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INSTITUTIONAL REVIEW BOARD

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

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This manual is available on the NMDP Network Website.

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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Table of Contents

1. Introduction 4
2. NMDP IRB as a sIRB 4
   - Background 4
   - Requirements for Using the NMDP sIRB 4
   - AAHRPP Accreditation 5
   - NMDP IRB Members 5
   - NMDP IRB Meeting Schedule 5
   - NMDP Single IRB Fees 5
3. Division of Responsibilities Between the NMDP IRB and the Local Institution 5
   - Responsibilities of the NMDP IRB 5
   - Responsibilities of Signatory/Local Institution 7
4. How to Enroll in the NMDP sIRB 10
5. Using the NMDP sIRB 11
   - Identifying Local Context Considerations 11
   - Opening a Study using the NMDP sIRB 12
   - Continuing Review 13
   - Amendment Review 13
   - Consent Form Revisions 13
   - Re-consent Requirements 14
   - Remote Consent Sessions and Electronic Consent Signatures 14
   - Short Forms for Non-English Speaking Participants 14
   - Fully-Translated Consent Documents 15
   - Annual Worksheet Review 15
   - Updating Information with the NMDP sIRB 16
   - Closing a Study at an Institution 17
6. Special Considerations Regarding Pediatric Study Participants 17
   - Assent Requirement 17
   - Documentation of Assent 18
   - Waiver of Assent Requirements 18
   - Consent at Age of Majority 18
7. Reportable Events, Protocol Exceptions, Protocol Deviations, and Adverse Events 19
   - Potential Unanticipated Problems 19
   - Potential Serious or Continuing Noncompliance 19
   - Protocol Exceptions 20
   - Protocol Deviations 20
   - Adverse Events 21
   - Reporting to OHRP and FDA 21
8. Communications 21
   - General Information 21
   - Study-Specific Information, Documents, and Notifications 21
   - Site-Specific Communication 22

Communicating with the NMDP Single IRB 22
9 . IRBManager 22
Appendix 1: List of Referenced Documents 23
Appendix 2: Key Terms 24

1. INTRODUCTION

This Manual introduces local institutions to the purpose and function of the 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

The National Institutes of Health (NIH) *Policy on the Use of a Single Institutional Review Board for Multi-site Research* (effective January 25, 2018) 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.

The Office for Human Research Protections (OHRP) 2018 Requirements at 45 CFR 46 (Revised Common Rule) mandates that all United States-based institutions engaged in federally funded 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 "cooperative research" Rule was 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 and cell therapy.

Requirements for Using the NMDP sIRB

The Blood and Marrow Transplant Clinical Trials Network®'s (BMT CTN) NIH grant includes a plan to use the NMDP IRB as the single IRB for BMT CTN research. Centers participating in BMT CTN research are 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®) or NMDP research. Centers participating in federally funded CIBMTR or NMDP research released after January 25, 2018, will be required to use the NMDP IRB as their IRB of record for the study.

If requested, the NMDP IRB may choose to serve as the single IRB for other multi-site research in the field of blood and marrow transplantation and cell therapy on a case-by-case basis.

AAHRPP Accreditation

NMDP is fully accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). NMDP received full accreditation in December 2014 and has remained accredited since that time.

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 and on an ad hoc basis as needed. The NMDP IRB meeting schedule can be found on the NMDP Network Website at https://network.nmdp.org/research/institutional-review-board/irb-meeting-schedule/. Meeting dates are subject to change if quorum is at risk.

NMDP Single IRB Fees

Fees for NMDP IRB's service as a single IRB for a study will be charged to the sponsor or network/consortium, as applicable. Individual participating research sites are not directly charged fees for relying on the NMDP IRB for a study.

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.

- *Single IRB Signatory Institution Enrollment and Local Context Form*
- *NMDP sIRB 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

For federally funded research, the NMDP IRB reports any unanticipated problem determination, serious noncompliance determination, continuing noncompliance determination, suspension, or termination to OHRP and FDA (if applicable). 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.

