Manual for Local Institutions
Using the NMDP IRB as a Single IRB

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This manual is available on the NMDP/Be The Match Network Website.
https://network.bethematchclinical.org/research/institutional-review-board/irb-applications-and-forms/

This manual was modeled after the NCI CIRB Handbook for Local Institutions formerly located on the NCI CIRB website at https://ncicirb.org.
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1 INTRODUCTION

This Manual introduces local institutions to the purpose and function of the National Marrow Donor Program (NMDP) Institutional Review Board (IRB) when it serves as a single Institutional Review Board (sIRB) for multi-site studies. The Manual provides information for enrolling in and using the NMDP sIRB.

NMDP IRB staff coordinate the work of the NMDP sIRB and provide support for local institutions. Study reviews are conducted by the NMDP IRB.

2 NMDP IRB AS A sIRB

Background

On June 21, 2016, the National Institutes of Health (NIH) released its Policy on the Use of a Single Institutional Review Board for Multi-site Research with an effective date of January 25, 2018. The Policy applies to domestic awardees of NIH-funded research and participating study sites, and requires that applications/proposals for NIH funding include a plan for use of a single IRB, which becomes part of the terms and conditions of the award.

On January 20, 2017, the final revised Common Rule was published in the Federal Register. The new Rule mandates that all United States-based institutions engaged in cooperative research rely on a single IRB as their reviewing IRB for the U.S.-conducted portions of the study, with certain exceptions. The compliance date for this new “cooperative research” Rule is January 20, 2020.

In response to both the NIH single IRB mandate and the new Common Rule regulations for cooperative research, the NMDP IRB will serve as a single IRB for multi-site research in the field of blood and marrow transplantation. The 2017 Blood and Marrow Transplant Clinical Trials Network® (BMT CTN) grant renewal included a plan to use the NMDP IRB as the single IRB for BMT CTN research. Centers participating in BMT CTN research will be required to use the NMDP IRB as their IRB of record for BMT CTN studies released after July 1, 2017. This requirement applies to BMT CTN Core, Affiliate and Consortium Centers.

The NMDP IRB will also serve as a single IRB for the Center for International Blood and Marrow Transplant Research® (CIBMTR®) Resource for Clinical Investigation in Blood and Marrow Transplantation (RCI BMT) program. Centers participating in federally-funded RCI BMT research released after January 25, 2018, where the NMDP IRB has been chosen as the single IRB for the study, will be required to use the NMDP IRB as their IRB of record for the RCI BMT study.
AAHRPP Accreditation

The NMDP is fully accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). The NMDP received full accreditation in December 2014.

NMDP IRB Members

The members of the NMDP IRB are a diverse group of distinguished healthcare professionals, donor advocates, and patient advocates with expertise in bone marrow transplantation and hematology/oncology. The majority of members are not affiliated with NMDP.

NMDP IRB Meeting Schedule

The NMDP IRB meets on the third Thursday of each month (with the exception of the second Thursday for July) and on an ad hoc basis as needed. The NMDP IRB meeting schedule can be found on the NMDP/Be The Match Network Website.

Requirements for Using the NMDP sIRB

Enrolling institutions must participate in a research study either through BMT CTN or through the CIBMTR RCI BMT program. Exceptions will be considered on a case-by-case basis.

3 Division of Responsibilities Between the NMDP IRB and the Local Institution

An IRB Authorization Agreement document is signed by the Signatory Institution in the enrollment process. This document outlines the responsibilities performed by the NMDP IRB and those performed by the local institution.

Responsibilities of the NMDP IRB

Serving as the sIRB, the NMDP IRB is the IRB of record and is responsible for both study review and review of local context considerations for enrolled Signatory Institutions.

NMDP IRB Membership

The NMDP IRB maintains membership that satisfies the requirements of 45 CFR 46 and 21 CFR 56. The NMDP IRB Office actively monitors NMDP IRB member composition and tenure and identifies possible future members to ensure the requirements are maintained.

Study-Specific Reviews

The NMDP IRB conducts the study-specific reviews as required by the regulations. This includes initial review, continuing review, and review of modifications to previously approved research. In addition, any other study-specific documents submitted to the NMDP IRB are reviewed per the NMDP IRB Standard Operating Procedures (SOPs) and federal regulations.
Review of Local Context Considerations
“Local Context” is considered the unique considerations for an institution and the Principal Investigator (PI) when conducting research. For example, the institution local context includes boilerplate language for inclusion in the consent form and compliance with applicable state and local laws. The PI local context includes the resources available to support research and the safeguards used to protect vulnerable populations. The Signatory Institution reports its local context considerations to the NMDP IRB for review using two Worksheets that reflect the organization, the Principal Investigator, and the specific protocol.

