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STANDARD OPERATING PROCEDURE

OBJECTIVE/SCOPE

To ensure that:

1. Principal Investigators submit all the materials pertinent for an informed review by the National Marrow Donor Program (NMDP) Institutional Review Board (IRB) for initial or continuing review of a study, or changes to a previously-approved study.
2. Principal Investigators submit proper documentation to the NMDP IRB to stop a study.
3. Study sites relying on the NMDP IRB as their IRB of record submit the required site-specific materials to the NMDP IRB.

MATERIALS

1. Annual Renewal or Updates to sIRB Enrollment and Local Context Instructions
2. Annual Status Report
3. Application for Continuing Review for Bio-Medical Studies
4. Application for Continuing Review for Social and Behavioral Studies
5. Financial Disclosure Form
6. Initial Application for Bio-Medical Studies
7. Initial Application for Social and Behavioral Sciences
8. IRB Authorization Agreement
9. IRBManager Manual for Researchers and Staff
10. IRB Request for Study Amendment
11. Major Protocol Exception Request Form
12. NMDP Single IRB Manual for Local Institutions
13. NMDP sIRB Study-Specific Local Context Worksheet
14. Notification of Study Closure
15. Reportable Event Form
16. Request to Rely on an External IRB Form

17. Revised NMDP sIRB Study-Specific Local Context Worksheet

18. Single IRB Signatory Institution Enrollment and Local Context Form

19. Site-Specific Documents Submission Form

20. Study Site Closure Form

21. Temporary Variance Request Form

SAFETY

Not applicable

DEFINITIONS

1. **2018 Revised Common Rule Requirements:** Revised Federal Policy for the Protection of Human Subjects (Revised Common Rule) requirements effective on January 21, 2019.

2. **Blood and Marrow Transplant Clinical Trials Network (BMT CTN):** A network funded 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. **Federalwide Assurance (FWA):** A document filed with the Department of Health and Human Services (DHHS) stating that the institution will comply with DHHS protection of human subjects regulations.

4. **IRB Authorization Agreement:** An agreement between two institutions that defines the scope of research that one institution's qualified IRB will be allowed to review on behalf of the other institution. Also referred to as a reliance agreement.

5. **IRBManager:** Web-based system for IRB application submission, IRB application review, and management of IRB-related study records.

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

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

8. **Resource for Clinical Investigations in Blood and Marrow Transplantation (RCI BMT):** A team within the CIBMTR dedicated to advancing the field of hematopoietic cell transplantation and cellular therapy by providing trial

management, survey research, and data management services for multi-center trials.

9. **Single IRB (sIRB):** One IRB that has been selected to serve as the IRB of record for the participating sites on a multi-site study.

RESPONSIBILITIES

1. NMDP IRB Staff

- Create applicable applications and forms in IRBManager.

2. Principal Investigator

- Submit required materials to the NMDP IRB as outlined in this SOP.

PROCEDURE

The information below outlines the information and accompanying materials the Principal Investigator must submit to the NMDP IRB for initial or continuing review, review of a change to an already NMDP IRB-approved study, to stop a study, or to determine if a study is exempt from regulation. Applicable NMDP IRB applications and forms are located in IRBManager. Submission instructions are found on the applications and forms. A link to the *IRBManager Manual for Researchers and Staff* can be found in IRBManager and on the NMDP/Be The Match Network Website for additional instructions on submitting forms.

1. **Materials required for initial review.**

1.1. The application for initial review and accompanying materials must be received, reviewed and approved by the NMDP IRB prior to the Principal Investigator initiating the study.

1.2. The same materials required for initial review must be received regardless of whether the study will be reviewed by the convened IRB, qualifies for review by expedited procedures, qualifies for an exempt determination, or a limited IRB review will be conducted.

1.3. Materials for initial review include, but are not limited to the following:

1.3.1. The Principal Investigator's professional qualifications to perform the research.

1.3.1.1. The Principal Investigator's curriculum vitae (CV).

1.3.1.2. Documentation that the Principal Investigator has received training in human subjects protection.

1.3.1.2.1. It shall be clarified with Principal Investigators outside of the U.S. that they are in compliance with their country's regulations and their own institution's training requirements for human subjects protection.

