STANDARD OPERATING PROCEDURE

OBJECTIVE/SCOPE

To outline the NMDP IRB procedures for suspending, terminating, or administratively closing research previously approved by the NMDP IRB, and for reporting suspension or termination to the appropriate authorities in compliance with federal regulatory requirements.

MATERIALS

Notification of Study Closure form

SAFETY

Not applicable

DEFINITIONS

1. **Administrative closure:** Closure of a research protocol with the NMDP IRB by the NMDP IRB office after the IRB approval period expires. Administrative closures are not reportable events, since the protocol approval is already expired, and there is no withdrawal of IRB approval.

2. **Blood and Marrow Transplant Clinical Trials Network (BMT CTN):** A network sponsored by the National Institutes of Health (NIH) that conducts large multi-institutional clinical trials addressing important issues in hematopoietic cell transplantation thereby furthering understanding of the best possible treatment approaches.

3. **Common Rule:** A Federal Policy for the Protection of Human Subjects codified in separate regulations by the Department of Health and Human Service (DHHS) and other Federal departments and agencies.

    3.1. **2018 Revised Common Rule Requirements:** Revised Federal Policy for the Protection of Human Subjects (Revised Common Rule) requirements effective on January 21, 2019.

    3.2. **Pre-2018 Common Rule Requirements:** Federal Policy for the Protection of Human Subjects (Common Rule) requirements originally published on June 18, 1991 and effective until January 21, 2019.

4. **IRB of record:** The IRB responsible for conducting the IRB reviews of a study on behalf of a participating study site.

5. **Research protocol:** General term used to refer to a study proposal, research project, concept paper, etc.

6. **Suspension of NMDP IRB approval:** An action taken by the IRB to temporarily withdraw approval for some or all research procedures on a protocol.

7. **Termination of NMDP IRB approval:** An action taken by the IRB to permanently withdraw approval for some or all research procedures on a protocol.

RESPONSIBILITIES

1. **NMDP Institutional Official**

   - Review, approve, and sign off on reports of suspensions or terminations prepared by NMDP IRB staff

2. **NMDP IRB Chair**

   - Make decisions on suspensions or terminations of approval of research that need to be made on an urgent basis.

3. **NMDP IRB Staff**

   - Prepare reports of suspensions or terminations
   - Distribute reports of suspensions or terminations to the appropriate personnel, organizations, and agencies
   - Send reminders to investigators to submit the Notification of Study Closure form
   - Perform administrative closures of research

4. **Principal Investigator**

   - Submit to the NMDP IRB proposed procedures for withdrawal of currently enrolled subjects that considers their rights and welfare
   - Submit the Notification of Study Closure form to the NMDP IRB when a study is closed

PROCEDURE

1. The NMDP IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to participants. (See P00064 NMDP Board of Directors Policy: Research Involving Human Subjects)

1.1. For BMT CTN studies, the NMDP IRB has the authority to suspend or terminate approval of research only for participating study sites that are using the NMDP IRB as their IRB of record for the study.

2. Process for suspending or terminating previously approved research

2.1. Decisions to suspend or terminate previously approved research shall be made by the full IRB at a convened meeting.

2.2. Decisions to suspend or terminate approval of research that need to be made on an urgent basis shall be made by the IRB Chair.

2.2.1. Should the IRB Chair be unavailable in an urgent situation, the Organizational Official, IRB Administrator or Institutional Official will designate one or more IRB members to substitute for the IRB Chair.

2.2.2. IRB members will be informed of urgent decisions to suspend or terminate approval of research at the next regularly scheduled meeting.

2.3. When IRB approval is suspended or terminated, the IRB shall consider actions to protect the rights and welfare of currently enrolled participants.

2.3.1. The Principal Investigator shall submit to the IRB proposed procedures for withdrawal of currently enrolled subjects that considers their rights and welfare. The IRB will review the proposed procedures. The IRB may mandate oversight or transfer responsibility to another Investigator to assure implementation of these procedures.

2.3.2. When a termination or suspension involves the withdrawal of currently enrolled participants from the research, the IRB shall require that the participants be notified.

2.3.3. When follow-up of participants for safety reasons is permitted or required, the IRB shall require that participants be so informed.

2.4. If the IRB suspends or terminates approval of a study, any adverse events or unanticipated problems involving risks to participants or others that would have required reporting had the former participants continued to be enrolled in the research should be reported to the NMDP IRB and others as required by the protocol and NMDP IRB policies and procedures.

3. Reporting suspension or termination of previously approved research

3.1. The Department of Health and Human Services (HHS) and U.S. Food and Drug Administration (FDA) regulations require prompt reporting of suspension or termination of previously approved research .