Access to Study-Level Documents

BMT CTN Research
All study-specific documents related to NMDP IRB reviews of BMT CTN studies are posted by the central study-level protocol coordinator 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.

CIBMTR and NMDP Research
All study-specific documents related to NMDP IRB reviews of CIBMTR or NMDP studies are either posted by the central study-level protocol coordinator to the study-specific website or are sent to participating study sites by the central study-level protocol coordinator.

Other Research
All study-specific documents related to NMDP IRB reviews of other studies where the NMDP IRB has agreed to serve as the single IRB are either posted by the central study-level protocol coordinator to the study-specific website or are sent to participating study sites by the central study-level protocol coordinator.

Notification of New Materials
Central study-level 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 studies reviewed by the NMDP IRB and opened by the institution with the NMDP IRB. Separate IRB Authorization Agreements exist for other studies not sponsored by BMT CTN.

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 Network Website.

Submission of Required Documents

The Signatory Institution Primary Contact or Local Context Representative (usually the local institution's IRB office) must complete and submit the following form to enroll in the NMDP sIRB:

- *Single IRB Signatory Institution Enrollment and Local Context Form*

This form 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.

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

- *NMDP sIRB Study-Specific Local Context Worksheet*

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 *Single IRB Signatory Institution Enrollment and Local Context 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 have a different FWA number from the Signatory Institution and meet all of 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 Components 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 HIPAA Privacy Reviews and Other Ancillary Reviews

The NMDP IRB does not serve as a HIPAA Privacy Board. The Signatory Institution is responsible for ensuring the conduct of any necessary privacy review required for HIPAA compliance as well as granting requests for waivers of HIPAA authorization. The Signatory Institution is responsible for the HIPAA authorization language required for a study, if applicable. 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.) and will be responsible for ensuring such required ancillary reviews are completed prior to commencement of the research at the Signatory Institution.

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 study 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 accepted by and on file with the NMDP IRB.
- No language changes may be made to the consent form with the exception of NMDP IRB-accepted boilerplate language.
- HIPAA authorization language must **not** be embedded in the consent form.

- The institution must submit the institutional consent form to the central study-level protocol coordinator for review prior to submitting the consent form to the NMDP IRB for approval.
- The institution must obtain NMDP IRB acceptance 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.

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 NMDP IRB is not set up to review research for compliance with the regulations at 45 CFR 46 Subpart C. Therefore, if an investigator wishes to enroll prisoners on a study, the investigator's local IRB must review the study for compliance with Subpart C regulations.

4 . How to Enroll in the NMDP sIRB

To enroll in the NMDP sIRB, institutions must submit the forms in IRBManager. The *Single IRB Signatory Institution Enrollment and Local Context* xForm can be started, saved, and completed once you have all the components in place.

1. Complete the *Single IRB Signatory Institution Enrollment and Local Context* xForm. As a part of completing this form, you will need to select the applicable IRB Authorization Agreement document(s), download the Agreement(s), have them completed, signed, and attached to the *Single IRB Signatory Institution Enrollment and Local Context Form* before submitting the xForm.
    a. For BMT CTN research, complete the Agreement that covers all BMT CTN studies.
    b. For any other study, complete the Agreement that covers the specific study.
2. Receive copy of IRB Authorization Agreement back with signature of NMDP's Signatory Official.
3. Receive confirmation from the NMDP IRB of Completion of Enrollment

Completing the *Single IRB Signatory Institution Enrollment and Local Context Form*

The *Single IRB Signatory Institution Enrollment and Local Context Form* is located in IRBManager. The form should be completed by the Signatory Institution Primary Contact or Local Context Representative (usually the local institution's IRB office). Follow the instructions for each section of the form.

Completing the IRB Authorization Agreement

Select the applicable IRB Authorization Agreement (IAA) document(s) when completing the *Single IRB Signatory Institution Enrollment and Local Context* xForm. 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 studies reviewed by the NMDP IRB and opened by the institution with the NMDP sIRB. Separate IRB Authorization Agreement documents exist for each CIBMTR, NMDP, or other 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 uploaded in IRBManager. 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 IRB Authorization Agreement, 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.