1.3.1.3. Principal Investigator's financial disclosure and conflict of interest statements, if applicable.

1.3.2. Information provided at the time of initial review may include, but is not limited to, the following:

1.3.2.1. Circumstances under which the informed consent will be administered.

1.3.2.1.1. In the case of studies involving the unrelated volunteer donor obtained through the Be the Match Registry, informed consent will be administered according to specific NMDP requirements by staff at an organization identified by the NMDP, such as the donor center coordinator.

1.3.2.2. Procedures for documentation of informed consent including any procedures for using witnesses, translators, and document storage.

1.3.2.2.1. In the case of studies involving the unrelated volunteer donor obtained through the Be the Match Registry, the NMDP procedure for documenting informed consent at the donor centers will be applicable.

1.3.2.3. Compensation to subjects for their participation.

1.3.2.4. Compensation for injured research subjects.

1.3.2.5. Provisions for protection of subject's privacy and maintenance of confidentiality of data.

1.3.2.6. Extra costs to subjects for their participation in the study.

1.3.2.7. Extra costs to third party payers because of subject participation.

1.3.2.8. Risks and benefits to being in the study.

1.3.2.9. IND or IDE number assigned by the FDA, if applicable.

1.3.2.10. Federalwide Assurance (FWA) number for the Principal Investigator's institution

1.3.3. The research protocol which includes and/or addresses, but is not limited to, the following:

1.3.3.1. Title of study.

1.3.3.2. Purpose of the study (including the expected benefits of the study).

1.3.3.3. Sponsor of the study.

1.3.3.4. The scientific or scholarly rationale for the study.

1.3.3.5. Results of previous related research.

1.3.3.6. Subject inclusion/exclusion criteria. Include justification for the subject population involved and assurance that the selection of the subjects is equitable, taking into account the purposes of the research and the setting in which the research will be conducted.

1.3.3.7. Study design including the appropriateness of the research method.

1.3.3.8. Description of procedures to be performed.

1.3.3.9. Provisions for managing adverse events.

1.3.4. Investigator's Brochure, if applicable.

1.3.5. Package insert (providing drug information), if applicable.

1.3.6. Device Manual, if applicable.

1.3.7. Data and safety monitoring plan, if research involves more than minimal risk (may be included in research protocol).

1.3.8. The proposed informed consent document(s).

1.3.9. IRB review letters from other IRBs that have reviewed the protocol (if applicable), including letters of disapproval and the reasons for the disapproval.

1.3.10. Documentation of review for scientific merit if such a review was conducted.

1.3.10.1. NMDP research receiving funding from the Department of the Navy must be reviewed for scientific merit.

1.3.11. Recruitment materials (if applicable), including advertisements to be seen or heard by potential subjects.

2. **Materials required for continuing review**

2.1. The materials required for continuing review must be received, reviewed and approved by the NMDP IRB prior to the end of the approval term.

2.2. Materials for continuing review may include, but are not limited to, the following:

2.2.1. Application for continuing review which may include, but is not limited to, the following:

2.2.1.1. Status of study (e.g. open for enrollment, closed to enrollment, etc.).

2.2.1.2. Number of subjects enrolled since the last review period, total number enrolled since the study was implemented, and total to be enrolled.

2.2.1.3. Summary of study progress and preliminary findings, including any multi-center trial reports, and the researcher's current risk-potential benefit assessment based on study results.

2.2.1.4. Summary of protocol exceptions and deviations.

2.2.1.5. Summary of unanticipated problems involving risks to subjects or others.

2.2.1.6. Withdrawal of subjects from the research, including the reasons for withdrawals, and complaints about the research since the last IRB review.

2.2.1.7. Summary of protocol amendments.

2.2.1.8. List of any relevant recent literature

2.2.2. Current informed consent documents, including tracked changes versions if there are amendments since the previous NMDP IRB review.

2.2.3. Approval/rejection letters from all other IRBs/ERBs reviewing the study, if applicable.

2.2.4. Research protocol (if amended since last submission to NMDP IRB).

2.2.5. Data Safety Monitoring Board (DSMB) progress report, if applicable.

2.2.6. Funding agency progress report, if applicable.

3. **Materials required for an Annual Status Report**

3.1. For studies initially reviewed by expedited procedures under the 2018 Revised Common Rule Requirements (or that have transitioned to the 2018 Revised Common Rule Requirements), investigators will complete the *Annual Status Report* in IRBManager with information about study status and subject enrollment, including recipients, donors, and/or other research participants. At this time the investigators will also have an opportunity to submit amendments that have not yet been implemented or to close the study.