- NMDP Single IRB Signatory Institution Local Context Worksheet
- NMDP Single IRB Study-Specific Local Context Worksheet

Review of Potential Unanticipated Problems and/or Serious or Continuing Noncompliance
The NMDP IRB reviews potential unanticipated problems involving risks to subjects or others and/or serious or continuing noncompliance when the local institution or other entity reports an incident, experience, or outcome to the NMDP IRB.

Notification of Determinations Regarding Research at the Local Institution
The NMDP IRB will promptly notify the local institution of its findings and actions with respect to any unanticipated problems, subject injuries, or subject complaints which are related to or may affect subjects participating in research at the local institution. Additionally, the NMDP IRB will ensure prompt notification to the local institution of any finding of serious or continuing noncompliance on, or any suspension or termination of IRB approval for, that portion of a study taking place at the local institution.

Reporting to OHRP and FDA
The NMDP IRB reports any unanticipated problem determination, serious noncompliance determination, continuing noncompliance determination, suspension, or termination to OHRP, the FDA, and the NMDP Signatory Official. The NMDP IRB reports for trial-wide and locally-occurring events.

Review of FCOI Management Plans
The NMDP IRB will review any researcher or research staff financial conflict of interest (FCOI) management plans submitted by the local institution and will decide whether to allow the research to continue at the local institution based on the management plan.

Documentation

BMT CTN Research
All study-specific documents related to NMDP IRB reviews of BMT CTN studies are posted by Emmes to the BMT CTN Data and Coordinating Center (DCC) study-specific SharePoint site. This website has restricted access. If you would like access, please send an email to bmtctnsp@emmes.com, along with your full name, center name, your role on BMT CTN studies, and your e-mail address.
**RCI BMT and other NMDP/CIBMTR Research**

All study-specific documents related to NMDP IRB reviews of RCI BMT or other NMDP/CIBMTR-sponsored studies are posted by the protocol coordinator to either the CIBMTR website or the NMDP/Be The Match Network Website, depending on the study.

**Notification of New Materials**

Protocol coordinators notify research staff and institutional designees of all study-wide NMDP IRB actions or new materials via broadcast emails with numbered memos, as well as access to the appropriate websites.

**Notification of Institution-Specific Documents**

NMDP IRB staff will provide institution-specific documents and approvals related to NMDP IRB review by email to research staff and institutional designees.

**Responsibilities of Signatory/Local Institution**

The Signatory Institution complies with the responsibilities as identified in the IRB Authorization Agreement document. The IRB Authorization Agreement for BMT CTN research covers only BMT CTN-sponsored studies reviewed by the NMDP IRB and opened by the institution with the NMDP IRB. Separate IRB Authorization Agreements exist for each RCI BMT or other NMDP/CIBMTR-sponsored study.

**Compliance with the NMDP IRB**

The Signatory Institution Principal Investigator and research staff must comply with the NMDP IRB’s requirements as defined in the NMDP IRB SOPs and in correspondence from the NMDP IRB. The NMDP IRB SOPs are available on the NMDP/Be The Match Network Website.

**Submission of Required Documents**

The Signatory Institution Primary Contact or Local Context Representative must complete and submit the following forms to enroll in the NMDP sIRB:

- NMDP Single IRB Signatory Institution Enrollment Form
- NMDP Single IRB Signatory Institution Local Context Worksheet

Additionally, for each study the Signatory Institution Principal Investigator wishes to open with the NMDP sIRB, the following form must be submitted:

- NMDP Single IRB Study-Specific Local Context Worksheet

These forms must be reviewed annually for necessary updates. However, updates to information should be submitted to the NMDP IRB as they occur. All information requested by the NMDP IRB shall be provided in a timely manner.

**Reporting of Components or Affiliate Institutions**

The Signatory Institution representative reports to the NMDP IRB the names of any Component or Affiliate Institutions that rely on the Signatory Institution’s oversight of the conduct of NMDP IRB-approved research by identifying them on the IRB Authorization Agreement document.
The Signatory Institution representative must also provide Component or Affiliate Institution information on the NMDP Single IRB Signatory Institution Enrollment Form.

Component Institutions meet all the following criteria:
- The FWA number for the Component Institution is the same as the Signatory Institution;
- The Component Institution operates under a different name than the Signatory Institution;
- The Signatory Institution has legal authority for the Component Institution;
- The local context considerations of the Component Institution are the same as the Signatory Institution;
- The boilerplate language and institutional requirements of the Component Institution are the same as the Signatory Institution; and
- The conduct of research at the Component Institution is monitored by the same office as the Signatory Institution.