3.2. Reports of suspensions or terminations will be prepared by the NMDP IRB staff and shall include the following:

3.2.1. Name of the institution conducting the research

3.2.2. Title of the research protocol and/or grant proposal being suspended or terminated

3.2.3. Name of the Principal Investigator (PI) on the research protocol

3.2.4. NMDP IRB study number and the number of any applicable federal award(s)

3.2.5. Description of the event resulting in suspension or termination

3.2.6. Findings of the NMDP or the NMDP IRB

3.2.7. Actions the NMDP is taking or plans to take

3.2.8. Reasons for the NMDP's or the NMDP IRB's actions

3.2.9. Plans for continued investigation or action, if applicable

3.3. The draft report will be reviewed by the NMDP Institutional Official.

3.4. If the suspension or termination of IRB approval is occurring only at a specific site in a multi-site study, the draft report will be forwarded to the site for review and comment.

3.4.1. The NMDP will make reasonable efforts to allow for the site's review/comment, but in no case will such opportunity interfere with timely submission of required reports.

3.4.2. Although NMDP will consider any comments submitted, the final content of the report is up to the discretion of the NMDP.

3.5. The final report will be reviewed and signed by the NMDP Institutional Official.

3.6. Once the NMDP Institutional Official has signed off on the report, it will be distributed to:

3.6.1. NMDP Organizational Official

3.6.2. Principal Investigator

3.6.3. Office of Human Research Protections (OHRP)

3.6.3.1. For research subject to pre-2018 Common Rule Requirements, reporting to OHRP is not required if, 1) the research is not federally funded, and 2) the relying institution did not "check the box" on its FWA (i.e., The relying institution did not elect on their FWA to apply the Common Rule and all of its subparts to all of its human subjects research regardless of the source of support.).

3.6.3.2. For research subject to 2018 Revised Common Rule Requirements, reporting to OHRP will only occur for federally-funded studies.

3.6.4. FDA, when the research is subject to FDA regulations

3.6.5. Department of Defense-Navy Human Research Protection Officer, when the research is subject to Department of Defense (DoD) regulations. NOTE: Reporting to DoD must occur within five days of completion of the report.

3.6.6. Other government agencies when the research is overseen or funded by those agencies, and they require reporting separate from that to OHRP.

3.6.7. Non-federal study sponsor or contract research organization, when appropriate

3.6.8. BMT CTN Data & Coordinating Center (DCC), for BMT CTN studies

3.6.9. Other sites involved in the research, when appropriate

3.6.10. NMDP legal counsel, when appropriate

3.7. The above reports will not be sent to federal agencies if the intended recipient of the report has already been made aware of the suspension or termination through other mechanisms, such as reporting by the PI, sponsor, or another organization.

3.8. Required reporting will be completed within 30 days of the IRB's decision to suspend or terminate the research. In rare instances, this deadline may be extended for good cause in the discretion of the Institutional Official in consultation with the Organizational Official, in which case a preliminary report would be submitted to the above people/agencies with a follow-up report submitted at a later date when more information is available.

4. Process for administrative closure of research

4.1. The NMDP IRB office may administratively close a study with the NMDP IRB under the following conditions:

4.1.1. NMDP IRB approval of the study has expired, and the investigator has not submitted continuing review materials for the study to the NMDP IRB within one year of the study's NMDP IRB expiration date.

4.1.2. NMDP IRB approval of the study has expired, and the investigator has not responded to the stipulations or reasons for deferral set forth by the IRB within one year of the study's NMDP IRB expiration date.

4.1.3. The investigator has communicated closure of the study to the NMDP IRB office; however, the investigator has failed to submit the Notification of Study Closure form within three months after such communication.

4.1.3.1. IRB staff will send monthly reminders to the investigator for two months requesting he/she complete and submit the Notification of Study Closure form.

4.1.3.2. Should the Notification of Study Closure form not be received by the IRB Office at the end of the third month, IRB staff will administratively close the study with the NMDP IRB.

4.2. The Principal Investigator will be informed in writing of the administrative closure with the NMDP IRB.

4.3. Should the Principal Investigator wish to reopen the study with the NMDP IRB one year or more beyond the NMDP IRB expiration date, he/she must submit a new NMDP IRB Initial Application form, including all required accompanying materials, as well as study progress and participant accrual information.

REFERENCES

1. 45 CFR 46.103(b)(5)(ii) and 45 CFR 46.113
2. 21 CFR 56.108(b)(3) and 21 CFR 56.113
3. Department of Defense Instruction 3216.02, 4.b.4
4. OHRP Guidance on Reporting Incidents to OHRP
5. FDA Information Sheets: Continuing Review After Study Approval
6. Policy #: P00064 NMDP Board of Directors Policy: Research Involving Human Subjects

Revision History

Revision	Brief Description of Revision
S00399 rev. 2	Added 4.1.3 and its subpoints.
S00399 rev. 3	Revised 3.6 re: timing of reports
S00399 rev. 4	Added the Notification of Study Closure form under Materials. Added definitions for BMT CTN and IRB of record. Added Responsibilities section. Added 1.1 and 3.48 specific to BMT CTN studies.
S00399 rev. 5	Added Common Rule definition and sections 3.4.3.1 and 3.4.3.2 with OHRP reporting requirements.
S00399 rev. 6	Revised section 3 to include provisions for sending draft report to participating site for comment.
S00399 rev.7	Added clarification to reporting to DoD in 3.6.5.

ADDENDA

Not applicable