4. **Materials required for requesting a change to an approved study**

4.1. Changes to a previously-approved study cannot be implemented until the Principal Investigator has received written approval from the NMDP IRB. The only exception is if the change is necessary to eliminate any immediate harm to the subject.

4.2. Materials for requesting a change to an approved study may include, but are not limited to, the following:

4.2.1. *IRB Request for Study Amendment* form, which includes rationale for the change.

4.2.2. Revised study documents, if applicable.

4.2.3. Approval/rejection letters from all other IRBs/ERBs reviewing the study amendment, if applicable.

5. **Materials required for requesting a temporary variance for a study**

5.1. Submit a *Temporary Variance Request Form* in IRBManager. (refer to S00693 NMDP IRB Protocol Exceptions, Deviations, and Temporary Variances)

6. **Materials required for stopping a study**

6.1. Materials submitted for stopping a study may include, but are not limited to, the following:

6.1.1. Progress report or published manuscript.

6.1.2. *Notification of Study Closure* form that may include, but is not limited to, the following information:

6.1.2.1. Study stop date.

6.1.2.2. Reason for stopping the study (e.g., study completed, funding ended, etc.).

6.2. The NMDP IRB must be notified immediately if a study is stopped for any reason other than completion of the study.

6.3. If a study is completed, it is acceptable to notify the NMDP IRB at the time of the continuing review.

6.4. If a study is stopped but will be reopened in the future, the study must be reviewed and approved by the NMDP IRB prior to restarting the study.

7. **Materials required when a NMDP investigator or research staff requests to rely on an external IRB**

7.1. *Request to Rely on an External IRB form*

7.2. *Financial Disclosure Form*

FOR SITES PARTICIPATING IN THE NMDP SINGLE IRB

The information below outlines the information and accompanying materials a participating study site must submit to the NMDP IRB when the study site is relying on the NMDP IRB as their IRB of record for a study. (Refer also to the *NMDP Single IRB Manual for Local Institutions*.) Applicable NMDP IRB forms are located in IRBManager. Submission instructions are found on the applications and forms. A link to the *IRBManager Manual for Researchers and Staff* can be found in IRBManager for additional instructions on submitting forms.

8. **Materials required for enrolling in the NMDP single IRB**

8.1. *Single IRB Signatory Institution Enrollment and Local Context Form.* This includes submission of the institution's required boilerplate consent language.

8.2. An IRB Authorization Agreement. This could be any of the following:

8.2.1. the BMT CTN IRB Authorization Agreement that covers all BMT CTN research released to sites after July 1, 2017,

8.2.2. a CIBMTR or NMDP/Be The Match study-specific IRB Authorization Agreement, or

8.2.3. an IRB Authorization Agreement specific to a study for which the NMDP IRB has agreed to serve as the single IRB.

9. **Materials required to open a study using the NMDP single IRB**

9.1. *NMDP sIRB Study-Specific Local Context Worksheet*

9.2. Documentation of current human research protection training for the site's Principal Investigator

9.3. Redlined version(s) of the site's study consent/assent form(s) approved by the central study-level protocol coordinator

9.4. Documentation of the central study-level protocol coordinator's approval of the site's study consent/assent form(s)

9.5. If applicable, any locally-developed recruitment material or participant-facing consent material.

10. **Materials required when submitting site-specific changes**

10.1. For consent form revisions

10.1.1. *IRB Request for Study Amendment* form

10.1.2. Redlined version(s) of the site's study consent/assent form(s) showing the study-wide changes

10.1.3. Documentation of the central study-level protocol coordinator's approval of the site's revised study consent/assent form(s)

10.2. For changes to the site's Principal Investigator (PI)

10.2.1. *Revised NMDP sIRB Study-Specific Local Context Worksheet*

10.2.2. Documentation of current human research protections training for the site's new PI

10.2.3. Redlined consent documents showing the change in PI

10.3. For site changes to previously submitted NMDP single IRB forms

10.3.1. For changes to the information on the institution's *Single IRB Signatory Institution Enrollment and Local Context Form*, start the *Annual Renewal or Updates to sIRB Enrollment and Local Context Instructions* xForm in IRBManager.