Affiliate Institutions meet all the following criteria:
- The local context considerations of the Affiliate Institution are the same as the Signatory Institution;
- The boilerplate language and institutional requirements of the Affiliate Institution are the same as the Signatory Institution; and
- The conduct of research at the Affiliate Institution is monitored by the same office as the Signatory Institution.

**Overseeing the Conduct of the Research**

The Signatory Institution Principal Investigator ensures the safe and appropriate performance of the research at the Signatory Institution and at all Component and Affiliates. This includes, but is not limited to:
- Ensuring the initial and ongoing qualifications of investigators and research staff;
- Monitoring protocol compliance;
- Maintaining compliance with state, local, or institutional requirements related to the protection of human subjects;
- Initiating changes in the research only after NMDP IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants.
- Enrolling individuals in the research only after NMDP IRB review and approval.
- Obtaining, documenting, and maintaining records of consent for each participant or each participant’s legally authorized representative as stipulated by the NMDP IRB.
- Providing a mechanism to receive and address concerns/complaints from local study participants and others about the conduct of the research;
- Notifying the NMDP IRB of any study-specific incidence, experience or outcome that rises to the level of an unanticipated problem involving risks to subjects or others and/or potential serious or continuing noncompliance. At the time the incident, experience or outcome is reported to the NMDP IRB, the local Institution must also provide a plan to manage it.
NOTE: As part of ensuring safe and appropriate performance of research the Signatory Institution has the authority to observe any aspect of the research process including observing the consent process. The NMDP IRB retains the authority to direct this to be done when necessary.

**Managing Conflicts of Interest**
The Signatory Institution is responsible for managing organizational conflicts of interest related to the study. The Signatory Institution must also obtain disclosures of and manage financial conflicts of interest (FCOI) of researchers and research staff at the local institution.

**Conducting Ancillary Reviews**
The Signatory Institution is responsible for ensuring the conduct of any necessary privacy review required for HIPAA compliance. Additionally, the Signatory Institution will conduct other ancillary reviews that may be required by the protocol or by the Signatory Institution (e.g., scientific review, biosafety, radiation safety, etc.).

**Creating the Institution-Specific Study Consent Form**
The local institution must follow the requirements listed below for incorporating the institutional boilerplate language into the NMDP IRB-approved template consent form to create the institution’s consent form to use for a specific study:

- The institution must use the NMDP IRB-approved template consent form.
- Institutional boilerplate language must be approved by the NMDP IRB.
- No language changes may be made to the consent form with the exception of NMDP IRB-approved boilerplate language.
- The institution must submit the institutional consent form to the protocol coordinator for review prior to implementing the consent form.
- The institution must obtain NMDP IRB approval of changes to the boilerplate language prior to implementation.
- The institution must obtain NMDP IRB approval of translations of the consent form prior to implementation.

NOTE: Including HIPAA Authorization language as part of boilerplate language is permitted. The NMDP IRB does not approve the HIPAA Authorization language, as it does not function as a Privacy Board; however, the NMDP IRB will accept HIPAA Authorization language when submitted as part of the boilerplate.

**Maintaining a Regulatory File**
The Signatory Institution Principal Investigator maintains a regulatory file for each study under NMDP IRB purview as per local institution and sponsor policy. The NMDP IRB does not have any additional requirements for the maintenance of the regulatory file at the local institution. The NMDP IRB maintains its own regulatory file of study reviews per NMDP IRB SOPs.

**Reviewing Research Involving Prisoners**
The Signatory Institution conducts a local full board review of any study enrolling prisoners, since the NMDP IRB is not constituted to review studies enrolling prisoners.
4 HOW TO ENROLL IN THE NMDP sIRB

To enroll in the NMDP sIRB, institutions must submit the forms as described below. The forms are available on the NMDP/Be The Match Network Website.

1. Complete and email the NMDP Single IRB Signatory Institution Enrollment Form
   a. For BMT CTN research, complete the Agreement that covers all BMT CTN studies.
   b. For RCI BMT or other NMDP/CIBMTR research, complete the Agreement that covers the specific study.
3. Complete and email the NMDP Single IRB Signatory Institution Local Context Worksheet
5. Receive confirmation from the NMDP IRB of Completion of Enrollment

Completing the NMDP Single IRB Signatory Institution Enrollment Form
The NMDP Single IRB Signatory Institution Enrollment Form is located on the NMDP/Be The Match Network Website. Follow the instructions for each section of the form. Save the completed form in Microsoft Word and email it to the NMDP IRB office at NMDPSIRB@nmdp.org.

Completing the IRB Authorization Agreement
The IRB Authorization Agreement (IAA) document is located on the NMDP/Be The Match Network Website. The IAA describes the arrangement with a Signatory Institution to rely on the NMDP IRB for review of studies. The IAA for BMT CTN research covers only BMT CTN-sponsored studies reviewed by the NMDP IRB and opened by the institution with the NMDP sIRB. Separate IRB Authorization Agreement documents exist for each RCI BMT or other NMDP/CIBMTR-sponsored study.

