STANDARD OPERATING PROCEDURE

OBJECTIVE/SCOPE
To ensure that the National Marrow Donor Program (NMDP) Institutional Review Board (IRB) has established processes for expedited review, emergency review, and for determining when studies are exempt from regulation.

MATERIALS
1. Documentation of IRB Review/Approval form
2. Exempt Notice of Action Form

SAFETY
Not applicable

DEFINITIONS
1. Annual Status Report: An annual report of study status and subject enrollment for studies eligible for expedited review in accordance with 2018 Common Rule Requirements.

2. Blood and Marrow Transplant Clinical Trials Network (BMT CTN): 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.

4. Center for International Blood and Marrow Transplant Research (CIBMTR): A research collaboration between the National Marrow Donor Program (NMDP)/Be The Match and the Medical College of Wisconsin.
5. **Expedited review:** A procedure through which certain kinds of research may be reviewed and approved without convening a meeting of the NMDP IRB.

6. **Exempt from regulation:** Research that qualifies for exemption from the requirements of 45 CFR 46.104(d)(1)-(8) or 21 CFR 56.104(c)-(d).

7. **Limited IRB Review:** A type of review process required for exempt categories under 45 CFR 46.104 (d)2(iii), (d)3(i)(c), and (d)7 and 8.

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

9. **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.

**RESPONSIBILITIES**

1. **NMDP IRB Administrator**
   - Determine if proposed research qualifies as exempt from regulation, and whether the exempt research meets the ethical standards in *The Belmont Report* and criteria for participant protection as outlined in 45 CFR 46.

2. **NMDP IRB Chair**
   - Conduct expedited reviews or designate another IRB member to conduct the review.
   - Indicate the expedited review action and sign the Documentation of IRB Review/Approval form.
   - Determine if proposed research qualifies as exempt from regulation, and whether the exempt research meets the ethical standards in *The Belmont Report* and criteria for participant protection as outlined in 45 CFR 46.

3. **NMDP IRB Staff**
   - Determine whether or not an expedited review process can be used for proposed research.

**PROCEDURE**

1. **Expedited review**
   1.1. The U.S. Food and Drug Administration (FDA) and Department of Health and Human Services (DHHS) have established a list of categories of research that may be reviewed by the NMDP IRB through an expedited review process. This list is published in the Federal Register and is amended as necessary. The NMDP IRB may use an expedited review process for any...
research study that 1) falls into one of the categories of research approved for expedited review and 2) does not involve more than minimal risk.

1.1.1. For NMDP/CIBMTR studies that receive funding from the Department of the Navy, the definition of minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain).

1.2. An expedited review process may also be used for minor changes in previously approved research during the time in which the approval was authorized if the changes do not in any way increase the risk to subjects. For example, an amendment to a research protocol that decreases the amount of blood to be collected for a specified test could be approved through an expedited review process.

1.3. An expedited review process may also be used for continuing review if the research falls into one or more of the regulatory categories that allow continuing review using the expedited procedure.

1.4. An expedited review process may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

1.5. The determination to use an expedited review process will be made at the discretion of the NMDP IRB staff upon pre-review of incoming materials. The IRB Administrator may be consulted for such determinations if needed.

1.6. Documentation of the expedited review determination will include the specific permissible category.

1.6.1. If an expedited reviewer determines that the research appearing on the expedited review list is more than minimal risk, the rationale for this determination must be documented.

1.6.2. For FDA-regulated clinical investigations, the NMDP IRB will continue to comply with FDA’s regulations at 21 CFR 56.110(b) and use the 1998 list for FDA-regulated clinical investigations.

1.7. The following process will be used for an expedited review:

1.7.1. The NMDP IRB Chair shall review the study or minor amendment to previously approved research.
1.7.1.1. The NMDP IRB Chair, at his/her discretion, may designate one or more members of the NMDP IRB to perform the expedited review in the following situations:

1.7.1.1.1. If the NMDP IRB Chair is unable to perform the expedited review in a timely manner.

1.7.1.1.2. If the NMDP IRB Chair feels the expertise of another IRB member(s) is better suited for review of a particular type of study.

1.7.1.1.3. If the NMDP IRB Chair has a financial or other conflict of interest pertinent to the research protocol or Principal Investigator.

1.7.1.1.3.1. If the designated IRB member(s) has a financial or other conflict of interest pertinent to the research protocol or Principal Investigator, he/she must disclose the conflict of interest so that another IRB member may be appointed to perform the expedited review.

1.7.1.2. To qualify as an expedited reviewer for a particular study, the IRB member, according to the judgment of the IRB Chair, must have the experience and education required to conduct expedited review for that type of study.