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 sIRB Study-Specific Local Context Worksheet.*

5 . USING THE NMDP SIRB

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 *Single IRB Signatory Institution Enrollment and Local Context Form* and the *NMDP sIRB 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.

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-accepted 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 accepted before it can be used. These changes include information captured in the consent form header, footer, and signature sections.

The boilerplate language document is submitted to the NMDP IRB when the Signatory Institution submits the *Single IRB Signatory Institution Enrollment and Local Context Form.* Once the NMDP IRB reviews and accepts the boilerplate language, the Signatory Institution Principal Investigator is required to incorporate the NMDP IRB-accepted 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 accepted 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 central study-level protocol coordinator 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. The site creates the institutional consent form(s) using the current NMDP IRB-approved template study consent form(s). With track changes on, insert institutional boilerplate language as applicable. Send the redlined version(s) of the form(s) to the central study-level protocol coordinator for pre-approval. This includes adult consent forms and minor assent forms.
2. Complete the *NMDP sIRB Study-Specific Local Context Worksheet* in IRBManager. (NOTE: You do not become associated with a specific study in IRBManager until this form is approved.) The following will need to be attached to the form. The form must also be signed by the site PI.
    a. Documentation of the site PI's training in human research protections (not GCP)

b. Redlined version(s) of consent/assent form(s) approved by the central study-level protocol coordinator
c. Copy of email documenting the central study-level protocol coordinator's approval of consent/assent form(s)
d. IRB Authorization Agreement (IAA) for the specific study, completed and signed by the site. If the study falls under a master IAA (e.g., master IAA for BMT CTN studies) that has already been executed, this step is not necessary.
e. If applicable, any locally-developed recruitment material or participant-facing consent material

3. Respond to any requests for additional information from the NMDP IRB.
4. 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 date.

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 central study-level protocol coordinator. Continuing review approvals apply to all sites relying on the NMDP IRB for the study at the time of continuing review. The NMDP IRB does not issue individual continuing review approval letters for sites.

Amendment Review

The Signatory Institution has no regulatory responsibilities for reviewing changes to previously approved research from the perspective of the NMDP IRB. NMDP IRB approvals for study-level amendments apply to all sites relying on the NMDP IRB for the study (with the exception of consent form revisions-see below).

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 previously-approved institutional consent form.
2. Send this tracked changes version to the central study-level protocol coordinator for approval.
3. After approval by the central study-level protocol coordinator, submit an *IRB Request for Study Amendment* xForm in IRBManager. Attach the tracked changes version of the consent form and documentation of the central study-level protocol coordinator's approval.

4. Receive an email from the NMDP IRB documenting approval of the study site's revised consent form, including the finalized consent form with the NMDP IRB approval date.

Re-consent Requirements

If the Study/Protocol Chair or the NMDP IRB requires study participants to be re-consented using the most recent amendment, the NMDP IRB notes this determination in the study-level 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.

Remote Consent Sessions and Electronic Consent Signatures

Remote consent sessions are acceptable to the NMDP IRB, provided:

1. The study protocol does not specify that the consent session must be done in person.
2. Phone or videoconference consent sessions are not prohibited by the participating research site's Standard Operating Procedures.
3. The research participant has the consent form in front of him/her (in either paper or electronic format) when the consent session is being discussed.
4. The research participant feels he/she is in a private space and is comfortable to discuss the study and ask questions.
5. The research participant is given the opportunity to ask questions.
6. **No research procedures may begin until the site has the signed consent document back from the research participant.**

Additionally, when obtaining consent remotely, researchers must:

1. Document in the research chart the conversation that took place, name of the study team member who provided the information, date and time.
2. Document how the informed consent document was transmitted to the research participant (e.g., email, fax, mail, etc.).
3. Document how the research participant's signature was obtained. For example:
    - Electronic signature
    - Scanned and emailed, faxed, or mailed back to the study team
    - Photograph of signature/signature page sent back to the study team
4. NOTE: For FDA-regulated research, the electronic signature program used by the site must be compliant with 21 CFR 11 regulations.