10.3.2. For changes to the site's *NMDP sIRB Study-Specific Local Context Worksheet*, other than study-site contacts, submit a *Revised NMDP sIRB Study-Specific Local Context Worksheet* in IRBManager.

10.4. For changes to the institutional boilerplate consent language

10.4.1. *Site-Specific Documents Submission* Form

10.4.2. Revised boilerplate consent language document

11. **Materials required when submitting translated documents (including consent forms) to the NMDP single IRB**

11.1. NMDP IRB-approved English language document corresponding to the translated document

11.2. Translated version(s) of the NMDP IRB-approved English language document

11.3. Translator's Certificate(s) of Accuracy or equivalent document(s)

11.3.1. In some cases an institution may use a native speaker of the non-English language employed by the institution, rather than a professional translator, to perform the translation. This is usually done for the purposes of cost savings. If a native speaker of the translation language performs the translation, the translation must be verified by another native speaker of that language.

11.3.1.1. The native speaker performing the translation should have recent experience translating similar documents.

11.3.2. This process may be accepted in lieu of providing a professional translator's Certificate of Accuracy. However, a Certificate of Accuracy from a professional translator is the preferred method of translation, and acceptance of a translated document without a Certificate of Accuracy is up to the discretion of the NMDP IRB.

12. **Materials required when requesting a major protocol exception**

12.1. *Major Protocol Exception Request Form* (refer to S00693 *NMDP IRB Protocol Exceptions, Deviations, and Temporary Variances*)

13. **Materials required when reporting unanticipated problems and/or serious or continuing non-compliance to the NMDP single IRB**

13.1. *Reportable Event Form* (refer to S00407 *Unanticipated Problems Involving Risks to Participants or Others* or S00213 *NMDP IRB Managing and Reporting Non-Compliance with Human Research Protection Program Requirements)*

14. **Materials required to close a study at a site using the NMDP single IRB**

14.1. For BMT CTN studies, the site must wait until notification from the BMT CTN Data and Coordinating Center that the site may close the study.

14.2. For studies other than BMT CTN studies, submit the *Study Site Closure Form*

REFERENCES

1. 21 CFR 56 Subpart C
2. 45 CFR 46 Subpart A
3. S00213 NMDP IRB Managing and Reporting Non-Compliance with Human Research Protection Program Requirements
4. S00407 Unanticipated Problems Involving Risks to Participants or Others
5. S00693 NMDP IRB Protocol Exceptions, Deviations, and Temporary Variances

Revision History

Revision	Brief Description of Revision
S00038 08/17/2001	New SOP
S00038 version 2.0	Annual Review: Added sections 1.10, 1.11, 2.1.8 & 2.1.9
S00038 version 3.0	Revised content and numbering of sections 1 and 2. Revised numbering of section 4.
S00038 rev. 4	Revised wording of 1.2.9 and added section 1.2.9.1.
S00038 rev. 5	Put into new format. Changed NMDP Registry to Be the Match Registry. Added section 5.
S00038 rev. 6	Added definition of Research protocol. Added 1.2.3.4, 1.2.7, 2.2.1.8 and 3.2.5. Clarifications made to other sections.
S00038 rev. 7	Deleted 3.2.5 scientific review comm. Report.
S00038 rev. 8	Added Responsibilities section. Updated website references to www.bethematchclinical.org. Added 1.2.1.2.1. Deleted 2.2.2 regarding adverse event reports. Revised 5.1 to accept submission of the Human Subjects Research Determination form.
S00038 rev. 9	Updated Objective/Scope. Added materials. Added definitions. Added responsibilities. Added section 3.2.2. Added section 6. Added section on Sites Participating in NMDP Single IRB. Added references.
S00038 rev. 10	Added references to IRBManager. Added forms in the Materials section. Added section 3 and section 5. Added procedures for accepting translations from a native speaker in lieu of a professional translator's Certificate of Accuracy. Revised sIRB site submissions to match submission procedures for IRBManager.
S00038 rev. 11	Removed reference to F00756 (archived). Removed section 7 regarding materials required to make an exempt determination and added 1.2.

ADDENDA

Not applicable