1.7.2. The reviewer(s) will receive all study documentation (Refer to SOP #: S00040, NMDP IRB Protocol Review)

1.7.3. The reviewer(s) will conduct the review according to procedures in SOP # S00040, NMDP IRB Protocol Review.

1.7.4. The reviewer(s) shall exercise the full authority of the NMDP IRB, except that they cannot disapprove the study. If the reviewer(s) does not find it acceptable to approve the study or amendment, the study or amendment will go before the full NMDP IRB for a non-expedited review.

1.7.4.1. For initial and continuing reviews, the reviewer(s) shall indicate their action and sign the Documentation of Review/Approval form, which shall be returned to the NMDP IRB Office.

1.7.4.2. For all other expedited reviews, the reviewer(s) documentation of review/approval via email is sufficient.

1.7.5. If the reviewer(s) approves the study with stipulations, but the investigator does not accept the stipulations, the study will go before the full NMDP IRB for review.

1.7.6. If the study is approved by the reviewer(s), the full NMDP IRB will be informed of the expedited review by including a summary of the study, or a summary of the amendment to the previously approved research, in the meeting packet.

1.7.7. The study summary will also include any specific findings regarding informed consent and vulnerable subjects. (Refer to SOP#: S00047, NMDP IRB Record Management)

1.7.8. The expedited review process shall follow the procedures set forth in SOP # S00040, NMDP IRB Protocol Review regarding the following:
1.7.8.1. Determination of review interval
1.7.8.2. Further review and approval of NMDP IRB actions within the NMDP
1.7.8.3. How Investigators should respond to stipulations and how that response is reviewed
1.7.8.4. When continuing reviews shall be conducted
   1.7.8.4.1. NOTE: Continuing review is not required for studies initially reviewed by expedited procedures under the 2018 Revised Common Rule Requirements that are not regulated by the FDA, unless the reviewer explicitly justifies why continuing review would enhance protection of research subjects. Instead, the investigators will be required to submit an Annual Status Report.
1.7.8.5. Consequences of the Investigator not providing continuing review information to the IRB, or of the IRB not reviewing and approving a research study by the date of IRB expiration
1.7.8.6. Review of changes in approved research
1.7.8.7. Completion of a study

2. Annual Status Report
   2.1. For studies initially reviewed by expedited procedures under the 2018 Revised Common Rule Requirements, investigators will complete an annual report with information about study status and subject enrollment, including recipients and donors. At that time, the investigators will also have an option to submit amendments that have not yet been implemented or close the study.
   2.2. Annual Status Reports are reviewed by administrative procedures unless there is a change in the study status requiring an IRB review.

3. Emergency exemption
   3.1. In the case of volunteer hematopoietic cell donors, who are by definition healthy research subjects, there is no justification for emergency use of an investigational drug, biologic, or investigational device.
   3.2. There are, however, cases where a volunteer donor is asked to make a donation on an urgent basis for a recipient enrolled in a research protocol that also requires NMDP IRB review and approval for the donor to participate. In these cases, a quorum of the NMDP IRB membership will be convened to review the research protocol on an urgent basis. The urgent review process will be the same as that outlined in SOP #: S00040, NMDP IRB Protocol Review.
   3.2.1. If a quorum of the NMDP IRB membership is not able to convene for an urgent review, the donation may be done as an emergency exemption, if approved by the NMDP Vice President of Medical & Quality Services or
the NMDP Vice President and Medical Director of Health Services Research. In the case of an emergency exemption the donor-patient pair must not be considered research subjects, and any resulting data must not be included in any subsequent publications or presentations of research.

3.2.2. In an emergency exemption, donor consent will be obtained, unless the legal and regulatory requirements for an exception to obtain consent are met.

3.3. The transplant center’s institutional policies and procedures for the emergency use of an investigational drug, biologic, or investigational device must be followed for a patient at that transplant center to access in an emergency situation an investigational product offered through a BMT CTN or RCI BMT research protocol.

4. **Exemption from regulation**

4.1. Any research study involving human subjects that falls into one of the research categories listed in 45 CFR 46.101(b)(1)-(6) is exempt from regulation.

4.1.1. FDA-regulated research cannot be exempt.

4.1.2. NMDP will follow the applicable Federal regulations in determining exempt status of research involving children as participants.

4.2. The IRB Chair or IRB Administrator will determine if proposed research is exempt from regulation.

4.2.1. Should the IRB Administrator have an apparent or real conflict of interest regarding the study, the determination of exemption will be made by the IRB Chair.

4.2.2. Should the IRB Chair have an apparent or real conflict of interest regarding the study, the determination of exemption will be made by the IRB Administrator.