Short Forms for Non-English Speaking Participants

The NMDP IRB has a Short Form for Non-English Speaking Research Participants translated into several languages. These forms can be found on the IRB webpages of the NMDP Network website.

If the Signatory Institution wishes to use their own Short Forms, they must first be approved by the NMDP IRB. The institution's Primary Contact should submit the *Site-specific Documents*

Submission xForm in IRBManager, accessible under the Site Management page, and attach the institution's template English Short Form. The template English Short Form will be reviewed at a convened NMDP IRB meeting.

Once the institution's template English Short Form has been approved by the NMDP IRB, the site may obtain NMDP IRB approval for their translated Short Forms on a study-by-study basis. The site may submit their study-specific translated Short Forms either at initial study-site review (via the *NMDP sIRB Study-Specific Local Context Worksheet* xForm) or with an amendment (using the *IRB Request for Study Amendment* xForm). The translated Short Form must match the template English version of the Short Form that has been approved by the NMDP IRB, and a translator's certificate(s) of accuracy or equivalent document(s) must also be submitted.

The site principal investigator must determine that there is sufficient justification for obtaining the subject's consent using the Short Form process, and that use of the Short Form consent process will provide the subject with sufficient opportunity to understand the information being presented. NMDP IRB policy does not require the re-consent of a subject with a fully translated consent form after the use of a Short Form. However, if the Signatory Institution has a stricter policy, the site should follow their local policy.

Fully-Translated Consent Documents

If the Signatory Institution wishes to translate the full consent document, the translated document must first be approved by the NMDP IRB before use. The consent document that is used for translation must be the NMDP IRB final approved consent document for the institution. Submit an *IRB Request for Study Amendment* xForm in IRBManager. Be sure to attach the following to the request:

1. Translated consent document(s), which should match the version number and approval date of the English version(s).
2. Translator's Certificate(s) of Accuracy or equivalent document(s)

Annual Worksheet Review

The *Single IRB Signatory Institution Enrollment and Local Context Form* should be updated on an ongoing basis if there are changes to the Component or Affiliate Institutions, institutional requirements, or any other institutional changes. Additionally, Signatory Institutions must review the form at least annually to verify the form reflects the current policies and procedures for the institution.

Using each institution's enrollment date, institutions will be notified annually. The Signatory Institution Primary Contact(s) (SIPC) receives an email notification from IRBManager requesting the SIPC review the previously submitted *Single IRB Signatory Institution Enrollment and Local Context Form* and make any necessary changes. The SIPC should review the form within a month after notification. A reminder will be sent after three weeks.

Updating Information with the NMDP sIRB

Institutional Boilerplate Language

For changes to the Signatory Institution's required boilerplate consent language outside of the institution's annual review, the Signatory Institution's Primary Contact must submit a *Site-specific Documents Submission* xForm in IRBManager accessible under the Site Management page.

Signatory Institution Primary Contacts or Signatory Official

For changes to the Signatory Institution's primary contacts or signatory official outside of the institution's annual review, the Signatory Institution's Primary Contact must submit an *Add/Remove sIRB Site Contacts* xForm in IRBManager accessible under the Site Management page.

Signatory Institution Enrollment and Local Context Form

For changes to the information on the institution's *Single IRB Signatory Institution Enrollment and Local Context Form* outside of the institution's annual review, the Signatory Institution's Primary Contact must submit the changes in IRBManager by clicking on the "copy" icon next to the form on the institution's Site Management page and making the changes within the form. Changes can be submitted on this form at any time, even if it is not time for the institution's annual review of the institutional information.

Study-Site Contacts

To add or remove site contacts for a specific study, a current study-site contact must submit an *Add/Remove Study-Site Contacts* xForm in IRBManager accessible under the specific study.

