.7—Appeal of Review Actions and Determinations, or resubmit rests with the principal investigator.

GBMC IRB actions and determinations shall be conveyed by the GBMC IRB office staff to the principal investigator and other key personnel as soon as possible after a final decision has been made.

The reviewer shall report their decision back to the convened IRB at the next scheduled meeting.

All GBMC IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer and Signatory Official on GBMC's Federalwide Assurance. (See also SOP Section 3.5—Minutes of the Meeting)

Post-Approval Responsibilities

Once the GBMC IRB has approved and accepted the external IRB as the IRB record, the GBMC principal investigator shall have the responsibility to comply with the IRB reliance agreement, study contract and any other applicable documents and/or determinations and requirements as dictated by the external IRB of record, lead principal investigator, coordinating center and/or study sponsor.

Even though GBMC does not provide IRB oversight when an external IRB is the IRB of record, the GBMC IRB shall remain responsible for all research that takes place at GBMC. The GBMC principal investigator shall have reporting obligations to the GBMC IRB that include but not be limited to the following:

1. Undergoing an independent annual review that shall include the submission of annual conflict of interest statements and evidence that current training in human subjects research is being maintained (See SOP Section 6.4—Independent Annual Reviews).
2. Submitting matters of local context (e.g. study team changes) for approval or acknowledgement (See SOP Section 6.6—Matters of Local Context).
3. Notifying the GBMC IRB of all adverse events, other reportable events and unanticipated problems occurring at GBMC (See SOP Section 6.7—Adverse and Other Reportable Events).
4. Notifying the GBMC IRB of protocol deviations occurring at GBMC (See SOP Section 6.8—Protocol Deviations/Violations).
5. Notifying the GBMC IRB of permanent project closures (See SOP Section 6.5—Permanent Project Closures).

Review Fee

The GBMC IRB shall charge a review fee of $200 for all initial reviews of requests to conduct cooperative research using an external IRB (See SOP Section 4.3—Review Fees

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Initial Review of Cooperative Research Using the CIRB
Section Number: 6.3
Effective Date: January 20, 2020
Last Revision:
Replaced SOP Revised On:

Cooperative research projects involving the use of the CIRB (Central Institutional Review Board) for the National Cancer Institute must be reviewed by the GBMC IRB.

The initial review of cooperative research using the CIRB involves a two-step process. This policy outlines the process and describes the procedures to be followed for the approval of cooperative research using the CIRB.

All cooperative research projects under the oversight of the CIRB shall have one designated principal investigator who shall have full responsibility for the conduct of the research and the study team personnel at GBMC.

Step 1. Approval from the CIRB to Conduct Proposed Cooperative Research

The principal investigator or designee shall submit to the CIRB the required "Study-Specific Worksheet About Local Context". This online worksheet must be submitted to the CIRB to open a study at the signatory institution (GBMC).

Once the "Study-Specific Worksheet" has been accepted and approved granting permission to conduct the study, a request to conduct cooperative research using the CIRB shall be submitted to the GBMC IRB.

Research activities cannot be initiated until the proposed project has been reviewed and approved by the GBMC IRB.

Step 2. Submission of Request to Conduct Cooperative Research Using the CIRB

All requests to conduct cooperative research using the CIRB shall be submitted to the GBMC IRB electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The GBMC IRB must receive project information in sufficient detail to make an informed decision. The electronic submission "package" shall contain but not be limited to the following:

- Complete project protocol
- Investigator brochure (if applicable)
- Informed consent form
- HIPAA research authorization

- Conflict of interest statements
- Evidence of current training in human subjects research
- CIRB correspondence documenting approval of the study-specific worksheet

The GBMC IRB recognizes the following two individuals as having the authority to review a request to conduct cooperative research using the CIRB:

1. IRB Chairperson
2. Vice Chairperson

All requests to conduct cooperative research using the CIRB shall be forwarded to the IRB Chairperson for review. If the IRB Chairperson has a conflict of interest with the proposed research activity, the submission shall then be forwarded to the IRB Vice Chairperson.

The reviewer/IRB shall take one of the following three actions when reviewing a request to conduct cooperative research using the CIRB:

1. Approve – signifies that the IRB has approved the cooperative research for initiation at GBMC and accepts the CIRB as the IRB of record.

2. Approve with conditions – signifies that the IRB has approved the submission but specific conditions must be satisfactorily met to secure full approval.

   When a submission is approved with conditions, the principal investigator shall be notified as to the pending approval and the conditions that must be met to secure full approval.

   If no responsive action is taken by the principal investigator within 90 days of being notified of the approved with conditions decision, the submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety to be reconsidered.

3. Disapprove – signifies that the IRB has found significant and sufficient fault with the request/submission and corresponding documents to warrant its disapproval.

   The proposed cooperative research cannot be initiated at GBMC and all executed documents shall be terminated to include the submission of a "Study Closure or Transfer of Study Review Responsibility Worksheet" to the CIRB.

   In the event that disapproval occurs, the principal investigator shall be notified as to the reason for the disapproval and the corrective action, if any, that could be taken to secure approval. No further action will be taken by the IRB. Any decision to appeal in accordance with SOP Section 4.7—Appeal of Review Actions and Determinations or resubmit rests with the principal investigator.

GBMC IRB actions and determinations shall be conveyed by the GBMC IRB office staff to the principal investigator and other key personnel as soon as possible after a final decision has been made.

All GBMC IRB actions and determinations shall be reported back to the fully convened IRB at the next scheduled meeting.

All GBMC actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer and Signatory on GBMC's Federalwide Assurance.

Post-Approval Responsibilities

Once the GBMC IRB has approved and accepted the CIRB as the IRB record, the GBMC principal investigator shall have the responsibility to comply with all CIRB determinations and requirements.

Even though GBMC does not provide IRB oversight when an external IRB is the IRB of record, the GBMC IRB shall remain responsible for all research that takes place at GBMC. The GBMC principal investigator shall have reporting obligations to the GBMC IRB that include but not be limited to the following:

6. Undergoing an independent annual review that shall include the submission of annual conflict of interest statements and evidence that current training in human subjects research is being maintained (See SOP Section 6.4—Independent Annual Reviews).
7. Submitting matters of local context (e.g. study team changes) for approval or acknowledgement (See SOP Section 6.6—Matters of Local Context).
8. Notifying the GBMC IRB of all adverse events, other reportable events and unanticipated problems occurring at GBMC (See SOP Section 6.7—Adverse and Other Reportable Events).
9. Notifying the GBMC IRB of protocol deviations occurring at GBMC (See SOP Section 6.8—Protocol Deviations/Violations).
10. Notifying the GBMC IRB of permanent project closures (See SOP Section 6.5—Permanent Project Closures).

Review Fee

The GBMC IRB shall charge a review fee of $200 for all initial reviews of requests to conduct cooperative research using the CIRB (See SOP Section 4.3—Review Fees).

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Independent Annual Reviews
Section Number: 6.4
Effective Date: January 20, 2020
Last Revision:
Replaced SOP Revised On:

The external IRB of record shall have the responsibility for conducting continuing review of ceded research projects in accordance with 45 CFR 46 (Federal Policy for the Protection of Human Subjects--Common Rule), 21 CFR 56 (Food and Drug Administration) and other regulations and laws as applicable; however, the GBMC IRB has determined that research ceded to an external IRB shall be subject to a local "independent annual review" that shall correspond with the annual continuing review performed by the external IRB of record.

At the time of GBMC IRB initial review and approval of cooperative research, all ceded projects shall be given an approval expiration date indicating when the project must undergo a local independent annual review. Independent annual review expiration dates are calculated to correspond with the approval expiration date as determined by the external IRB of record. It is the responsibility of the principal investigator to submit for an independent annual review prior to the GBMC IRB determined annual review due date or as soon as possible after receiving documentation of the external IRB's continuing review approval.

As a courtesy, independent annual review reminder emails in the form of a "Project Expiration Reminder" shall be sent out automatically via IRBNet 60 and 30 days prior to a project's annual review due date. If the project does not undergo an independent annual review prior to the GBMC IRB determined annual review due date, IRBNet will send a final notice on the due date of the annual review. Failure to submit for the independent annual review may result in a directive to cease all research activity until the independent annual review has been performed by the GBMC IRB.

Independent annual reviews are performed by the convened IRB.

All independent annual review submissions must be sent electronically via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements. The electronic submission "package" for an independent annual review shall contain but not be limited to the following documents:

1. Request for independent annual review of projects with external IRB oversight
2. Conflict of interest statements from the principal investigator and all co-investigators on the study team
3. Evidence of current human subjects research training from the principal investigator, co-investigators and study coordinator
4. Copy of external IRB continuing review approval letter

Once an independent annual review has been completed, the GBMC IRB's action shall be conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations. Independent annual review follow-up letters shall clearly state the due date for the next annual review.

IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer and Signatory Official on GBMC's Federalwide Assurance. (See also SOP Section 3.5—Minutes of the Meeting)

Review Fee

The GBMC IRB shall charge a review fee of $100 for all independent annual reviews of cooperative research using an external IRB (See SOP Section 4.3—Review Fees).

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Permanent Project Closures
Section Number: 6.5
Effective Date: January 20, 2020
Last Revision:
Replaced SOP Revised On:

Principal investigators have the responsibility of informing the GBMC IRB when a project ceded to an external IRB of record has been completed. The GBMC IRB requests that, upon the completion of a project, a "Request for Review of Project Closure (Permanent)" form be submitted as a final report.

All closure of project submissions shall be reviewed by the convened GBMC IRB and acknowledged. The IRB's acknowledgement shall be formally conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible after the convened meeting as described in SOP Section 4.6—Notification and Documentation of Review Actions and Decisions. IRB office records shall be coded to indicate that the project is now permanently closed.

Once a project is permanently closed, the IRB shall retain individual project files for six years. Once the six year retention time frame has elapsed, the project files (both hard copy and those maintained electronically in IRBNet) shall be permanently deleted and/or destroyed.

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Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Matters of Local Context
Section Number: 6.6
Effective Date: January 20, 2020
Last Revision:
Replaced SOP Revised On:

Principle investigators have the responsibility of submitting to the GBMC IRB for review all changes in research that are matters of local context. Matters of local context include but are not limited to the following:

1. Project team changes
2. Revisions/amendments
3. Updates/reports

The GBMC IRB requests that the matters of local context be submitted using a "Request for Review of Matters of Local Context" form. All matters of local context shall be reviewed by the convened GBMC IRB.

When matters of local context requiring a vote are reviewed by the convened IRB, a primary reviewer shall be appointed. The IRB Assistant shall assign each matters of local context submission to a qualified IRB member for review. The IRB member shall summarize and present the nature of the local matter to the convened IRB. The IRB Assistant shall not assign a matters of local context submission to any IRB member who has a conflicting interest in the local matter and/or project undergoing review.

All decisions made by the GBMC IRB regarding a submission for matters of local context shall be conveyed by the IRB office staff to the principal investigator and other key project personnel as soon as possible as described in SOP Section 4.6—Notification and Documentation of Review Actions and Determinations.

IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer and Signatory Official on GBMC's Federalwide Assurance. (See also SOP Section 3.5—Minutes of the Meeting)

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Name of SOP: Adverse and Other Reportable Events
Section Number: 6.7
Effective Date: January 20, 2020
Last Revision:
Replaced SOP Revised On:

Federal regulations 45 CFR 46.108(a)(4) and 21 CFR 56.108(b)(1-3) require the IRB to follow written procedures for ensuring the prompt reporting to the IRB, appropriate institutional officials, and governmental departments and/or agency heads of any:

5. unanticipated problems involving risks to subjects or others
6. serious or continuing noncompliance with Federal regulations
7. serious or continuing noncompliance with requirements or determinations of the IRB
8. suspension or termination of IRB approval

This policy outlines the procedures for prompt reporting to the GBMC IRB of adverse events, unanticipated problems and all other reportable events.

All reporting requirements of the external IRB of record and/or the overall principal investigator's participating institution shall also be followed as dictated in all applicable agreements and/or contracts.

Definitions

Adverse Event (AE): An AE is defined as "any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse Events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research."

Serious Adverse Event (SAE): A SAE is defined as "any adverse event temporally associated with the subject's participation in research that meets any of the following criteria:

7. results in death;
8. is life-threatening (places the subject at immediate risk of death from the event as it occurred);
9. requires inpatient hospitalization or prolongation of existing hospitalization;
10. results in a persistent or significant disability/incapacity;
11. results in a congenital anomaly/birth defect; or

12. any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition"

Unanticipated Problem (UP): An unanticipated problem is defined as "any incident, experience, or outcome that meets all of the following criteria:

4. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
5. related or possibly related to participation in the research; and
6. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized."

Possibly related to the research means that "there is a reasonable possibility that the adverse event, incident, experience or outcome may have been caused by the procedures involved in the research".

Internal Adverse Event: An adverse event that occurs in study participants who were enrolled through GBMC or a GBMC affiliated study site.

External Adverse Event: An adverse event that occurs in study participants who were not enrolled through GBMC or a GBMC affiliated study site.

Reporting Requirements for Internal Adverse Events

All internal adverse events that meet the above-definition of a serious adverse event or an unanticipated problem shall be reported to the GBMC IRB within 5 business days of the investigator becoming aware of the event.

All internal events that meet the above-definition of an adverse event but do not meet the above-definition of a serious adverse event or unanticipated problem shall be reported to the GBMC IRB within 10 business days of the investigator becoming aware of the event.

All internal adverse events that are reported to an outside entity (e.g. external IRB of record, sponsor, FDA) with study oversight shall be reported to the GBMC IRB within 10 business days of the investigator becoming aware of the event.

All subject deaths that occur while on study shall be reported to the GBMC IRB within 48 hours of the investigator becoming aware of the event unless the event is clearly unrelated to the study procedures or related to natural progression of a disease process.

Reporting Requirements for External Adverse Events

The "OHRP advises that it is neither useful nor necessary under the HHS regulations at 45 CFR part 46 for reports of individual adverse events occurring in subjects in multicenter studies to be distributed routinely to investigators or IRBs at all institutions conducting the research."

Only external adverse events that meet the following criteria need to be reported to the GBMC IRB:

5. events that are determined by the sponsor to be an unanticipated problem involving risks to subjects or others
6. events that result in a modification to the protocol, informed consent document and/or investigator brochure
7. events that result in suspension of all or parts of the research
8. events that result in early termination of the research

External adverse events shall be reported to the GBMC IRB within 10 business days of the investigator becoming aware of the event.

Other Reportable Events

In addition to the above-mentioned adverse events, serious adverse events, and unanticipated problems, the GBMC IRB considers the following to be reportable events:

8. new or updated safety information relating to the study or study product
9. DSMB/DMC or other independent safety monitoring group report
10. any externally imposed suspension or termination of the research due to new or increased risks
11. a breach of confidentiality or violation of HIPAA
12. unresolved participant complaints
13. adverse audit results or enforcement actions
14. any other problem indicating that the research places subjects or others at an increased risk of harm or otherwise adversely affects the rights, welfare or safety of subjects or others

The above mentioned other reportable events shall be reported to the GBMC IRB within 10 business days of the investigator becoming aware of the event.

For reasons of confidentiality, subject names must not be included in any reportable event submission. Subject identifiers such as enrollment numbers should be used instead.

GBMC IRB Review Process for Reported Events

All reported events shall be screened by the GBMC IRB office staff. The IRB office staff shall either place the submitted item on the agenda for the next scheduled meeting of the convened IRB or forward it to the IRB Chairperson or his designee for review.

The following internal events shall be promptly forwarded to the GBMC IRB Chairperson or his designee for immediate review:

7. Death of a subject or life-threatening circumstances
8. Serious adverse events that are unresolved
9. Unanticipated problems resulting in risks to subjects or others
10. Serious or continuing noncompliance with Federal regulations
11. Serious or continuing noncompliance with requirements or determinations of the IRB
12. Any other event involving risks to subjects or others

The IRB Chairperson or designee shall report the review findings back to the convened IRB at the next scheduled meeting. The principal investigator shall be notified of all review findings and if any corrective action is required or additional information is needed.

If the GBMC IRB determines that corrective action is necessary, the required action may include:

10. Frequent progress or status reports to the IRB
11. Suspension of all or parts of the research
12. Termination of the research
13. Other actions as determined by the IRB

If the GBMC IRB determines that the event is of a magnitude that it must be reported to other appropriate authorities, those authorities may include:

5. GBMC institutional officials
6. External IRB of record
7. The Office for Human Research Protection (OHRP)
8. The Food and Drug Administration (FDA)
9. Other governmental departments or agency heads as appropriate

The IRB Coordinator shall be responsible for notifying the following GBMC officials regarding the reportable event within 5 business days of the IRB's determination:

4. Chief Medical Officer
5. Vice President for Legal Affairs and General Counsel
6. Vice President for Quality and Patient Safety

The IRB Chairperson shall be responsible for notifying all appropriate governmental departments and/or agencies within 15 business days of GBMC officials being notified of the reportable event unless otherwise dictated in the IRB reliance agreement. A copy of all correspondence and/or reports shall be forwarded to the above-mentioned GBMC officials.

[All quoted passages within this policy have been taken from the OHRP "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" dated 1/15/07]

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Protocol Deviations/Violations
Section Number: 6.8
Effective Date: January 20, 2020
Last Revision:
Replaced SOP Revised On:

As previously stated in Section 6.7—Adverse and Other Reportable Events--Federal regulations 45 CFR 46.108(a)(4) and 21 CFR 56.108(b)(1-3) require the IRB to follow written procedures for ensuring the prompt reporting to the IRB, appropriate institutional officials, and governmental departments and/or agency heads of any:

9. unanticipated problems involving risks to subjects or others
10. serious or continuing noncompliance with Federal regulations
11. serious or continuing noncompliance with requirements or determinations of the IRB
12. suspension or termination of IRB approval

This policy outlines the procedures for prompt reporting to the GBMC IRB.

All reporting requirements of the external IRB of record and/or the overall principal investigator's participating institution shall also be followed as dictated in all applicable agreements and/or contracts.

The term "protocol deviation" is not defined by either OHRP human subjects regulations (45 CFR 46) or FDA human subjects regulations (21 CFR 50). For GBMC IRB purposes, a protocol deviation is any modification or departure from the defined procedures and treatment plans set forth in the IRB-approved protocol.

Protocol deviations/violations range in seriousness according to how the changes may impact subject safety. The GBMC IRB has divided protocol deviations/violations into two categories—major and minor.

A major protocol deviation/violation is defined as any change that may impact subject safety or alter the risk/benefit ratio, compromise the integrity of the study data, and/or affect a subject's willingness to participate in the study. Major protocol deviations/violations include but are not limited to the following:

- Enrollment of a subject before IRB approval of study
- Enrollment of a subject after IRB approval of study has expired
- Enrollment of a subject who did not meet inclusion/exclusion criteria
- Failure to obtain informed consent prior to initiating study procedures
- Inappropriate documentation of informed consent (e.g. missing subject signature)
- Use of a non-IRB approved informed consent

- Use of an invalid informed consent (e.g. outdated version)
- Failure to perform a study specific procedure (impacting subject safety)
- Out of window visit and/or procedure (impacting subject safety)
- Performing study procedures not approved by the IRB
- Drug/study medication dispensing or dosing error
- Incorrect storage/handling of study drug/medication, biological samples, etc.
- Loss or destruction of samples or data
- Failure to follow protocol safety and monitoring requirements
- Any lapse in study approval where there is a continuation of research activities
- Any event requiring prompt reporting according to the protocol or IRB of record
- Any other deviation impacting subject safety

A minor protocol deviation/violation is defined as a one-time change that does not significantly affect the safety of the subject. Minor protocol deviations/violations include but are not limited to the following:

- Use of recruitment method and/or material not approved by the IRB
- Missing original signed and dated informed consent (copy available)
- Copy of signed informed consent not given to subject
- Missing pages of executed informed consent
- Failure to perform a study specific procedure (not impacting subject safety)
- Out of window visit and/or procedure (not impacting subject safety)
- Failure of subject to return unused study drug/medication
- Improper investigational product accountability
- Failure to follow Federal regulations
- Failure to follow requirements or determinations of the GBMC IRB and/or external IRB of record

Minor protocol deviations/violations that occur repetitively may be determined to be a major deviation by the GBMC IRB and require corrective action.

All major protocol deviations/violations shall be reported to the GBMC IRB within 5 business days of the investigator becoming aware of the event.

All major protocol deviations/violations resulting in the death of a subject shall be reported to the GBMC IRB within 48 hours of the investigator becoming aware of the event.

All minor protocol deviations/violations shall be submitted to the GBMC IRB on an individual basis or no less than every quarter (every 90 days) in the form of a summary report.

All emergency situations involving the implementation of a non-IRB approved protocol deviation to eliminate apparent immediate hazards to a subject shall be reported to the GBMC IRB within 48 hours of the event taking place.

Protocol deviations/violations that occur at a non-GBMC affiliated site in a multi-center research study do not need to the reported to the GBMC IRB.

All protocol deviations/violations shall be screened by the GBMC IRB office staff. The IRB office staff shall either place the submitted item on the agenda for the next scheduled meeting of the convened GBMC IRB or forward it to the IRB Chairperson or his designee for review.

The following protocol deviations/violations shall be promptly forwarded to the GBMC IRB Chairperson or his designee for immediate review:

1. All major deviations/violations that could possibly be classed as a:
   a. serious noncompliance,
   b. continuing noncompliance, or
   c. unanticipated problem involving risks to subjects or others

2. All major deviations/violations resulting in the death of a subject

3. All deviations/violations being conducted under an emergency situation

The GBMC IRB Chairperson or his designee shall report the review findings back to the convened IRB at the next scheduled meeting. The principal investigator shall be notified of all review findings and if any corrective action is required or additional information is needed.

If the GBMC IRB determines that corrective action is necessary, the required action may include:

14. Monitoring of the informed consent process
15. Re-consenting of currently enrolled subjects
16. Monitoring of research activities
17. Suspension of all or parts of the research
18. Termination of the research
19. Other actions as determined by the IRB

If the GBMC IRB determines that the event is of a magnitude that it must be reported to other appropriate authorities, those authorities may include:

10. GBMC institutional officials
11. External IRB of record
12. The Office for Human Research Protection (OHRP)
13. The Food and Drug Administration (FDA)
14. Other governmental departments or agency heads as appropriate

The IRB Coordinator shall be responsible for notifying the following GBMC officials regarding the reportable event within 5 business days of the IRB's determination:

7. Chief Medical Officer
8. Vice President for Legal Affairs and General Counsel

9. Vice President for Quality and Patient Safety

The IRB Chairperson shall be responsible for notifying all appropriate governmental departments and/or agencies within 15 business days of GBMC officials being notified of the reportable event unless otherwise dictated in the IRB reliance agreement. A copy of all correspondence and/or reports shall be forwarded to the above-mentioned GBMC officials.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Cooperative Research Using GBMC as IRB of Record
Section Number: 6.9
Effective Date: January 20, 2020
Last Revision:
Replaced SOP Revised On:

Federal regulations allow for the use of and, under certain circumstances, mandate the use of a single IRB of record for multi-site cooperative research projects (45 CFR 46.114 and 21 CFR 56.114).