The IRB Authorization Agreement should be completed by the Signatory Institution and signed by the Signatory Official at the Signatory Institution. Once completed and signed, the IAA should be emailed to the NMDP IRB office at NMDPSIRB@nmdp.org. The IAA will be signed by the NMDP Signatory Official, and a fully-executed document will be returned to the Signatory Institution via email.

The Signatory Official must be a senior institutional official who has the authority to commit the entire institution named on the FWA, as well as all of the institutional components that have been listed in the IAA, to a legal binding agreement. This person must also have the authority to assure compliance of the institution and all its components to the Terms of the FWA.

Completing the NMDP Single IRB Signatory Institution Local Context Worksheet
The NMDP Single IRB Signatory Institution Local Context Worksheet is located on the NMDP/Be The Match Network Website. The Worksheet should be completed by the Signatory
Institution Primary Contact or Local Context Representative. Save the completed form in Microsoft Word and email it to the NMDP IRB office at NMDPSIRB@nmdp.org.

**Confirmation of Enrollment Completion**
The NMDP IRB staff will verify that all enrollment steps have been completed. At this point, an email will be sent to the Signatory Institution Primary Contact confirming the requirements for enrollment are complete, and that Signatory Institution Principal Investigators can begin to open studies using the NMDP Single IRB Study-Specific Local Context Worksheet.

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### 5 USING THE NMDP sIRB

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#### Identifying Local Context Considerations

Local context considerations are identified and reported to the NMDP IRB by the Signatory Institution and Signatory Institution Principal Investigators via the Signatory Institution Local Context Worksheet and the Study-Specific Local Context Worksheet.

Local context considerations for the Signatory Institution include, but are not limited to:
- State and local laws,
- Institutional oversight of research
- Conflict of interest policy,
- Informed consent processes,
- Boilerplate language for inclusion in the consent form,
- Community descriptors, and
- Any other institutional requirements.

Study-specific local context considerations include, but are not limited to:
- Resources available to support research,
- Subject recruitment and selection,
- Safeguards for vulnerable populations,
- Informed consent processes
- Privacy and confidentiality protections, and
- Any unique study-specific considerations.

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#### Consent Form and Institutional Boilerplate Language

The NMDP IRB expects that institutional boilerplate language will be inserted into the NMDP IRB-approved template consent form, and that existing language will not be deleted or replaced. The submitted boilerplate language must indicate if it is to replace existing language.

No changes can be made to the NMDP IRB-approved template consent form except NMDP IRB-approved boilerplate language, removal of instruction/notes from the coordinating Group, and dates embedded to track changes. Any change made to the template consent forms needs to be captured as institutional boilerplate and approved before it can be used. These changes include information captured in the consent form header and footer.
The boilerplate language is submitted to the NMDP IRB via the NMDP Single IRB Signatory Institution Local Context Worksheet. Once the NMDP IRB reviews and approves the boilerplate language, the Signatory Institution Principal Investigator is required to incorporate the NMDP IRB-approved boilerplate language into the NMDP IRB-approved template consent form, as appropriate.

**Study-Specific Changes**
Principal Investigators (PI) must limit their changes to the consent form to those approved as part of the institutional boilerplate language. If a PI determines that additional changes to the consent form should be made for a specific study, they should submit those changes to the Study/Protocol Chair and Network Group to be considered for submission to the NMDP IRB as a study-wide amendment.

**Opening a Study using the NMDP sIRB**

Confirmation of a Signatory Institution’s enrollment in the NMDP sIRB is required prior to opening a new study. The steps to opening a study are:

1. Identify a NMDP IRB-approved study the Signatory Institution Principal Investigator (SIPI) wants to open.
2. The SIPI or designee completes the NMDP Single IRB Study-Specific Local Context Worksheet. The Worksheet must be signed by the SIPI.
3. Create the institutional consent form(s) using the current NMDP IRB-approved template consent form(s), and send the redlined version(s) of the form(s) to the protocol coordinator for approval. This includes adult consent forms and minor assent forms.
4. Email the following to the NMDP IRB at NMDPSIRB@nmdp.org:
   - a. Completed/Signed NMDP Single IRB Study-Specific Local Context Worksheet
   - b. Documentation of the SIPI’s training in human research protections
   - c. Redlined version(s) of consent/assent form(s) approved by the protocol coordinator
   - d. Copy of email documenting the protocol coordinator’s approval of consent/assent form(s)
5. Respond to any requests for additional information from the NMDP IRB.
6. Receive an email from the NMDP IRB documenting approval for the study site, including the finalized consent/assent form(s) with the NMDP IRB approval period.