Study-Site Principal Investigator

A change in a study-site's principal investigator must be approved by the NMDP IRB. A current study-site contact must submit the following in IRBManager:

1. *Revised NMDP sIRB Study-Specific Local Context Worksheet* xForm, accessible under the specific study
2. Attach documentation of new PI's training in human research protections (not GCP)
3. Attach redlined consent documents showing change in PI
    - If for some reason the consent documents are not being updated with the PI change, (e.g., study is closed to accrual) attach a document explaining the rationale for not updating the consent documents.

    NOTE: The **new** PI will need to sign off on the xForm in IRBManager.

If the principal investigator change is temporary (e.g., temporary leave of absence), the above process must still be completed, so that the NMDP IRB has on record the temporary investigator in charge. The site will indicate on the xForm whether the change in PI is permanent or temporary. The above process must be completed again when the permanent investigator returns from leave.

Study-Specific Local Context Worksheet

For changes to a site's Study-Specific Local Context Worksheet, other than study-site contacts, a current study-site contact must submit a *Revised NMDP sIRB Study-Specific Local Context Worksheet* in IRBManager, accessible under the specific study. Some examples of changes to this form might include deciding to now include minors in your site's enrollment population, creating site-specific recruitment material, changing the roles of who is authorized to obtain consent, or disclosing and submitting a new financial conflict of interest management plan.

Closing a Study at an Institution

The Protocol/Study Chair has ultimate responsibility for submitting a *Notification of Study Closure* when an entire study is to be closed with the NMDP IRB. The NMDP IRB's acceptance of a study closure also applies to all sites relying on the NMDP IRB for the study. The NMDP IRB does not issue individual closure letters for sites.

An exception is when a site wants to close a study at their site prior to the study closing with the NMDP IRB as a whole. In this case, 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:

1. The study is closed to accrual at the local institution.
2. 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.
3. 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 prior to the study closing as a whole, a current study-site contact must complete the *Study Site Closure Form* in IRBManager, accessible under the specific study. The site must also upload documentation from the central study-level protocol team approving premature study closure at the site.

6 . Special Considerations Regarding Pediatric Study Participants

Assent Requirement

The NMDP IRB determines whether assent of a child is required to participate in research. The NMDP IRB also makes a determination regarding the age range for obtaining assent of the child on a study. 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 accepted by the NMDP IRB. However, local institutions may follow their own policies and procedures for how assent is documented. If local institutional policies and procedures for documenting assent differ from the above (e.g., separate assent forms are not required), this information must be provided to the NMDP IRB as part of the local context considerations via the *Single IRB Signatory Institution Enrollment and Local Context Form.*

The NMDP IRB reserves the right to determine how assent must be documented on a study-by-study basis.

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. To request a waiver of assent, a current study-site contact must submit a *Major Protocol Exception Request Form* in IRBManager, accessible under the specific study.

Consent at Age of Majority

A study participant who has not yet reached the age of majority cannot provide legally effective informed consent. When a study participant reaches the age of majority, the NMDP IRB requires consent of the study participant if there are ongoing interactions or interventions with participants or the study involves the continued analysis of specimens or data for which the participant's identity is readily identifiable to the investigator(s). The Signatory Institution may follow their local policies and procedures for how age of majority consent is documented, as described in their *Single IRB Signatory Institution Enrollment and Local Context Form*.

If the Signatory Institution has a standard Age of Majority consent form, it must be approved by the NMDP IRB on a study-by-study basis prior to use. The site may submit their study-specific Age of Majority consent form either at initial study-site review (via the *NMDP sIRB Study-Specific Local Context Worksheet* xForm) or with an amendment (using the *IRB Request for Study Amendment* xForm).

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; and

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.

Unanticipated problems occurring at your institution that meet all three criteria above must be reported to the NMDP IRB using the *Reportable Event Form* in IRBManager. The Principal Investigator and institutional contacts will be notified of the NMDP IRB's determination, including review of the management plan and whether any additional action is required, if applicable.

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.