The GBMC IRB will consider being the IRB of record for multi-site cooperative research projects that are no greater than minimal risk. "Minimal risk means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests" [45 CFR 46.102(j) and 21 CFR 56.102(i)].

The initial review of requests for the GBMC IRB to be the IRB of record involves a three-step process. This policy outlines the process and describes the procedures to be followed for the GBMC IRB to be the IRB of record for multi-site cooperative research.

Research activities cannot be initiated at any collaborating site(s) until the proposed activities have been approved by the GBMC IRB and the GBMC IRB has formally accepted the responsibility of being the IRB of record for the collaborating sites(s) and a corresponding IRB reliance agreement(s) has been executed.

Step 1. Initial Request for the GBMC IRB to be the IRB Record for Cooperative Research

All requests for the GBMC IRB to be the IRB of record for multi-site cooperative research shall be initially handled by the IRB office staff. All requests will be considered on a case-by-case basis. Contact the IRB Office to discuss the details of the proposed research project and the steps that will need to be taken in order for the GBMC IRB to agree to be the IRB of record for the proposed multi-site cooperative research.

The GBMC IRB approval obtained during this step (Step 1) of the review process is a preliminary approval and grants permission to pursue execution of an IRB reliance agreement (See Step 2) and final review and acceptance of GBMC IRB as IRB of record (See Step 3).

Step 2. Review and Execution of the IRB Reliance Agreement

Once the GBMC IRB has preliminarily agreed to be the IRB of record for the proposed multi-site cooperative research, the IRB Coordinator shall contact the point person(s) at the collaborating institution(s) and begin the process of entering into and executing an IRB reliance

agreement(s). The reliance agreement(s) will dictate the respective responsibilities of the IRBs and institutions.

Reliance agreements shall be reviewed by GBMC Legal Counsel and the IRB Coordinator prior to execution. The GBMC recognized signatory for executing all IRB reliance agreements is the Chief Medical Officer who serves as the GBMC IRB Institutional Official.

Step 3. Final Review and Acceptance of GBMC as IRB of Record for Cooperative Research

Once the GBMC IRB has preliminarily agreed to be the IRB of record for the proposed multi-site cooperative research, the principal investigator and/or other key personnel as appropriate shall make one of two submissions via IRBNet as described in SOP Section 4.2—Submission Deadlines and Requirements:

1. New Project Submission. If the proposed research is being presented to the GBMC IRB for the first time, an application for new research project shall be submitted to include a formal request that the GBMC IRB be the IRB of record and all necessary information and documentation regarding the other collaborating site(s) and their study team.

2. Amendment/Modification Submission. If the proposed research has already undergone GBMC IRB review and is a currently active study under the oversight of the GBMC IRB, a revisions and amendments form shall be submitted to include a formal request that the GBMC IRB be the IRB of record and all necessary information and documentation regarding the other collaborating site(s) and their study team.

The above-mentioned submissions shall be reviewed by the convened GBMC IRB.

The GBMC IRB shall take one of the following three actions when reviewing either of the two above-referenced submissions:

4. Approve – signifies that the IRB has approved the submission and corresponding documents as received and has formally accepted the role of IRB of record.

5. Approve with conditions – signifies that the IRB has approved the submission and corresponding documents but specific conditions must be satisfactorily met to secure full approval and GBMC IRB acceptance as the IRB of record.

   When a submission is approved with conditions, the principal investigator shall be notified as to the pending approval and the conditions that must be met to secure full approval and the IRB's acceptance as the IRB of record.

   If no responsive action is taken by the principal investigator within 90 days of being notified of the approved with conditions decision, the submission shall be administratively withdrawn by the IRB office staff, and it must be resubmitted in its entirety to be reconsidered.

6. Disapprove – signifies that the IRB has found significant and sufficient fault with the submission and corresponding documents to warrant its disapproval.

   In the event that disapproval occurs, the principal investigator shall be notified as to the reason for the disapproval and the corrective action, if any, that could be taken to secure full approval and GBMC IRB acceptance as the IRB of record. No further action will be taken by the IRB. Any decision to appeal in accordance with SOP Section 4.7—Appeal of Review Actions and Determinations or resubmit rests with the principal investigator.

GBMC IRB actions and determinations shall be conveyed by the GBMC IRB office staff to the principal investigator and other key personnel as soon as possible after a final decision has been made.

All GBMC IRB actions and determinations are reported back to institutional (GBMC) officials on a monthly basis in the form of meeting minutes. The minutes are submitted to the Chief Medical Officer and Signatory Official on GBMC's Federalwide Assurance. (See also SOP Section 3.5—Minutes of the Meeting)

Step 3 (Final Review and Acceptance of GBMC as IRB of Record for Cooperative Research) may take place concurrently with Step 2 (Review and Execution of the IRB Reliance Agreement) above. However, the IRB reliance agreement must be fully executed prior to the GBMC IRB's final acceptance of being the IRB of record.

Post Approval Responsibilities

Once the appropriate IRBNet submission (See Step 3 above) has been made and the GBMC IRB has formally agreed to be the IRB of record for the multi-site cooperative research, the GBMC principal investigator and the principal investigator of the relying institution shall have the responsibility to comply with the IRB reliance agreement, study contract and any other applicable documents and/or determinations and requirements as dictated by the GBMC IRB as the IRB of record.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: General Requirements and Guidelines for Informed Consent
Section Number: 7.1
Effective Date: January 1, 2005
Last Revision: September 18, 2023
Replaced SOP Revised On:

OVERVIEW

This policy describes general requirements and guidelines [both Federal (HHS and FDA) and Institutional (GBMC)] regarding the informed consent of human subjects in research.

Informed consent is more than just obtaining a signature on a form for enrolling a prospective human subject in research. It is a process of education and information exchange. In brief, the informed consent document communicates to a prospective subject the purpose, procedures, risks and benefits of the research, the subject's rights in participating in the research, and the freedom to decline to participate without any penalties. It is the principal investigator or designee's responsibility to educate prospective subjects to a level of understanding whereby they can make a truly informed decision as to whether to participate in the research.

GENERAL REQUIREMENTS (FEDERAL)

The Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) both set forth, in 45 CFR 46.116(a) and 21 CFR 50.20 respectively, the following general requirements for informed consent and the involvement of a human subject in research:

1. No investigator shall enroll or involve a human subject in research until "legally effective informed consent of the subject or the subject's legally authorized representative" has been obtained [45 CFR 46.116(a)(1)] [21 CFR 50.20]
2. Consent shall only be sought "under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence" [45 CFR 46.116(a)(2)] [21 CFR 50.20]
3. "The information that is given to the subject or the legally authorized representative shall be in a language understandable to the subject or the legally authorized representative." [45 CFR 46.116(a)(3)] [21 CFR 50.20]
4. "The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information" [45 CFR 46.116(a)(4)]
5. "Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research." The information presented in this concise presentation

section of the informed consent must be "organized and presented in a way that facilitates comprehension." [45 CFR 46.116(a)(5)(i)]

6. The information contained in the informed consent must be in sufficient detail regarding the research, and it "must be organized and presented in a way that does not merely provide lists of isolated facts" [45 CFR 46.116(a)(5)(ii)]
7. The informed consent presentation (whether it be written or oral) shall not contain "any exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights, or release or appears to release the investigator, the sponsor, the institution, or its agents from liability." [45 CFR 46.116(a)(6)] [21 CFR 50.20]

DELEGATION OF AUTHORITY TO CONSENT RESEARCH SUBJECTS

The informed consent process begins when a prospective research subject is contacted by the principal investigator regarding participating in a research project. The principal investigator may delegate authority to consent and enroll prospective subjects to another individual; however, this individual should be qualified to do so by education, training, experience and understanding of the scientific content of the research. The principal investigator is responsible for providing adequate supervision of those to whom tasks are delegated. Prospective research subjects should not be approached about their potential participation in a research project prior to the project being reviewed and approved by the GBMC IRB.

GBMC IRB REVIEW AND APPROVAL OF INFORMED CONSENT DOCUMENTS

The GBMC IRB shall review all informed consent documents for adherence to any local requirements and compliance with federal regulations regarding the required elements of informed consent (See SOP Section 7.2—Elements of Informed Consent) and for assurance of the adequacy of the information contained in the informed consent. Informed consent documents shall not be used unless they have been reviewed and approved by the IRB. Any changes in the informed consent documents or processes must be submitted via IRBNet to the IRB for review and approval prior to implementation (See SOP Section 4.2—Submission Deadlines and Requirements and SOP Section 5.8—Changes in Research Activity: Revisions and Amendments).

Only the most recent version of a GBMC IRB-approved informed consent document shall be used when consenting research subjects. GBMC IRB-approved informed consent documents shall be stamped on each page with an approval stamp that includes the date approved. IRB approved and stamped informed consent documents for use with project participants are posted in the project's electronic IRBNet file.

WRITTEN DOCUMENTATION OF INFORMED CONSENT

Unless a waiver is granted in accordance with 45 CFR 46.117(c) (HHS) and in the case of FDA regulated research 21 CFR 56.109(c), informed consent shall be documented using a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative.

For complete policy details regarding the documentation of informed consent, see SOP Section 7.3—Documentation of Informed Consent.

INFORMED CONSENT OF ADULTS

Informed consent may only be obtained from adult subjects who have the legal and mental capacity to give consent. For subjects without that capacity, permission must be obtained from a legal guardian or a legally authorized representative with appropriate authority to make decisions regarding the activities called for in the research. A legally authorized representative (LAR) is defined by 45 CFR 46.102 (HHS) and 21 CFR 50.3 (FDA) 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."

INFORMED CONSENT OF CHILDREN

Both the Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) at 45 CFR 46.402(a) and 21 CFR 50.3(o) respectively define children as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted."

Maryland law (Maryland Code Annotated Health-General §9.5-101) defines a child as meaning "an individual under the age of 18 years".

For complete policy details regarding the informed consent of children, see SOP Section 5.16—Research Involving Children and SOP Section 7.14—Child Assent and Parental Permission.

POSTING OF INFORMED CONSENT FORMS FOR CLINICAL TRIALS SUPPORTED BY A FEDERAL DEPARTMENT OR AGENCY

The Revised 2018 Common Rule at 45 CFR 46.116(h)(1) states that "For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Web site that will be established as a repository for such informed consent forms." This requirement applies to non-exempt clinical trials that have received initial IRB approval on or after January 21, 2019 and non-exempt clinical trials that received initial IRB approval prior to January 21, 2019 and were transitioned to comply with the Revised 2018 Common Rule.

Informed consent forms must be posted on one of the following two federal websites:

1. ClinicalTrials.gov, or
2. Regulations.gov (Docket ID: HHS-OPHS-2018-0021)

The informed consent forms must be posted on one of the two above-mentioned websites "after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol". [45 CFR 46.116(h)(3)]

The above-mentioned Federal informed consent form posting requirement has limited applicability at GBMC.