4.3. The IRB Chair or IRB Administrator will determine whether the exempt research meets the ethical standards in *The Belmont Report* and criteria for participant protection as outlined in 45 CFR 46.

4.3.1. This criteria includes, but is not limited to, the following:

4.3.1.1. The research involves no more than minimal risk to participants.

4.3.1.2. Selection of participants is equitable.

4.3.1.3. There are adequate provisions to maintain the confidentiality of data and the privacy of participants.

4.3.1.4. The participants will be informed:

4.3.1.4.1. that the activity involves research,

4.3.1.4.2. of the research procedures,

4.3.1.4.3. that participation is voluntary,
4.3.1.4.4. of the investigator’s name and contact information.

4.3.2. Should the IRB Chair or IRB Administrator feel that the exempt research raises ethical concerns or requires measures to protect participants, modifications to the research may be required prior to a final determination of exempt status.

4.4. Determinations of exemption will be documented on the Exempt Notice of Action.

4.4.1. Documentation of the exemption will include the exemption category listed in 45 CFR 46.104.

4.4.2. Documentation of the exemption will be kept on file at the NMDP.

4.4.3. The Exempt Notice of Action will be sent to the Principal Investigator.

4.4.3.1. The Exempt Notice of Action will include a directive that any changes to the study must be reviewed by the NMDP IRB prior to implementation to determine whether the research continues to qualify for exemption from regulation.

5. Limited IRB Review

5.1. 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).

5.2. Expedited review procedures will be followed to review research for which limited IRB review is required.

5.3. For the purposes of conducting the limited IRB review, the reviewer must make a determination that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

5.4. For the purposes of conducting the limited IRB review required by §46.104(d)(7) and (d)(8), the reviewer must make a determination that the broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of 45 CFR 46.116(a)(1)-(4), (a)(6), and (d) and that the broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with 45 CFR 46.117.

5.4.1. The NMDP IRB does not use broad consent as an alternative consent process. Thus, exemption categories 7 and 8 will not be considered under the auspices of the NMDP IRB.

REFERENCES
1. 21 CFR 56
2. 45 CFR 46 Subparts A, B & D
3. SOP#: S00040, NMDP IRB Protocol Review
4. SOP#: S00047, NMDP IRB Record Management
5. The Belmont Report
6. OPRR Guidance on 45 CFR 46.101(b)(5): Exemption for Research and Demonstration Projects on Public Benefit and Service Programs

8. Department of Defense Instruction (DoDI) 3216.02, 6.b

**Revision History**

<table>
<thead>
<tr>
<th>Revision</th>
<th>Brief Description of Revision</th>
</tr>
</thead>
<tbody>
<tr>
<td>S00041 08/17/2001</td>
<td>New SOP</td>
</tr>
<tr>
<td>S00041 version 2.0</td>
<td>Annual Review: Added Exempt from Review definition, added sections 1.5.3 – 1.5.6</td>
</tr>
<tr>
<td>S00041 version 3.0</td>
<td>Added an Applicable Reference Document. Added section 3.4. Formatting changes.</td>
</tr>
<tr>
<td>S00041 rev. 4</td>
<td>Put into new SOP format. Changed language from “exempt from review” to “exempt from regulation.” Added applicable reference documents. Added 1.3. Revised 1.4. Added 1.6.1.1 and sub-points. Added 1.6.3, 1.6.4.1, 1.6.5, 1.6.8 and sub-points. Revised 3.1, 3.2 and their sub-points. Added 3.3, 3.4 and their sub-points.</td>
</tr>
<tr>
<td>S00041 rev. 5</td>
<td>Added definition of Research protocol. Added 1.4, 1.7.1.2, 2.3.1, 3.3.1.4.1. Clarifications made to several sections. Added Reference Document on OHRP Guidance on Expedited Review Categories.</td>
</tr>
<tr>
<td>S00041 rev. 6</td>
<td>Added 1.1.1. Added DoDI reference doc.</td>
</tr>
<tr>
<td>S00041 rev. 7</td>
<td>Revised section 3.2 and 3.3 to state that the IRB Chair or IRB Administrator (not both) will make exemption determinations.</td>
</tr>
<tr>
<td>S00041 rev. 8</td>
<td>Added section 3.1.1 stating that FDA-regulated research cannot be exempt.</td>
</tr>
<tr>
<td>S00041 rev. 9</td>
<td>Added Materials. Added definitions for CIBMTR and RCI BMT. Added Responsibilities section. Reworded 1.5 to state that the IRB Administrator may be consulted if needed. Added 2.4 regarding emergency exemptions for recipients.</td>
</tr>
</tbody>
</table>

**ADDENDA**

Not applicable