**Continuing Review**

The Signatory Institution has no regulatory responsibilities for continuing review from the perspective of the NMDP IRB. The NMDP IRB is responsible for the continuing review required by the Federal regulations. The Protocol/Study Chair has ultimate responsibility for submitting the required continuing review materials to the NMDP IRB. Any site-specific information required for completion of the continuing review materials will be solicited from the site by the protocol coordinator.
Amendment Review

The Signatory Institution has no regulatory responsibilities for reviewing changes to previously approved research from the perspective of the NMDP IRB.

Consent Form Revisions

When study-wide consent form revisions have been approved by the NMDP IRB, study sites that have already had their institutional study consent form approved by the NMDP IRB should follow the steps below to incorporate the revisions:

1. With the tracked changes on, make the revisions to the institutional consent form.
2. Send this tracked changes version to the protocol coordinator for approval.
3. After approval by the protocol coordinator, send the tracked changes version (along with documentation of the protocol coordinator’s approval) to the NMDP IRB for approval and insertion of new approval period in the form’s footer.

Annual Worksheet Review

The NMDP Single IRB Signatory Institution Enrollment Form, the NMDP Single IRB Signatory Institution Local Context Worksheet, and the NMDP Single IRB Study-Specific Local Context Worksheets should be updated on an ongoing basis if there are changes to the Component or Affiliate Institutions, boilerplate language, other institutional requirements, or any other institutional or study-specific changes. Additionally, the NMDP IRB implemented an annual Worksheet review process to ensure that institutions and PIs review Worksheets at least annually to verify the Worksheets reflect the current policies and procedures for the institution, the PI, and the study. This is not part of the regulatory-required continuous review process.

NMDP Single IRB Signatory Institution Enrollment Form and NMDP Single IRB Signatory Institution Local Context Worksheet

Using each institution’s enrollment date, institutions will be contacted annually. The Signatory Institution Primary Contact(s) (SIPC) receives an email notification from the NMDP IRB requesting the SIPC review the NMDP Single IRB Signatory Institution Enrollment Form and the NMDP Single IRB Signatory Institution Local Context Worksheet. The SIPC will then submit a revised form with updates, or may respond via email confirming there are no changes.

If the NMDP IRB does not receive a response, a reminder email is sent two weeks after the initial email notification. After a month, if no correspondence is received from the institution regarding the forms, the NMDP IRB notes that there were no annual revisions received that year, and no further reminder emails are sent.

NMDP Single IRB Study-Specific Local Context Worksheet

Using the study-specific approval date for the study site, the Signatory Institution Principal Investigator is also contacted annually. The PI and the study site coordinator (SSC) receive an email notification from the NMDP IRB requesting that the PI or SSC review the Study-Specific Local Context Worksheet. The PI or SSC will then submit a revised Worksheet with any updates, or may respond via email confirming there are no changes.
If the NMDP IRB does not receive a response, a reminder email is sent two weeks after the initial email notification. After a month, if no correspondence is received from the institution regarding the Worksheet, the NMDP IRB notes that there were no annual revisions received that year, and no further reminder emails are sent.

**Re-consent Requirements**

If the Study/Protocol Chair or the NMDP IRB requires study participants to be consented using the most recent amendment, the NMDP IRB notes this determination in the Notice of Action letter. The institution should follow the instructions in the letter from the NMDP IRB for obtaining re-consent. If local policy requires re-consent when the Study/Protocol Chair or NMDP IRB do not, those local policies should be followed.

**Updating Information with the NMDP sIRB**

Follow the steps below to update information, including contacts, that was previously submitted to the NMDP sIRB:

1. Select the appropriate form on the NMDP/Be The Match Network Website that needs to be updated.
   - NMDP Single IRB Signatory Institution Enrollment Form
   - NMDP Single IRB Signatory Institution Local Context Worksheet
   - NMDP Single IRB Study-Specific Local Context Worksheet
2. Indicate on the top of the form that this is a Revised Submission and include the date.
3. Include the name of the Signatory Institution to indicate who is submitting the revision.
4. If the revision is on the Study-Specific Local Context Worksheet, also identify the Protocol ID Number and Protocol Title.
5. Complete the appropriate sections or questions with the updated information.
6. Submit the revised form via email to NMDPSIRB@nmdp.org.

**Closing a Study at an Institution**

Studies should only be closed at a local institution by the institution’s Principal Investigator when all the following criteria are met at the local institution:

- The study is closed to accrual at the local institution.
- All study participants on this study at the local institution have completed study intervention(s) and follow-up activities OR no study participants were enrolled at the local institution.
- There will be no further research activities for this study (this includes recruitment, enrollment, data collection, data analysis, data submission, etc.) at the local institution.
To close a study at a local institution with the NMDP IRB, complete the NMDP Single IRB Study Site Closure Form and email it to NMDPSIRB@nmdp.org.