Noncompliance occurring at your institution that meets the criteria above for serious and/or continuing noncompliance must be reported to the NMDP IRB using the *Reportable Event Form* in IRBManager. The Principal Investigator and institutional contacts will be notified of the NMDP IRB's determination, including review of the management plan and whether any additional action is required, if applicable.

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 is intended by the investigator and may or may not 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 submit the *Major Protocol Exception Request Form* in IRBManager. 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. Major protocol exceptions must be documented by the investigator as part of their study records.

A **minor protocol exception** is a protocol exception that is not intended by the investigator and cannot be prevented. 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 central study-level protocol team 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 central study-level protocol team and be submitted to the NMDP IRB at the time of the study's next continuing review.

Adverse Events

Internal Adverse Events

Internal adverse events (events occurring at your site) 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 as described above.

External Adverse Events

External adverse events (events occurring at a different site) will be reported to the NMDP IRB, if necessary, by the site where the event occurred and/or the central study-level protocol team. If you receive an external adverse event report (e.g., Investigator Safety Letter) from the central study-level protocol team, you do not need to submit it to the NMDP IRB.

Reporting to OHRP and FDA

The NMDP IRB will report determinations of unanticipated problems and/or serious or continuing noncompliance to OHRP and any other applicable agencies (e.g., FDA) according to NMDP IRB SOPs. Individuals included on the original correspondence will also be included on the reports to the agencies.

8 . COMMUNICATIONS

General Information

General information regarding NMDP IRB policies and procedures can be found on the NMDP 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, such as template consent documents, can be found on the appropriate study website (e.g., the study-specific BMT CTN SharePoint website) or will be communicated to participating sites by the central study-level protocol coordinator.

When trial-wide study-specific notifications are required, the appropriate central study-level 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 and appropriate study or regulatory staff.

Communicating with the NMDP Single IRB

Relying institutions may communicate directly with the NMDP sIRB regarding questions or concerns by emailing IRBstaff@nmdp.org.

9 . IRBMANAGER

IRBManager is an online submission, workflow, and data management system for the NMDP IRB. Institutions and study-sites relying on the NMDP IRB will submit forms for NMDP IRB review through IRBManager. These forms are then electronically routed through the required review process. Through IRBManager, site investigators and research staff have access to see their studies. IRBManager is a fully web-based system, which means that users can log in anywhere they have internet access.

For instructions on using IRBManager, refer to the **IRBManager for Researchers and Staff User Guide** on the IRB webpages of the NMDP Network website.

APPENDIX 1: LIST OF REFERENCED DOCUMENTS

Add/Remove sIRB Site Contacts Form

Add/Remove Study-Site Contacts Form

IRB Authorization Agreement – All BMT CTN Studies

IRB Request for Study Amendment Form

Major Protocol Exception Request Form

NMDP IRB Standard Operating Procedures

NMDP sIRB Study-Specific Local Context Worksheet

Notification of Study Closure

Reportable Event Form

Revised NMDP sIRB Study-Specific Local Context Worksheet

Single IRB Signatory Institution Enrollment and Local Context Form

Site-specific Documents Submission Form

Study Site Closure Form

APPENDIX 2: KEY TERMS

1. **Affiliate institutions** have a different FWA number than the Signatory Institution, and 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 Signatory Institution Enrollment and Local Context Form;
    - 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 Signatory Institution Enrollment and Local Context Form; and
    - The conduct of research at the Affiliate Institution is monitored by the same office as the Signatory Institution.

2. **Boilerplate language** is required wording added by the Signatory Institution Principal Investigator to the NMDP IRB-approved consent form template. 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 institution, institution-specific injury language, institution-specific pregnancy language, and other institution-specific information. An institution's boilerplate language must be accepted by the NMDP IRB. Updates to boilerplate language must also receive NMDP IRB acceptance 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 Enrollment and Local Context Form;
    - 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 Enrollment and Local Context Form; 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 is intended by the investigator and may or may not 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 is not intended by the investigator and cannot be prevented.

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 and Local Context Form* annually for necessary updates.

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; and

    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.