Although GBMC applies the Revised 2018 Common Rule to all research, GBMC does not apply this informed consent form posting requirement to non-federally funded, investigator-initiated research projects.

BROAD CONSENT

The Revised 2018 Common Rule at 45 CFR 46.116(d) includes an option for obtaining broad consent. Broad consent is an alternative consent process for the storage, maintenance, and secondary use of identifiable private information or identifiable biospecimens for future, yet-to-be-specified research. The use of broad consent requires that a sophisticated tracking system be maintained which GBMC currently does not have in place. For this reason, GBMC does not permit the use of broad consent.

GBMC IRB INFORMED CONSENT FORM TEMPLATES

The GBMC IRB has made available in IRBNet (See "Forms and Templates") various informed consent templates (e.g., adult consent, child assent, oral telephone scripts). These templates include the required and suggested additional elements of informed consent. In the case of investigator-initiated projects, it is strongly recommended that researchers use the GBMC IRB provided templates to develop their informed consent documents, modifying them as appropriate for their specific research needs.

OBSERVATION OF CONSENT PROCESSES AND RESEARCH ACTIVITIES

An IRB has the authority to observe or have a third party observe consent processes and research activities [45 CFR 46.109(g) and 21 CFR 56.109(f)]. In order to ensure that consent processes are appropriate and approved processes are being followed, the GBMC IRB may determine that special monitoring is necessary. Projects that could require special monitoring include but are not limited to the following:

- Projects involving significant or high risk
- Projects involving particularly complicated procedures or interventions
- Projects involving vulnerable populations
- Projects being conducted by inexperienced investigators and/or project teams
- Projects where a complaint has been submitted regarding the consent process
- Other projects as determined necessary by the IRB

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Elements of Informed Consent
Section Number: 7.2
Effective Date: January 1, 2005
Last Revision: September 18, 2023
Replaced SOP Revised On:

Both the Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) at 45 CFR 46.116(b) and 21 CFR 50.25(a) respectively list basic elements of informed consent that must be provided to each subject or their legally authorized representative, unless specifically waived by the IRB.

The GBMC IRB shall review all informed consents regardless of format (e.g., written, oral scripts) to determine if the following basic elements of informed consent have been addressed:

1. "A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental."
2. "A description of any reasonably foreseeable risks or discomforts to the subject."
3. "A description of any benefits to the subject or to others which may reasonably be expected from the research."
4. "A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject."
5. "A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained." Consent documents for FDA-regulated research must also make note of the "possibility that the Food and Drug Administration may inspect the records" [21 CFR 50.25(a)(5)].
6. "For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained."
7. "An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject."
8. "A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled."

   [All of the quoted passages above have been taken from 45 CFR 46.116(b) and 21 CFR 50.25(a) unless stated otherwise.]

The Revised 2018 Common Rule that went into effect on January 21, 2019, added a ninth basic element of consent. All informed consent documents subject to the 2018 Requirements shall include:

"One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

(ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies." [45 CFR 46.116(b)(9)]

[The above quoted ninth basic element of consent only appears in the Revised 2018 Common Rule. It is not an addition to the FDA regulations.]

The GBMC IRB shall also review all informed consents for the following additional elements of informed consent listed at 45 CFR 46.116(c) (HHS) and 21 CFR 50.25(b) (FDA) respectively. These additional elements shall be provided to each subject or their legally authorized representative when appropriate:

1. "A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable."
2. "Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent."
3. "Any additional costs to the subject that may result from participation in the research."
4. "The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject."
5. "A statement that 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."
6. "The approximate number of subjects involved in the study."

The Revised 2018 Common Rule that went into effect on January 21, 2019, added three more additional elements of informed consent. All research subject to the 2018 Requirements shall include:

1. "A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit." [45 CFR 46.116(c)(7)]

2. "A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions." [45 CFR 46.116(c)(8)]
3. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)." [45 CFR 116(c)(9)]

   [The above quoted three additional elements of consent only appear in the Revised 2018 Common Rule. They are not an addition to the FDA regulations.]

Informed consent documents for applicable FDA-regulated clinical trials must include the following statement as a way of informing subjects that the clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank ClinicalTrials.gov. The statement must be incorporated into the informed consent document verbatim:

"A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

All informed consent documents submitted to the GBMC IRB are pre-reviewed by the GBMC IRB office staff prior to their release for final review by the convened IRB or expedited review. If any required elements of informed consent are found to be lacking in an informed consent document at the time of pre-review, the IRB office staff shall attempt to have the informed consent document revised to conform to the basic elements of informed consent as set forth in 45 CFR 46.116(b) and 21 CFR 50.25(a). Should an informed consent document be reviewed by the convened IRB or reviewed by way of expedited review and found to be lacking any of the required elements of informed consent, the document shall be either disapproved or conditionally approved pending satisfactory revisions.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Documentation of Informed Consent
Section Number: 7.3
Effective Date: January 1, 2005
Last Revision: September 18, 2023
Replaced SOP Revised On:

Unless a waiver is granted in accordance with 45 CFR 46.117(c) (HHS) and in the case of FDA-regulated research 21 CFR 56.109(c), informed consent shall be documented using a written informed consent form. The informed consent form must be approved by the IRB and signed by the subject or the subject's legally authorized representative. The individual signing the informed consent form shall be given a copy of the signed document.

The GBMC IRB reviews all informed consent documents. Only GBMC IRB-approved informed consent documents shall be used when consenting subjects. It is the responsibility of the principal investigator to make certain that all applicable federal regulations and institutional requirements regarding the consenting of subjects be adhered to.

An informed consent document may be in either of the following two formats:

1. Long Form – A long form is a full length standard written consent form that contains all the required basic elements of informed consent (See SOP Section 7.2—Elements of Informed Consent). This written informed consent is to be given to the subject or the subject's legally authorized representative to read. It may also be read orally to the subject or the subject's legally authorized representative. [45 CFR 46.117(b)(1) and 21 CFR 50.27(b)(1)]

2. Short Form – A short form is a written consent stating that the required basic elements of informed consent have been presented orally to the subject or the subject's legally authorized representative. A written summary of the oral presentation shall be reviewed and approved by the IRB prior to use. [45 CFR 46.117(b)(2) and 21 CFR 50.27(b)(2)].

   A short form is typically used for consenting a non-English-speaking subject when there is no translated long form consent available in a language understandable to the potential subject or the subject's legally authorized representative (See SOP Section 7.5—Informed Consent of Non-English-Speaking Subjects).

Long form consent forms shall be signed by the subject or the subject's legally authorized representative. The individual signing the informed consent form shall be given a copy of the signed document. [45 CFR 46.117(a) and 21 CFR 50.27(a)]

When a short form method is used, there shall be a witness to the oral presentation. The subject or the subject's legally authorized representative shall sign the short form document only; however, the witness shall sign both the short form document and a copy of the oral presentation

summary with the person obtaining the consent also signing a copy of the summary. A copy of the oral presentation summary and the short form itself shall be given to the subject or the subject's legally authorized representative [45 CFR 46.117(b)(2) and 21 CFR 50.27(b)(2)].

For certain types of research, an IRB may waive the requirement to obtain signed informed consent from either individual subjects or all subjects participating in a research project. A waiver of signed informed consent means that subjects are to be provided with all the information necessary to give informed consent, but they do not need to sign a consent document. An IRB may waive the requirement to obtain a signed informed consent if it determines the following:

1. "That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality" [45 CFR 46.117(c)(1)(i) (HHS)], or
2. "That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context" [45 CFR 46.117(c)(1)(ii) (HHS)].

In the case of FDA-regulated research, only the second criterion listed above is permitted as a determination to waive the requirement to obtain a signed informed consent [21 CFR 56.109(c)(1)].

Examples of research where the GBMC IRB will consider waiving the requirement to obtain signed informed consent include but are not limited to:

1. Hard copy anonymous surveys or questionnaires
2. Oral telephone surveys or interviews
3. Online anonymous surveys or questionnaires

In instances where the GBMC IRB waives the requirement to obtain signed informed consent, it shall be required that a written description of the research be provided to all subjects. This written description shall include all the required elements of informed consent. Depending on the type of research being conducted, the required description can be provided to subjects in the following ways:

1. As a written hard copy "information sheet"
2. In an introductory statement to an online questionnaire
3. Incorporated into an oral phone script

In all instances, no signatures shall be required.

All information sheets, online questionnaire scripts and oral phone scripts must be reviewed and approved by the GBMC IRB prior to implementation.

All waivers of the requirement to obtain signed informed consent given by the GBMC IRB shall be documented in the IRB meeting minutes as described in SOP Section 3.5—Minutes of the Meeting.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Child Assent and Parental Permission
Section Number: 7.4
Effective Date: September 18, 2023
Last Revision:
Replaced SOP Revised On:

Both the Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) at 45 CFR 46.408(a) and 21 CFR 50.55(a) respectively state that an IRB must "determine that adequate provisions are made for soliciting the assent" of children when the children are capable of providing assent.

Children are defined as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." [45 CFR 46.402(a)] [21 CFR 50.3(o)]

Maryland law (Maryland Code Annotated Health-General §9.5-101) defines a child as meaning "an individual under the age of 18 years".

The IRB shall also apply, as applicable, Maryland law (Maryland Code Annotated Health-General §20-102) which states that a minor has the same capacity as an adult to consent to medical treatment if they are (1) married, (2) the parent of a child, or (3) living separate and apart from their parent, parents, or guardian, and are self-supporting, regardless of the source of their income.

"Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent." [45 CFR 46.402(b)] [21 CFR 50.3(n)].

It is the responsibility of the IRB to determine whether children are capable of assent, and the IRB shall consider the following when determining whether children are capable of providing assent, with the judgment being made for all children or for each child that will be participating in a proposed research project [45 CFR 46.408(a)] [21 CFR 50.55(b)]:

1. Age of the children
2. Maturity level
3. Psychological state

The IRB may determine it is not necessary that children be assented if one of the following two conditions apply [45 CFR 46.408(a)] [21 CFR 50.55(c)(1)(2)]:

1. "The capability of some or all of the children is so limited that they cannot reasonably be consulted," or

2. “The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research”

Should the IRB determine that assent of the children is not necessary, the determination and condition applied shall be documented in the meeting minutes as described in SOP Section 3.5—Minutes of the Meeting.

Should the IRB determine that assent of the children is required, it is the responsibility of the IRB to “also determine whether and how assent must be documented” [45 CFR 46.408(e)] [21 CFR 50.55(g)]. The GBMC IRB uses the following guidelines to determine how assent shall be documented:

1. Children up to 7 years of age: Written documentation is not required; however, verbal assent should be obtained and documented when the children are capable.

2. Children 7 to 12 years of age: Written documentation is required using a simplified assent form appropriate for the age and comprehension level of the children.

3. Children 13 to 17 years of age: Written documentation is required using a form that is appropriate for the age and comprehension level of the children. Depending on the complexity of the research project, the form can be either very similar or identical to the parental permission form.

Children who reach the age of seven (7) and are still actively participating in a research project should document their willingness to continue participation by the signing of a simplified assent form appropriate for their age and comprehension level as stated above in #2.

Children who reach the age of 18 and are still actively participating in a research project should be re-approached to confirm that they are still willing to continue their participation. Their willingness to continue should be documented by the signing of an adult informed consent form that is in accordance with and to the extent required by 45 CFR 46.116 and, as applicable, 21 CFR 50 Subpart B—Informed Consent of Human Subjects.