6 SPECIAL CONSIDERATIONS REGARDING PEDIATRIC STUDY PARTICIPANTS

Assent Requirement

The NMDP IRB makes a determination whether assent of a child is required to participate in research and the age range for obtaining assent of the child. The NMDP IRB’s determination is included in the NMDP IRB’s Notice of Action (approval letter) sent to the Study/Protocol Chair. Signatory Institutions enrolled in the NMDP sIRB must comply with the NMDP IRB’s age range determination for the child to provide assent to be enrolled in the study.

Documentation of Assent

The protocol team shall submit minor assent forms to the NMDP IRB for review. NMDP IRB-approved template assent forms will be provided to sites along with the NMDP IRB-approved template consent forms.

Principal Investigators must comply with the determinations of the NMDP IRB regarding the assent process and age range. Institutions are expected to use the NMDP IRB-approved template assent forms and insert institutional boilerplate assent language that has been approved by the NMDP IRB. If local institutional policies require a different process for documenting assent, this information must be provided to the NMDP IRB as part of the local context considerations via the NMDP Single IRB Signatory Institution Local Context Worksheet.

Waiver of Assent Requirements

The NMDP IRB may waive its assent requirement for an individual child upon request of the Principal Investigator if the capability of that child is so limited that they cannot reasonably be consulted. A waiver must be obtained before a child is enrolled on a study. The NMDP IRB cannot approve a waiver of assent retrospectively. Requests should be submitted via email to NMDPSIRB@nmdp.org, and should include the reason why the individual child cannot provide assent.

Consent at Age of Majority

When a study participant reaches the age of majority, the NMDP IRB requires consent of the study participant be obtained per local institution policies and procedures as described in the NMDP Single IRB Signatory Institution Local Context Worksheet. A study participant who has not yet reached the age of majority cannot provide legally effective informed consent.
7 REPORTABLE EVENTS, PROTOCOL EXCEPTIONS, PROTOCOL DEVIATIONS, AND ADVERSE EVENTS

Potential Unanticipated Problems

The Signatory Institution is responsible for reporting potential unanticipated problems involving risks to subjects or others to the NMDP IRB for review. The Signatory Institution determines who does the reporting to the NMDP IRB. The reporting designee or the Principal Investigator decides whether a study-specific incident, experience, or outcome meets the regulatory definition of an unanticipated problem and requires reporting to the NMDP IRB. The regulatory definition of an unanticipated problem is as follows:

1. The incident, experience, or outcome is unexpected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents (such as the IRB-approved research protocol and informed consent document), and the characteristics of the subject population being studied while the protocol was followed as written;

2. There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research; and

3. The incident, experience, or outcome suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

If the Principal Investigator is unsure if the incident, experience, or outcome is a potential unanticipated problem, it should be reported to the NMDP IRB for a determination using the NMDP IRB Reportable Event Form for Potential Unanticipated Problems or Potential Serious or Continuing Noncompliance found on the NMDP/Be The Match Network Website.

Potential Serious or Continuing Noncompliance

The Signatory Institution is responsible for reporting potential serious or continuing noncompliance reports to the NMDP IRB. The Signatory Institution determines who does the reporting to the NMDP IRB. The Signatory Institution or Principal Investigator makes the decision whether an incident, experience, or outcome could meet the definition of serious or continuing noncompliance and therefore requires reporting to the NMDP IRB. The NMDP IRB definitions of serious noncompliance and continuing noncompliance are as follows:

**Serious noncompliance** is defined as noncompliance that violates the rights and welfare of research subjects, increases risks to subjects, or compromises the integrity of data.

**Continuing noncompliance** is defined as a series or pattern of more than one incident of noncompliance that indicates a deficiency in knowledge, ability, or willingness to comply with a law, regulation, or policy governing human subjects research.
If the Signatory Institution or Principal Investigator is unsure if the incident, experience, or outcome is potential serious or continuing noncompliance, the incident, experience or outcome should be reported to the NMDP IRB for a determination using the NMDP IRB Reportable Event Form for Potential Unanticipated Problems or Potential Serious or Continuing Noncompliance found on the NMDP/Be The Match Network Website.

**Protocol Exceptions**

A protocol exception is defined by the NMDP IRB as a one-time, temporary departure from the IRB-approved protocol procedures that is identified before it occurs and intended for one specific study subject. Protocol exceptions do not have the intention of amending the protocol as a systematic change. The NMDP IRB categorizes protocol exceptions as either major or minor.