In addition to determining the need for assenting children, the IRB has the responsibility of determining that adequate provisions are made for soliciting the permission of each child’s parents or guardian; however, waiver of parental permission by the IRB is permitted under 45 CFR 46.408(c) (HHS) if specific criteria are met. The FDA does not have a comparable waiver of parental permission to match 45 CFR 46.408(c); however, according to the July 2017 FDA guidance “IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects”, the FDA will not “object to an IRB approving a consent procedure that does not include, or alters, some or all of the elements of informed consent set forth in 21 CFR 50.25” for minimal risk clinical investigations.

When parental permission is required, the parents or guardian shall provide informed consent on behalf of the child as follows and in accordance with 45 CFR 46.408(b) (HHS) and, as applicable, 21 CFR 50.55(e) (FDA):

1. “Research not involving greater than minimal risk” (45 CFR 46.404) (21 CFR 50.51) shall require the permission of at least one parent or guardian with the IRB determining on a case-by-case basis whether the permission of one parent is sufficient.

2. “Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects” (45 CFR 46.405) (21 CFR 50.52) shall require the permission of at least one parent or guardian with the IRB determining on a case-by-case basis whether the permission of one parent is sufficient.

3. “Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition” (45 CFR 46.406) (21 CFR 50.53) shall require the permission of both parents or guardian.

Federal regulations at 45 CFR 46.408(d) and 21 CFR 50.55(f) state that “Permission by parents or guardians shall be documented in accordance with and to the extent required by” 45 CFR 46.117 and 21 CFR 50.27 (Documentation of Informed Consent). The GBMC IRB, in most cases, will require written documentation of parental permission; however, in certain cases, documentation of permission may be waived and an information sheet used instead [45 CFR 46.117(c)(2)] [21 CFR 56.109(d)].

For additional information regarding IRB review of research involving children as subjects, see SOP Section 5.16—Research Involving Children.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Informed Consent of Non-English-Speaking Subjects
Section Number: 7.5
Effective Date: September 18, 2023
Last Revision:
Replaced SOP Revised On:

The GBMC IRB acknowledges that there may be non-English-speaking individuals who may ask or be asked to participate in research projects that are being conducted at GBMC. Federal regulations at 45 CFR 46.116(a)(3) (HHS) and 21 CFR 50.20 (FDA) under General Requirements for Informed Consent state that the information given to potential subjects or their legally authorized representatives must be in a language that is understandable to them.

The GBMC IRB recognizes two methods for obtaining the consent of non-English-speaking subjects or their legally authorized representatives:

1. Translated Long Form Consent Document
2. Translated Short Form Consent Document

If it is anticipated that some or all of the subjects to be enrolled for a proposed research project will not be able to read or understand a consent document written in the English language, it is the preference of the GBMC IRB that a long form consent document be used. This method requires translation of the English consent form by either a valid translator service or an individual who is known to be bilingual. The English consent form shall be translated into a language understandable to the potential subjects or their legally authorized representatives. All long form translated consent documents shall be reviewed and approved by the GBMC IRB prior to use.

When a non-English-speaking individual seeks to enroll unexpectedly in a currently active research project and there is no IRB-approved long form consent document in the language of the potential subject, Federal regulations at 45 CFR 46.117(b)(2) and 21 CFR 50.27(b)(2) permit the use of a short form consent document which states that the required elements of informed consent have been presented orally to the subject or the subject's legally authorized representative. The required elements of informed consent may be presented to the subject in the form of a summary. The summary may be written in English, and it is permissible to use the English language long form consent document as the summary. A witness must be present at the time of the oral presentation and should be fluent in both English and the language of the subject or the legally authorized representative. The oral presentation and the short form written consent document shall be in a language understandable to the subject or the subject's legally authorized representative. Both the short form consent document and the summary shall be reviewed and approved by the GBMC IRB prior to use. The short form consent document and summary may undergo expedited review if the English language long form consent document has already been approved by the convened IRB.

All long form consent documents, short form consent documents and summaries used when consenting non-English-speaking subjects shall be appropriately signed as described in SOP Section 7.3—Documentation of Informed Consent.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Waiver or Alteration of Informed Consent
Section Number: 7.6
Effective Date: January 1, 2005
Last Revision: September 18, 2023
Replaced SOP Revised On:

Federal regulations state that no investigator shall enroll or involve a human subject in research until "legally effective informed consent of the subject or the subject's legally authorized representative" has been obtained [45 CFR 46.116(a)(1)] [21 CFR 50.20]. However, under certain circumstances, an IRB may approve a consent process that does not include, or that alters, some or all of the required basic elements of informed consent or the IRB may even waive the requirement to obtain informed consent.

Before an IRB can waive or approve any alterations of informed consent, certain conditions must be met.

Under the Revised 2018 Common Rule (2018 Requirements) at 45 CFR 46.116(f)(3), an IRB may waive or approve the alteration of informed consent if it finds and documents the following:

1. The research involves no more than minimal risk to the subjects;
2. The research could not practicably be carried out without the requested waiver or alteration;
3. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
4. The waiver or alteration will not adversely affect the rights and welfare of the subjects, and
5. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

The Revised 2018 Common Rule at 45 CFR 46.116(g) also allows an IRB to "approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subjects or the subject's legally authorized representative" if either of two criteria are met. The two criteria are as follows:

1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens

For the most part, FDA regulations do not permit waivers of informed consent except for specific emergency situations as described in 21 CFR 50.23 or emergency research as described in 21

CFR 50.24. An example of when a waiver of informed consent could be approved under FDA regulations is when a patient is in a life-threatening situation where an investigational therapy may be beneficial but there is not enough time to obtain legal informed consent. The FDA exceptions from the general requirements of informed consent at 21 CFR 50.23 and 21 CFR 50.24 have limited applicability at GBMC.

In July 2017 the FDA released a new guidance entitled "IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects". This guidance allows IRBs to waive or alter the informed consent requirements using the Revised 2018 Common Rule criteria (see above list) until the FDA is able to harmonize its regulations with those of the Common Rule for waiver of consent.

All waivers or alterations of informed consent must be approved by the GBMC IRB prior to implementation and shall be documented in the IRB meeting minutes as described in SOP Section 3.5—Minutes of the Meeting.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: HIPAA Privacy Rule Overview
Section Number: 8.1
Effective Date: August 19, 2024
Last Revision:
Replaced SOP Revised On:

HIPAA is an acronym for the Health Insurance Portability and Accountability Act. HIPAA was passed as federal law on August 21, 1996. HIPAA mandated the creation of national standards to protect sensitive patient health information from being disclosed without the patient's consent or knowledge. HIPAA assigned the Secretary of Health and Human Services (HHS) to set regulatory standards for the privacy of important health information, laying the groundwork for the Privacy Rule which went into effect on April 14, 2003. The Privacy Rule establishes the conditions under which protected health information may be used or disclosed by covered entities for research purposes.

Research is defined in the Privacy Rule as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge" (45 CFR 164.501 – Definitions).

Protected health information (PHI) is defined in the Privacy Rule as individually identifiable health information that is transmitted by electronic media, maintained in electronic media, or transmitted or maintained in any other form or medium, excluding certain educational and employment records (45 CFR 160.103 – Definitions). It can be further said that PHI is any information in a medical record or designated data set that can be used to identify an individual either separately or with other pieces of information. All formats of PHI are covered by the Privacy Rule. These formats include, but are not limited to, spoken PHI, PHI written on paper, electronic PHI, and physical or digital images that could identify the subject of the health information.

There is no formal list of HIPAA/PHI identifiers in the Privacy Rule. What the Privacy Rule does recognize [at 45 CFR 164.514(b)(2)(i)] are 18 identifiers that must be removed from protected health information to render it fully de-identified and no longer subject to the Privacy Rule.

The 18 identifiers are as follows and are quoted directly from 45 CFR 164.514(b)(2)(i):

1. "Names;
2. All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census:
    a. The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and

   b. The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;
4. Telephone numbers;
5. Fax numbers;
6. Electronic mail addresses;
7. Social security numbers;
8. Medical record numbers;
9. Health plan beneficiary numbers;
10. Account numbers;
11. Certificate/license numbers;
12. Vehicle identifiers and serial numbers, including license plate numbers;
13. Device identifiers and serial numbers;
14. Web Universal Resource Locators (URLs);
15. Internet Protocol (IP) address numbers;
16. Biometric identifiers, including finger and voice prints
17. Full face photographic images and any comparable images; and
18. Any other unique identifying number, characteristic, or code"

When the above 18 identifiers are removed from a data set and the information contained in the data set is no longer individually identifiable, the requirements of the Privacy Rule no longer apply. Researchers may use or disclose de-identified health information without restriction. However, to be used as part of a research study, the information must be de-identified prior to it being obtained by the researcher.

[See also SOP Section 8.5--De-Identified Protected Health Information (PHI)]

The Privacy Rule permits researchers to use and disclose individually identifiable health information for research purposes; however, the Privacy Rule in general requires that researchers obtain an individual's written authorization prior to the use or disclosure, unless a full or partial waiver of authorization is granted. [45 CFR 164.508(a)]

Under the Privacy Rule, a full or partial waiver of authorization may be granted by either an Institutional Review Board (IRB) or a privacy board [45 CFR 164.512(i)(i)(A)(B)].

GBMC recognizes the GBMC IRB as having the authority to grant:

1. Full Waivers of HIPAA Research Authorization
2. Partial Waivers of HIPAA Research Authorization
3. Alterations of HIPAA Research Authorization

Full waivers occur when the IRB determines that no authorization will be required to use and/or disclose PHI for a particular research project. A full waiver is most often granted for retrospective chart review projects.

Partial waivers occur when the IRB determines that no authorization will be required for use and/or disclosure of PHI for the sole purpose of screening and/or recruiting prospective subjects as part of a research project.

Alterations of HIPAA research authorization occur when the IRB approves a request to remove some PHI, but not all, or alter the requirements for a HIPAA authorization.

[See also SOP Section 8.3--Waivers or Alterations of HIPAA Authorization]

The Privacy Rule also permits researchers to access PHI, without an individual's authorization, for preparatory to research activities. These activities include but are not limited to reviewing PHI to:

1. Assist in formulating a research hypothesis
2. Determine the feasibility of conducting a specific research project
3. Assist in preparing a research protocol
4. Develop eligibility criteria
5. Determine if there is a sufficient population of research subjects
6. Other similar uses that precede the development of an actual protocol

[See also SOP Section 8.4—Preparatory to Research Activities]

The GBMC IRB has the following forms available in IRBNet to assist researchers in complying with the Privacy Rule as it relates to the conduct of human subjects research and the use and disclosure of protected health information:

1. HIPAA Research Authorization Form (For Study Subject)
2. HIPAA Research Authorization Waiver Request
3. Preparatory to Research Activity Request

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: HIPAA Research Authorizations
Section Number: 8.2
Effective Date: January 1, 2005
Last Revision: August 19, 2024
Replaced SOP Revised On:

The Privacy Rule permits researchers to use and disclose individually identifiable health information for research purposes; however, the Privacy Rule in general requires that researchers obtain an individual's written authorization prior to the use or disclosure. [45 CFR 164.508(a)]

The GBMC IRB has made available in IRBNet (See "Forms and Templates") a HIPAA Research Authorization Form template for use with study subjects. This template contains the core elements and statements as required by the Privacy Rule.

A valid HIPAA research authorization must contain, at the very least, the following six elements, unless the IRB has approved a waiver or alteration of one or more of the elements:

1. "A description of the information to be used or disclosed that identifies the information in a specific and meaningful fashion."
2. "The name or other specific identification of the person(s), or class of persons, authorized to make the requested use or disclosure."
3. "The name or other specific identification of the person(s), or class of persons, to whom the covered entity may make the requested use or disclosure."
4. "A description of each purpose of the requested use or disclosure."
5. "An expiration date or an expiration event that relates to the individual or the purpose of the use or disclosure."
6. "Signature of the individual and date. If the authorization is signed by a personal representative of the individual, a description of such representative's authority to act for the individual must also be provided." [All quoted passages have been taken from 45 CFR 164.508(c)(1)]

In addition to the above-mentioned six elements, a valid HIPAA research authorization must contain statements that notify an individual of the following:

1. "The individual's right to revoke the authorization in writing, and either: (A) The exceptions to the right to revoke and a description of how the individual may revoke the authorization;" or (B) reference to the corresponding section(s) of the covered entity's Notice of Privacy Practices.
2. The covered entity's ability or inability to condition treatment, payment, enrollment, or eligibility for benefits on the authorization, including research related treatment and, if applicable, the consequences of refusing to sign the authorization.

3. "The potential for information disclosed pursuant to the authorization to be subject to redisclosure by the recipient and no longer be protected" by the Privacy Rule. [All quoted passages have been taken from 45 CFR 164.508(c)(2)]

A valid HIPAA research authorization "must be written in plain language" [45 CFR 164.508(c)(3)] that is understandable to the subject.

The Privacy Rule at 45 CFR 164.508(b)(3)(i) allows a HIPAA research authorization to be combined with an informed consent document. The GBMC IRB accepts both stand-alone HIPAA research authorizations and HIPAA research authorizations that are combined with an informed consent document. The GBMC IRB has made available in IRBNet (See "Forms and Templates") an adult informed consent template with an incorporated HIPAA research authorization section that combines the two documents. If an investigator prefers using a stand-alone HIPAA research authorization, the HIPAA research authorization section of the GBMC IRB informed consent template may be deleted and a separate HIPAA research authorization be used.

If the research study is sponsored and the sponsor supplies either a combined informed consent-HIPAA authorization document or a stand-alone HIPAA research authorization form, the GBMC IRB will accept these sponsor-supplied documents. However, should the sponsor not supply the required HIPAA authorization either in the informed consent document or by way of a stand-alone HIPAA research authorization, a separate GBMC HIPAA research authorization form must be used and signed by the study subject.

HIPAA research authorization forms shall only be signed by an adult study subject who has legal and mental capacity to give permission to the use and disclosure of the individually identifiable health information. For subjects without that capacity or for individuals under the age of 18 years, authorization shall be obtained from the parent, legal guardian, or legally authorized representative of the subject. The individual signing the HIPAA research authorization form shall be given a copy of the signed document [45 CFR 164.508(c)(4)].

All stand-alone HIPAA research authorizations and HIPAA research authorizations that are combined with an informed consent document and included in an electronic submission "package" submitted via IRBNet shall be reviewed by the GBMC IRB. The GBMC IRB shall review the submitted documents to ensure that all required Privacy Rule elements and statements are present. All follow-up letters shall specify the approved method of HIPAA authorization (e.g. the informed consent document is HIPAA compliant and does not require a separate HIPAA research authorization form).

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Waivers or Alterations of HIPAA Authorization
Section Number: 8.3
Effective Date: January 1, 2005
Last Revision: August 19, 2024
Replaced SOP Revised On:

The Privacy Rule permits researchers to use and disclose individually identifiable health information for research purposes; however, the Privacy Rule in general requires that researchers obtain an individual's written authorization prior to the use or disclosure [45 CFR 164.508(a)] unless a full or partial waiver of authorization is granted by an IRB.

A full waiver is granted by an IRB when it is determined that no authorization will be required for the use and/or disclosure of individually identifiable health information for a specific research project. This most often occurs when it is not possible to obtain an individual's written authorization, such as for a retrospective chart review project.

A partial waiver is most often granted by an IRB when it is determined that individually identifiable health information will be accessed for the sole purpose of screening and/or recruiting prospective subjects as part of a specific research project. It must be noted that a partial waiver for recruitment purposes does not eliminate the need to obtain written HIPAA research authorization from an individual as part of the study enrollment process.

An IRB may also approve a request to alter a HIPAA research authorization where some, but not all, of the required elements or statements of a valid authorization are removed. (See SOP Section 8.2—HIPAA Research Authorizations for a list of the required elements and statements). The most common alteration request is to present the required HIPAA authorization elements and statements to an individual orally and to have the individual give their authorization orally. This would typically take place when an IRB has also waived the requirement for written informed consent.

For an IRB to approve a waiver or alteration of a HIPAA research authorization, it must determine that the following three Privacy Rule criteria are met:

1. The use or disclosure of protected health information must involve no more than minimal risk to the privacy of individuals based on:
   a. "An adequate plan to protect the identifiers from improper use and disclosure.
   b. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
   c. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use of disclosure of protected health information would be permitted" under the Privacy Rule.

2. "The research could not practicably be conducted without the waiver or alteration; and
3. The research could not practicably be conducted without access to and use of the protected health information." [All quoted passages have been taken from 45 CFR 164.512(i)(2)(ii)]

Once an IRB has granted either a waiver or alteration, the action must be documented with the following [45 CFR 164.512(i)(2)]:

1. A statement identifying the IRB and the date on which the alteration or waiver of authorization was approved.
2. A statement that the IRB has determined that the alteration or waiver, in whole or in part, of authorization satisfies the criteria at 45 CFR 164.512(i)(2)(ii) (See criteria listed above).
3. A brief description of the protected health information for which use or access has been determined to be necessary by the IRB.
4. A statement that the alteration or waiver of authorization has been reviewed and approved under either normal or expedited review procedures.
5. Documentation of the alteration or waiver of authorization must be signed by the IRB chair or other member, as designated by the chair, of the IRB as applicable.

Requests for a waiver or alteration of HIPAA research authorization can be reviewed by the convened IRB or by expedited review procedures.

The GBMC IRB recognizes the following two individuals as having the authority to grant HIPAA research authorization waivers or alterations under expedited review procedures:

3. IRB Chairperson
4. IRB Vice Chairperson

The above-mentioned two individuals are also recognized as having the authority to grant HIPAA research authorization waivers or alterations, as appropriate, for research projects under the oversight of an external IRB.

When a request for a waiver or alteration of HIPAA research authorization is reviewed by the convened IRB, a majority of the members must be present at the meeting, including at least one member whose primary concerns are in nonscientific areas. For the request to be approved by the convened IRB, it must be approved by a majority of the IRB members present. Majority is defined as being fifty percent of the members present plus one.

No IRB member who has a conflicting interest shall participate in the review of a request for a waiver or alteration of HIPAA research authorization.

The GBMC IRB has made available in IRBNet (See "Forms and Templates") a "Request for Full, Partial Waiver or Alteration of HIPAA Authorization" form. This form shall be submitted electronically via IRBNet.

Once a request for a full, partial waiver or alteration of HIPAA authorization has been reviewed by the GBMC IRB and a decision (to either approve or disapprove) has been made regarding the request, the "For IRB Use Only Below This Line" section of the request form shall be filled out by the IRB Office staff. The form shall be signed by the IRB chairperson or his designee and posted in the appropriate electronic IRBNet file (submission package).

All decisions made by the convened IRB to either approve or disapprove a request for a full, partial waiver or alteration of HIPAA authorization shall be documented in the meeting minutes.

All decisions made by way of an expedited or ceded review procedure shall be reported back to the convened IRB at the next scheduled meeting and documented in the meeting minutes.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Preparatory to Research Activities
Section Number: 8.4
Effective Date: August 19, 2024
Last Revision:
Replaced SOP Revised On:

The Privacy Rule permits researchers to access protected health information (PHI) for activities performed in preparation for conducting research. These activities include but are not limited to reviewing PHI to:

7. Assist in formulating a research hypothesis
8. Determine the feasibility of conducting a specific research project
9. Assist in preparing a research protocol
10. Develop eligibility criteria
11. Determine if there is a sufficient population of research subjects
12. Other similar uses that precede the development of an actual protocol

This access is permitted to take place without an individual's authorization, a waiver or alteration of authorization, or a data use agreement provided representation of the following is obtained from the researcher:

1. "Use or disclosure is sought solely to review protected health information as necessary to prepare a research protocol or for similar purposes preparatory to research;
2. No protected health information is to be removed from the covered entity by the researcher in the course of the review; and
3. The protected health information for which use or access is sought is necessary for the research purposes." [45 CFR 164.512(i)(ii)]

The GBMC IRB has made available in IRBNet (See "Forms and Templates") a "Representations of Activities Preparatory to Research Form" for use when requesting approval to conduct preparatory to research activities.

The above-mentioned preparatory to research request form requires researchers to attest to and/or abide by the following:

1. That access to and use of the described PHI shall be solely as necessary to prepare a research protocol or for similar purposes preparatory to research.
2. That access to the described PHI is necessary for the research purposes.
3. That PHI accessed preparatory to research cannot be moved, copied, duplicated, exported, transmitted, or otherwise removed from GBMC and may not be used to contact potential subjects.

4. That a list of prospective subjects may be retained, provided, the list does not leave GBMC, whether hardcopy or electronic, and potential subjects are not contacted until IRB approval of the study is granted.
5. That PHI access shall not be used for any other purpose and the PHI shall not be shared with individuals outside of GBMC without approval by the GBMC IRB.

The "Representations of Activities Preparatory to Research Form" shall be submitted to the GBMC IRB electronically via IRBNet.

The GBMC IRB recognizes the following two individuals as having the authority to grant researchers approval to conduct preparatory to research activities:

5. IRB Chairperson
6. IRB Vice Chairperson

Once a request to conduct preparatory to research activities has been reviewed and a decision (to either approve or disapprove) has been made regarding the request, the "For IRB Use Only Below This Line" section of the request form shall be filled out by the IRB Office staff. The form shall be signed by the IRB chairperson or his designee and posted in the appropriate electronic IRBNet file (submission package).

No preparatory to research activities shall be initiated until approval has been granted by the GBMC IRB.

All decisions made regarding requests to conduct preparatory to research activities shall be reported back to the convened IRB at the next scheduled meeting and documented in the meeting minutes.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: De-Identified Protected Health Information (PHI)
Section Number: 8.5
Effective Date: August 19, 2024
Last Revision:
Replaced SOP Revised On:

The Privacy Rule allows a covered entity or its business associates to use or disclose health information that is not individually identifiable (de-identified protected health information) without restriction. Health information is not individually identifiable if it does not identify an individual and if the covered entity has no reasonable basis to believe it can be used to identify an individual. [45 CFR 164.514(a)].