A **major protocol exception** is a protocol exception that may adversely affect one or both of the following:

- the safety, rights, or welfare of the subject(s)
- the scientific validity of the research

Major protocol exceptions must be approved by the NMDP IRB prior to implementation. To request a major protocol exception, the relying institution’s investigator must complete the NMDP IRB Major Protocol Exception Request Form, found on the NMDP/Be The Match Network Website, and submit it via email to IRBStaff@nmdp.org. If the relying institution has obtained approval for the major protocol exception request from the study sponsor or FDA prior to IRB submission, documentation of such approval must be submitted with the IRB submission. The relying institution’s investigator must maintain a copy of the IRB approval with the corresponding request for major protocol exception documentation in their study records.

A **minor protocol exception** is a protocol exception that does not fit the criteria of a major protocol exception. Minor protocol exceptions do not require NMDP IRB approval prior to implementation but must be documented by the investigator as part of their study records.

A list of protocol exceptions that occurred since the study’s last continuing review must be compiled by the sponsoring organization (e.g., BMT CTN) and be submitted to the NMDP IRB at the time of the study’s next continuing review.

**Protocol Deviations**

A protocol deviation is defined by the NMDP IRB as a departure from the IRB-approved protocol procedures that is unintentional and discovered after it occurs. When a protocol deviation is discovered, the relying institution’s investigator should assess the event and determine whether it could be considered an unanticipated problem involving risks to participants or others or potential serious or continuing non-compliance, and if so, follow the appropriate reporting procedures. Protocol deviations must be documented by the investigator as part of their study records. A list of protocol deviations that occurred since the study’s last
continuing review must be compiled by the sponsoring organization (e.g., BMT CTN) and be submitted to the NMDP IRB at the time of the study’s next continuing review.

**Adverse Events**

Adverse events are only to be reported to the NMDP IRB if the Principal Investigator assesses the event as meeting or possibly meeting the criteria of an unanticipated problem or serious or continuing noncompliance as described above.

**Reporting Forms**

Potential unanticipated problems and potential serious or continuing non-compliance must be reported to the NMDP IRB using the NMDP IRB Reportable Event Form. The Form requests a management plan, when applicable.

Major protocol exceptions must be requested of the NMDP IRB using the NMDP IRB Major Protocol Exception Request Form.

Institution contacts listed on the form will receive or be copied on an email indicating the NMDP IRB’s determination, including review of the management plan and whether any additional action is required, if applicable.

**Reporting to OHRP and FDA**

The NMDP IRB will report determinations of unanticipated problems and/or serious or continuing noncompliance to OHRP and FDA, as applicable. Individuals included on the original correspondence will also be included on the report to OHRP and FDA.

## 8 Submission of Locally-Developed Materials

Locally-developed materials include:

1. Translated Short Forms*, consent forms, or any other translated document targeted to the study participant that requires review by the NMDP IRB
   a. IRB-approved English language document(s) corresponding to the translated document
   b. Translated version(s) of the IRB-approved English language document
   c. Translator’s Certificate(s) of Accuracy or equivalent document(s)

2. Assent document(s) that differ from the NMDP IRB-approved template assent form due to local institutional policies (e.g., minor information sheet)
3. Institutional template consent at age of majority forms
4. Study-specific recruitment materials or advertisements
Those materials that are not study-specific can be submitted to the NMDP IRB along with the NMDP Single IRB Signatory Institution Local Context Worksheet. Materials that are to be used for a single study should be submitted along with the NMDP Single IRB Study-Specific Local Context Worksheet.

*An institution may choose to use either their local institution’s Short Form, or the NMDP IRB’s Short Form. The institution’s policy regarding the use of the Short Form should be indicated on the NMDP Single IRB Signatory Institution Local Context Worksheet.

9 **COMMUNICATIONS**

**General Information**

General information regarding NMDP IRB policies and procedures can be found on the NMDP/Be The Match Network Website. The NMDP IRB will communicate updates to policies, procedures, or forms to Signatory Institutions via broadcast emails.

**Study-Specific Information, Documents, and Notifications**

Study-specific information relating to the NMDP IRB and study-specific documents approved by the NMDP IRB can be found on the appropriate study website, i.e., either the study-specific BMT CTN SharePoint website or the study-specific CIBMTR website.

When trial-wide study-specific notifications are required, the appropriate BMT CTN or CIBMTR protocol coordinator will send a broadcast email to the appropriate stakeholders.

**Site-Specific Communication**

Site-specific determinations of the NMDP IRB for institutions relying on the NMDP IRB will be communicated by the NMDP IRB staff directly to the relying institution’s Principal Investigator.