Sections 164.514(b)(1) and (2) of the Privacy Rule outline two methods by which health information can be designated as de-identified:

1. Expert Determination—The Expert Determination method allows a covered entity or its business associates to utilize a person with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable. This expert is responsible for determining that there is only a very small risk that the anticipated recipient of the data set could use the provided information, along or in combination with other reasonably available information, to identify individuals in the data set. Additionally, this person is responsible for documenting the methods and results of the analysis that justify such a determination. [45 CFR 164.514(b)(1)]

2. Safe Harbor—This is the most common method used. The Safe Harbor method allows a covered entity or its business associates to de-identify individually identifiable health information by removing the following identifiers [quoted directly from 45 CFR 164.514(b)(2)(i)] of the individual or of relatives, employers, or household members of the individual:
   a. "Names;
   b. All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census:
      (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and
      (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
   c. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;

d. Telephone numbers;
e. Fax numbers;
f. Electronic mail addresses;
g. Social security numbers;
h. Medical record numbers;
i. Health plan beneficiary numbers;
j. Account numbers;
k. Certification/license numbers;
l. Vehicle identifiers and serial numbers, including license plate numbers;
m. Device identifiers and serial numbers;
n. Web Universal Resource Locators (URLs);
o. Internet Protocol (IP) address numbers;
p. Biometric identifiers, including finger and voice prints;
q. Full face photographic images and any comparable images; and
r. Any other unique identifying number, characteristic, or code except as permitted in" (c) above.

Additionally, "The covered entity does not have actual knowledge that the information could be used alone or in combination with other information to identify an individual who is a subject of the information" [45 CFR 164.514(b)(2)(ii).

Health information that is de-identified following the Expert Determination or Safe Harbor method, as described above, is no longer protected by the Privacy Rule because it does not fall within the definition of protected health information (PHI).

The Privacy Rule, at 45 CFR 164.514(c), states that a covered entity may assign a code or other means of record identification to allow information de-identified by one of the above two methods to be re-identified provided that:

1. "The code or other means of record identification is not derived from or related to information about the individual and is not otherwise capable of being translated so as to identify the individual; and
2. The covered entity does not use or disclose the code or other means of record identification for any other purpose, and does not disclose the mechanism for re-identification."

Should a covered entity or business associate successfully re-identify a subject(s) of de-identified information, the health information would again be protected by the Privacy Rule, as it would meet the definition of PHI. Disclosure of a code or other means of record identification designed to enable coded or otherwise de-identified information to be re-identified is also considered a disclosure of PHI.

As stated above, the Privacy Rule allows a covered entity or its business associates to use or disclose health information that is not individually identifiable (de-identified protected health information) without restriction; however, to be used as part of a research activity, the information must be de-identified prior to it being obtained for use with the proposed research.

Researchers must bear in mind that, if there is a mere chance or manner to link the data back to an individual person, then the health information is not considered to be de-identified.

Research involving the use of de-identified protected health information or coded private information where the researcher would never have the ability to link the data back to an individual person may qualify for a not human subjects research determination. All proposed activities that may qualify for a not human subjects research determination shall be screened by the IRB Coordinator as set forth in SOP Section 5.4—Not Human Subjects Research.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Limited Data Sets
Section Number: 8.6
Effective Date: August 19, 2024
Last Revision:
Replaced SOP Revised On:

The Privacy Rule permits covered entities to use or disclose protected health information (PHI) in the form of a "limited data set" without an individual's authorization and without a waiver or alteration of authorization. A limited data set is protected health information that excludes "direct identifiers" of an individual, relatives of the individual, or household members. [45 CFR 164.514(e)(1) and (2)]

The following direct identifiers must be excluded from a limited data set for it to be compliant with the Privacy Rule at 45 CFR 164.514(e)(2)(i)-(xvi):

1. "Names;
2. Postal address information, other than town or city, State, and zip code;
3. Telephone numbers;
4. Fax numbers;
5. Electronic mail addresses;
6. Social security numbers;
7. Medical record numbers;
8. Health plan beneficiary numbers;
9. Account numbers;
10. Certificate/license numbers;
11. Vehicle identifiers and serial numbers, including license plate numbers;
12. Device identifiers and serial numbers;
13. Web Universal Resource Locators (URLs);
14. Internet Protocol (IP) address numbers;
15. Biometric identifiers, including finger and voice prints; and
16. Full face photographic images and any comparable images"

Information that may be included in a limited data set is as follows:

- Dates such as admission, discharge, service, date of birth, date of death
- City, state, five digit or more zip code, and
- Ages in years, months or days or hours

A limited data set may only be used or disclosed by a covered entity "for the purposes of research, public health, or health care operations" [45 CFR 164.514(e)(3)(i)].

Additionally, a limited data set may only be used or disclosed by a covered entity "if the covered entity obtains satisfactory assurance, in the form of a data use agreement … that the limited data

set recipient will only use or disclose the protected health information for limited purposes" [45 CFR 164.514(e)(4)(i)].

A data use agreement shall include the following contents as outlined at 45 CFR 164.514(e)(4)(ii):

1. Establish how the information in the limited data set can be used or disclosed.
2. Establish who is permitted to use or receive the limited data set.
3. Stipulate that the recipient will:
    a. "Not use or further disclose the information other than as permitted by the data use agreement or as otherwise required by law;
    b. Use appropriate safeguards to prevent use or disclosure of the information other than as provided for by the data use agreement;
    c. Report to the covered entity any use or disclosure of the information not provided for by its data use agreement of which it becomes aware;
    d. Ensure that any agents to whom it provides the limited data set agree to the same restrictions and conditions that apply to the limited data set recipient with respect to such information; and
    e. Not identify the information or contact the individuals."

To use or disclose a limited data set for research purposes, GBMC must enter into a data use agreement with the recipient of the limited data set, even if the recipient is a GBMC employee. All data use agreements for the use or disclosure of a limited data set for research purposes shall be signed by GBMC's Executive Vice President and Chief Medical Officer and the recipient of the limited data set.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Post-Approval Monitoring (PAM) Overview
Section Number: 9.1
Effective Date: January 1, 2025
Last Revision:
Replaced SOP Revised On:

An IRB has the authority to "approve, require modifications in (to secure approval), or disapprove all research activities" [45 CFR 46.109(a) and 21 CFR 56.109(a)]. Furthermore, an IRB has the authority to "suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects" [45 CFR 46.113 and 21 CFR 56.113].

When a research project is reviewed and approved by an IRB, it is the responsibility of the principal investigator to comply with the provisions of the IRB-approved protocol and adhere to all federal regulations, state and local laws, GBMC institutional policies, and GBMC IRB specific policies governing human subject research. To ensure that compliance is maintained, GBMC has in place a Post-Approval Monitoring (PAM) Program where internal audits of research projects are conducted.

The purpose of GBMC's PAM Program is to monitor protocol and regulatory compliance, identify areas for improvement, provide tools for maintaining compliance, and take corrective action when necessary.

The GBMC IRB is responsible for all research that takes place at GBMC and has oversight of GBMC's PAM Program. Audits are performed by an IRB Office staff member and/or IRB committee member.

GBMC's PAM Program applies to the following:

- Research projects that are reviewed and approved by the GBMC IRB with the GBMC IRB being the IRB of record
- Research projects that are reviewed and approved by the GBMC IRB but are ceded to an external IRB with the external IRB being the IRB of record

There are two types of PAM audits:

- Not-for-cause
- For-cause

Not-for-cause audits are routine, targeted audits. All currently active research projects have the potential for being audited if certain prioritized criteria are met [See SOP Section 9.2—Post-Approval Monitoring (PAM) Not-for-Cause Audits].

For-cause audits are directed audits that generally take place due to concerns regarding research protocol compliance, and/or research subject rights and welfare. A for-cause audit may also be initiated due to complaints, repeated errors, or a lack of responsiveness by the principal investigator to GBMC IRB requests. GBMC recognizes the following two individuals as having the authority to determine the need and to call for a for-cause audit:

- GBMC IRB Chairperson
- GBMC Chief Medical Officer

Not-for-cause audits are performed on a quarterly basis. For-cause audits can take place at any time.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Post-Approval Monitoring (PAM) Not-for-Cause Audits
Section Number: 9.2
Effective Date: January 1, 2025
Last Revision:
Replaced SOP Revised On:

Introduction

After a research project is reviewed and approved by an IRB, there is the expectation that the principal investigator will comply with the provisions of the IRB-approved protocol and adhere to all federal regulations, state and local laws, GBMC institutional policies, and GBMC IRB specific policies governing human subject research. As a way of monitoring compliance, GBMC has in place a Post-Approval Monitoring (PAM) Program where internal audits of research projects are conducted.

There are two types of audits:

- Not-for-cause
- For-cause

This policy describes the process and outlines the procedures to be followed for conducting not-for-cause audits at GBMC.

Not-for-cause audits are routine, targeted audits.

Not-for-cause audits are conducted on a quarterly basis beginning with January of the calendar year. The goal is to audit a minimum of eight (two per quarter) research projects per calendar year that are currently active with subjects enrolled. A principal investigator shall have no more than one research project audited per calendar year.

Selection Process for Not-for Cause Audits

Research projects to be audited are selected at the discretion of the IRB Coordinator using, but not limited to, any of the following criteria where the project:

- Is IRB-approved (by either the GBMC IRB or an external IRB of record)
- Is active and ongoing
- Is prospective (retrospective projects are excluded from not-for-cause audits)
- Has subjects currently enrolled
- Involves the enrollment of minors
- Involves the enrollment of individuals with impaired decision-making capacity
- Involves the enrollment of vulnerable populations

- Is investigator-initiated
- Has a new and/or inexperienced principal investigator
- Has a new and/or inexperienced project coordinator
- Has had IRB determinations requiring a specific action(s) in response
- Has been audited before with recommendations for improvement

Not all criteria must be met to be selected for a not-for-cause audit.

Not-for-cause audits are not conducted on projects that have been exempted from IRB oversight or determined to be not human subject research.

Notification of and Preparation for a Not-for-Cause Audit

Once a research project has been selected to undergo a not-for-cause audit, the IRB Coordinator shall notify the principal investigator and project coordinator of the impending audit in writing. The notifying correspondence shall identify the research project that has been selected for auditing and include a request to schedule the audit at a mutually agreeable time. The audit shall take place within 30 days from the date of the initial notification correspondence, unless a delay is requested.

If the principal investigator would like to request a delay, the principal investigator shall have five (5) business days (after receipt of initial notification correspondence) to request a delay in writing.

Requests for delay shall be reviewed by the IRB Chairperson and a final decision made within five (5) business days. The IRB Coordinator shall notify the principal investigator in writing, as soon as possible, after the decision is made.

If the IRB Chairperson has a conflict of interest with the research project to be audited, the request for delay shall be given to the IRB Vice Chairperson.

The IRB Coordinator shall supply the principal investigator and project coordinator with a copy of the "Post-Approval Monitoring Audit Checklist" that will be used as a guide for conducting the audit. The checklist shall be supplied as an attachment to the initial correspondence notifying the principal investigator and project coordinator of the impending audit. The checklist may be used by the principal investigator as a means of preparing for the audit.

It is the responsibility of the principal investigator (or designee) to ensure that the individual conducting the audit has access to all relevant information (e.g. study files, regulatory documentation) pertaining to the research project at time of audit. This may include, but is not limited, to the following:

- Project contracts and/or other applicable agreements
- Documentation of a Site Initiation Visit
- Proof that subjects have met eligibility requirements
- Screening and enrollment log

- Subject (signed) informed consent forms
- Subject (signed) HIPAA research authorization forms (if standalone)
- Sponsor correspondence relating to amendments and revisions
- Adverse event reports submitted to the sponsor
- Protocol deviation reports submitted to the sponsor
- Investigational product (drug or device) administration and accountability records
- Subject withdrawal or drop out documentation
- Subject payment/compensation accounting documentation
- Delegation of Authority Log
- FDA Form 1572 – Statement of Investigator
- Project team personnel curriculum vitae
- Project team personnel evidence of project specific training
- Project team personnel evidence of Good Clinical Practice training
- Project team personnel evidence of licensure
- Computer files pertaining to the research project being audited

On the day of the audit, the principal investigator (or designee) shall make available to the auditor a conference room or quiet area for use while conducting the audit. The principal investigator shall appoint a designated individual to be available to the auditor to assist with documentation retrieval, answer any questions or provide clarification as needed throughout the course of the audit.

Prior to the day of the audit, the IRB Coordinator shall make known to the principal investigator and study coordinator who the auditor will be. Not-for-cause audits are performed by an IRB Office staff member and/or IRB committee member.

Not-for-Cause Audit Completion and Distribution of Final Report

Once a not-for-cause audit has been conducted and completed, the IRB Coordinator shall review the audit findings and prepare a summary report to include, as needed, recommendations for improvement and/or the identification of deficiencies requiring corrective action. The report shall be given to the IRB Chairperson for review within five (5) business days of audit completion. If the IRB Chairperson has a conflict of interest with the research project being audited, the report shall be given to the IRB Vice Chairperson.

The IRB Chairperson shall have five (5) business days to review the report. The IRB Chairperson can either approve the report as written or request revisions be made to the document. The IRB Coordinator shall make any requested revisions to the report within five (5) business days. Once the report has received final approval from the IRB Chairperson, the IRB Coordinator shall send the finalized report to the principal investigator and project coordinator.

The final report shall be distributed to the convened IRB at the next scheduled meeting.

Post-Audit Findings and Results

If no deficiencies are identified in the final audit report, no response is required by the principal investigator.

If recommendations for improvement are made in the final report, the principal investigator is not obligated to formally respond to the recommendations.

If deficiencies are identified in the final report requiring responsive action, the principal investigator shall have ten (10) business days (after receipt of the final report) to respond in writing with a corrective action plan for resolving the identified deficiencies.

If the principal investigator disagrees with the audit findings as presented in the final report, the principal investigator shall have five (5) business days (after receipt of the final report) to make an appeal in writing.

Appeals shall be reviewed by the IRB Chairperson and a final decision made within five (5) business days. The IRB Coordinator shall notify the principal investigator in writing, as soon as possible, after the decision is made.

If the IRB Chairperson has a conflict of interest with the research project being audited, the appeal request shall be given to the IRB Vice Chairperson for review and determination.

If the audit identifies a matter of serious or continuing protocol noncompliance and/or a serious concern relating to a research subject's rights and welfare, the research project may be suspended in whole or in part until the identified issue(s) can be resolved.

Audit Completion and Close-Out

An audit shall be considered complete and closed-out once all deficiencies identified in the final report are addressed and resolved and no further audit-related activities are necessary. The IRB Coordinator shall notify the principal investigator in writing when it has been determined that the audit is complete.

If no deficiencies are identified in the final audit report, the principal investigator shall be informed in the initial post-audit correspondence that the audit is complete with no further action being necessary.

Research projects that have undergone an audit with deficiencies identified may be subject to future targeted audits to further monitor compliance.

Filing and Storage of Audit Results and Documentation

The IRB Office shall keep on file indefinitely (or until the research project's file is purged) all documentation relating to the audit to include but not be limited to:

- Pre-audit notification correspondence
- Audit checklist
- Final audit report

- Post-audit correspondence
- Corrective action plans, if required

In addition to the hard-copy audit file maintained in the IRB Office, the IRB Coordinator shall create a special event package in the research project's electronic file in IRBNet. At a minimum, the following documents will be uploaded into the special event package:

- Post-audit correspondence
- Final audit report

The principal investigator is responsible for keeping their own documentation of the audit in their research project records.

Failure to Cooperate with the Performance of an Audit

Principal investigators and research project team members are expected to fully cooperate with a Post-Approval Monitoring (PAM) audit. Failure to cooperate with an audit shall be considered a serious non-compliance with GBMC IRB policy.

Failure to cooperate may include but not be limited to:

- Refusal and/or failure to respond to initial notifications and communications requesting that an audit be scheduled
- Refusal and/or failure to make all necessary and/or requested documents and records available for review and use during an audit
- Denying access to areas where project procedures and activities are conducted
- Refusal and/or failure to respond to post-audit communications
- Refusal and/or failure to submit corrective action plans, if required
- Other actions that delay or prevent an audit from taking place or being conducted

Failure to cooperate may result in disciplinary action and/or suspension or termination of the research project being audited.

GREATER BALTIMORE MEDICAL CENTER
Institutional Review Board
Standard Operating Policies and Procedures (SOP)

Name of SOP: Post-Approval Monitoring (PAM) For-Cause Audits
Section Number: 9.3
Effective Date: January 1, 2025
Last Revision:
Replaced SOP Revised On:

Introduction

After a research project is reviewed and approved by an IRB, there is the expectation that the principal investigator will comply with the provisions of the IRB-approved protocol and adhere to all federal regulations, state and local laws, GBMC institutional policies, and GBMC IRB specific policies governing human subject research. As a way of monitoring compliance, GBMC has in place a Post-Approval Monitoring (PAM) Program where internal audits are conducted.

There are two types of audits:

- Not-for-cause
- For-cause

This policy describes the process and outlines the procedures to be followed for conducting for-cause audits at GBMC.

For-cause audits are directed audits that generally take place due to concerns regarding identified or suspected serious protocol non-compliance and/or research subject rights and welfare. A for-cause audit may also be initiated in cases where there are unresolved complaints, continuing non-compliance with GBMC IRB policies and procedures, or a lack of compliance with GBMC IRB determinations.

For-cause audits may be conducted at any time, with little notice to the principal investigator.

Selection Process for For-Cause Audits

GBMC recognizes the following two individuals as having the authority to request a for-cause audit:

- GBMC IRB Chairperson
- GBMC Chief Medical Officer

Indications for a for-cause audit include, but are not limited to:

- Serious and/or continuing non-compliance with the IRB-approved protocol
- Serious and/or continuing non-compliance with GBMC IRB policies

- Serious and/or continuing non-compliance with GBMC IRB determinations
- Serious and/or continuing unanticipated problems involving risk to subjects or others
- Unresolved subject complaints
- Whistleblower complaints that require investigation

All research conducted at GBMC can be subject to a for-cause audit. This includes:

- Active research projects under the oversight of the GBMC IRB
- Active research projects under the oversight of an external IRB
- Research projects that have been permanently closed
- Both prospective and retrospective research projects
- Research projects determined to be exempt from IRB oversight

For-cause audits are not conducted on projects that have been determined to be not human subject research.

Notification of and Preparation for a For-Cause Audit

Once a for-cause audit has been formally requested, the IRB Coordinator shall notify the principal investigator and project coordinator of the impending audit in writing. The correspondence shall identify the research project that is under investigation and the reason(s) for the audit. The audit shall take place within three business days from the date of the notifying correspondence. It is not acceptable to request a delay for a for-cause audit.

The IRB Coordinator shall supply the principal investigator with a list of relevant information (e.g. study files, regulatory documentation) pertaining to the research project in question to be supplied at time of audit. It is the responsibility of the principal investigator to make certain that the requested information is available at time of audit.

On the day of the audit, the principal investigator (or designee) shall make available to the auditor a conference room or quiet area for use while conducting the audit. The principal investigator shall appoint a designated individual to be available to the auditor to assist with documentation retrieval, answer any questions or provide clarification as needed throughout the course of the audit.

For-cause audits are conducted by the IRB Coordinator and/or IRB committee member.

For-Cause Audit Completion and Distribution of Final Report

Once a for-cause audit has been conducted and completed, the IRB Coordinator shall review the audit findings and prepare a summary report to include, as needed, recommendations for improvement and/or the identification of deficiencies requiring corrective action. The report shall be given to the IRB Chairperson for review within five (5) business days of audit completion with a copy given to GBMC's Chief Medical Officer. If the IRB Chairperson has a conflict of interest with the research project being audited, the report shall be given to the IRB Vice Chairperson.

The IRB Chairperson shall have five (5) business days to review the report. The IRB Chairperson can either approve the report as written or request revisions be made to the document. The IRB Coordinator shall make any requested revisions to the report within five (5) business days. Once the report has received final approval from the IRB Chairperson, the IRB Coordinator shall send the finalized report to the principal investigator and project coordinator.

The final report shall be distributed to the convened IRB at the next scheduled meeting.

Post-Audit Findings and Results

If the final audit report does not identify any deficiencies or other matters relating to the reason(s) for the for-cause audit, no response is required by the principal investigator.

If the final audit report identifies deficiencies or other matters relating to the reason(s) for the for-cause audit and the identified issues involve serious or continuing non-compliance and/or serious concerns relating to a research subject's rights and welfare, the research project may be suspended in whole or in part until the identified issue(s) can be resolved

The principal investigator shall have ten (10) business days (after receipt of the final report) to respond in writing with a corrective action plan for resolving the identified deficiencies.

If the principal investigator disagrees with the audit findings as presented in the final report, the principal investigator shall have ten (10) business days (after receipt of the final report) to make an appeal in writing.

Appeals shall be reviewed by the IRB Chairperson and a final decision made within five (5) business days. The IRB Coordinator shall notify the principal investigator in writing, as soon as possible, after the decision is made.

If the IRB Chairperson has a conflict of interest with the research project being audited, the appeal request shall be given to the IRB Vice Chairperson for review and determination.

Audit Completion and Close-Out

An audit shall be considered complete and closed-out once all deficiencies identified in the final report are addressed and resolved and no further audit-related activities are necessary. The IRB Coordinator shall notify the principal investigator in writing when it has been determined that the audit is complete.

If no deficiencies are identified in the final audit report, the principal investigator shall be informed in the initial post-audit correspondence that the audit is complete with no further action being necessary.

Research projects that have undergone an audit with deficiencies identified may be subject to future targeted audits to further monitor compliance.

Filing and Storage of Audit Results and Documentation

The IRB Office shall keep on file indefinitely (or until the research project's file is purged) all documentation relating to the audit to include but not be limited to:

- Pre-audit notification correspondence
- Audit checklist
- Final audit report
- Post-audit correspondence
- Corrective action plans, if required

In addition to the hard-copy audit file maintained in the IRB Office, the IRB Coordinator shall create a special event package in the research project's electronic file in IRBNet. At a minimum, the following documents will be uploaded into the special event package:

- Post-audit correspondence
- Final audit report

The principal investigator is responsible for keeping their own documentation of the audit in their research project records.

Failure to Cooperate with the Performance of an Audit

Principal investigators and research project team members are expected to fully cooperate with a Post-Approval Monitoring (PAM) audit. Failure to cooperate with an audit shall be considered a serious non-compliance with GBMC IRB policy.

Failure to cooperate may include but not be limited to:

- Refusal and/or failure to respond to initial notifications and communications requesting that an audit be scheduled
- Refusal and/or failure to make all necessary and/or requested documents and records available for review and use during an audit
- Denying access to areas where project procedures and activities are conducted
- Refusal and/or failure to respond to post-audit communications
- Refusal and/or failure to submit corrective action plans, if required
- Other actions that delay or prevent an audit from taking place or being conducted

Failure to cooperate may result in disciplinary action and/or suspension or termination of the research project being audited.