**Communicating with the NMDP Single IRB**

Relying institutions may communicate directly with the NMDP sIRB regarding questions or concerns by emailing NMDPSIRB@nmdp.org. IRB staff will respond via email or phone.
APPENDIX 1: LIST OF REFERENCED DOCUMENTS

IRB Authorization Agreement – All BMT CTN Studies

NMDP IRB Major Protocol Exception Request Form

NMDP IRB Reportable Event Form

NMDP IRB Standard Operating Procedures

NMDP Single IRB Signatory Institution Enrollment Form

NMDP Single IRB Signatory Institution Local Context Worksheet

NMDP Single IRB Study Site Closure Form

NMDP Single IRB Study-Specific Local Context Worksheet
APPENDIX 2: KEY TERMS

1. **Affiliate institutions** are defined by the NMDP IRB as meeting all of the following criteria:
   - The local context considerations of the Affiliate Institution are the same as the Signatory Institution. Local context considerations are reported by the Signatory Institution in the Institutional Local Context Worksheet;
   - The boilerplate language and institutional requirements of the Affiliate Institution are the same as the Signatory Institution. The boilerplate language and institutional requirements are reported by the Signatory Institution in the Institution Local Context Worksheet; and
   - The conduct of research at the Affiliate Institution is monitored by the same office as the Signatory Institution.

2. **Boilerplate language** is the information added by the Signatory Institution Principal Investigator to the NMDP IRB-approved consent form after the NMDP IRB approves it. Boilerplate language provides information that is institution-specific and addresses local context considerations for the Signatory Institution and its Component and Affiliate Institutions. This information may include contact information for the Signatory Institution Principal Investigator, institution-specific injury language, institution-specific pregnancy language, and other institution-specific information. Updates to boilerplate language must also receive NMDP IRB approval prior to implementation.

3. **Component institutions** are defined by the NMDP IRB as meeting all the following criteria:
   - The Component Institution operates under a different name from the Signatory Institution, but the Signatory Institution has legal authority for the Component Institution;
   - The FWA number for the Component Institution is the same as the Signatory Institution;
   - The local context considerations of the Component Institution are the same as the Signatory Institution. Local context considerations are reported by the Signatory Institution in the Signatory Institution Local Context Worksheet;
   - The boilerplate language and institutional requirements of the Component Institution are the same as the Signatory Institution. The boilerplate language and institutional requirements are reported by the Signatory Institution in the Signatory Institution Local Context Worksheet; and
   - The conduct of research at the Component Institution is monitored by the same office as the Signatory Institution.
4. **Continuing noncompliance** is a series or pattern of more than one incident of noncompliance that indicates a deficiency in knowledge, ability, or willingness to comply with a law, regulation, or policy governing human subjects research.

5. **Major protocol exception** is a protocol exception that may adversely affect one or both of the following:
   - the safety, rights, or welfare of the subject(s)
   - the scientific validity of the research

6. **Minor protocol exception** is a protocol exception that does not fit the criteria of a major protocol exception.

7. **Protocol deviation** is a departure from the IRB-approved protocol procedures that is unintentional and discovered after it occurs.

8. **Protocol exception** is a one-time, temporary departure from the IRB-approved protocol procedures that is identified before it occurs and intended for one specific study subject.

9. **Serious noncompliance** is noncompliance that violates the rights and welfare of research subjects, increases risks to subjects, or compromises the integrity of data.

10. **Signatory institution** is the institution that signs the IRB Authorization Agreement document and has a direct relationship with the NMDP IRB. The responsibilities of the Signatory Institution are listed on the IRB Authorization Agreement document. Signatory Institution Principal Investigators must be “employed by” or "have a relationship with" the Signatory Institution to be eligible to open studies.

11. **Signatory institution primary contact** is the person who acts as the point of contact for the NMDP IRB should the NMDP IRB have any questions about the research being conducted at the Signatory Institution, Component Institution(s), or Affiliate Institution(s). The Signatory Institution Primary Contact receives or is copied on all correspondence from the NMDP IRB to the Signatory Institution and the Signatory Institution Principal Investigator(s). This individual is also responsible for reviewing the Signatory Institution Enrollment Form and the Signatory Institution Local Context Worksheet annually for necessary updates, and may also assist with other Worksheet completion.

12. **Signatory institution principal investigator** is an investigator at the Signatory Institution who is a member of the group coordinating the study and therefore is able to open studies with the NMDP sIRB. The Signatory Institution Principal Investigator is responsible for the research at their institution and all research activities conducted by the research staff (including any research activity at Component or Affiliate Institutions) for all studies opened in their name.

13. **Unanticipated problem** is defined as follows:
1. The incident, experience, or outcome is unexpected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents and the characteristics of the subject population being studied while the protocol was followed as written;

2. There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research; and

3. The incident, experience, or outcome suggests that the research places participants or others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.