1. PURPOSE

1.1 The purpose of this Standard Operating Procedure (SOP) is to outline the process for determining the IDE regulatory requirements for a Division of Microbiology and Infectious Diseases (DMID)-funded device clinical study.

2. SCOPE

2.1 This SOP applies to all Division of Microbiology and Infectious Diseases (DMID) staff members.

2.2 This SOP applies to clinical trials funded by contract or cooperative agreement that use a device that is not FDA cleared or approved.

3. DEFINITIONS

3.1 **Abbreviated IDE:** It refers to the Abbreviated regulations under 21 CFR 812.2(b) for an investigation of a Non-Significant Risk (NSR) device. The IRB must review and approve the study but no specific notification or approval from the FDA is required.

3.2 **Investigational Device Exemption (IDE):** An IDE allows an investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification [510(k)] submission to FDA.

3.3 **Non-Significant Risk (NSR) Device:** An investigational device that does not present a potential for serious risk to the health, safety, or welfare of a subject. IRB approval is required with an IRB risk determination of NSR. The FDA considers an NSR device study to have an approved IDE after IRB approval and must meet the abbreviated IDE requirements under 21 CFR 812.2(b).

3.4 **Significant Risk (SR) Device**: A device that presents a potential for serious risk to the health, safety, or welfare of a subject. Significant risk devices may include implants, devices that support or sustain human life, and devices that are substantially important in diagnosing, curing, mitigating, or treating disease or in preventing impairment to human health.

For other definitions, see DMID glossary.

4. RESPONSIBILITIES

4.1 ORA Director or Designee has the responsibility to:

4.1.1 Review risk determination, and requests with supporting documentation.

4.1.2 Determine risk.

4.1.3 Determine regulatory requirement.

4.2 DMID Branch/Office (Program staff, Medical Officer) has the responsibility to:

4.2.1 Make the initial risk determination based on communication with the device manufacturer, owner, and/or supplier, (the entity).

4.2.2 Prepare the risk determination document and submit to the Office of Regulatory Affairs (ORA).

4.3 The Regulatory Affairs Manager (RAM) has the responsibility to:

4.3.1 Communicate with the FDA, if FDA assistance is needed to determine risk; and determine whether the study will be conducted under an IDE, an abbreviated IDE or without an IDE.

5. PROCEDURE

5.1 A DMID-funded device clinical study will be considered a significant risk (SR) study and must be conducted under an IDE unless ORA approves that the study is a non-significant risk (NSR) study, and can be conducted under an abbreviated IDE, or approves that the study as an exempted study and can be conducted without an IDE.

5.2 A device clinical study must be conducted under an IDE if required by Food and Drug Administration (FDA) regulations.

5.3 Program staff will conduct discussions with the device owner (entity) regarding information known about the device, to include the mechanism of action and the level of risk to study volunteers.

5.3.1 It is recommended that the Program staff review the FDA Guidance entitled “Significant Risk and Nonsignificant Risk Medical Device Studies”.

5.3.2 The Program staff must determine an initial assessment of risk as SR, NSR or exempted for the device.

5.4 The Program staff will complete the request form “Request to Conduct a DMID-Funded Clinical Study as IDE, Abbreviated IDE or without an IDE” based on the communication with the entity.

5.4.1 Form: DMID-RA-FORM-00002

- https://cqms.niaid.nih.gov:443/prd/index.cfm?initialRequest=https%3A%2F%2Fcqms.niaid.nih.gov%3A443%2Fprd%2Fmain%2Findex.cfm%3Fevent%3DshowFile%26ID%3DZERO4PNMUJHGZD3I5N%26static%3Dfalse

5.5 The Program staff will provide the ORA Director the completed request form, the risk assessment of SR or NSR, the clinical protocol and any other supporting information, if not in protocol, such as:

5.5.1 Description of the device

5.5.2 Prior investigation

5.5.3 Investigation plan

5.5.4 Note: The clinical protocol or summary is essential because the proposed use of a device with the device information is used to determine the potential risk to subjects.

5.6 The ORA Director will review the information, consult with Program staff and the RAM assigned to the programmatic branch, and will approve or disapprove the request based on the risk of the device, FDA Risk determination guidance, and IDE regulatory requirements.

5.7 The ORA Director will complete the review and inform the Program staff if the request is approved or disapproved, with rationale. When the risk determination is unclear, the FDA may be contacted by ORA for help with the risk determination.

5.7.1 The ORA Director will send a copy of the completed Form to the Regulatory Information Management system (RIM) for archiving or to be stored with the IDE.

5.7.2 The final determination will be provided to program staff.

5.8 The Program Staff will communicate the risk determination to the clinical site investigator(s) for IRB to review.

5.8.1 The IRB reviews DMID's risk determination and may modify the determination if the IRB disagrees with DMID.

5.8.2 The Program Staff will provide a copy of the IRB's final determination document to ORA for archiving or stored with the IDE in the RIM.

5.9 If the FDA were not consulted (per section 5.7) during the Program risk determination process, when DMID submits the IDE application for a SR or an Abbreviated IDE for a NSR, the FDA may disagree with an IRB's determination for an SR or NSR study, and change to classify the study as NSR or SR. In such a case, the FDA will return the IDE application to ORA with the recommendation that the application be presented to the IRB as an NSR or SR study.

5.9.1 The RAM will relay the FDA's decision to change the classification to the program staff and upload the document to the RIM.

6. REFERENCES

6.1 U.S. Code of Federal Regulations 21 CFR 812 "Investigational Device Exemptions": https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-812

6.2 FDA "Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Frequently Asked Questions About Medical Devices": https://www.fda.gov/regulatory-information/search-fda-guidance-documents/frequently-asked-questions-about-medical-devices

6.3 FDA "Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Significant Risk and Nonsignificant Risk Medical Device Studies": https://www.fda.gov/regulatory-information/search-fda-guidance-documents/significant-risk-and-nonsignificant-risk-medical-device-studies

6.4 U.S. Code of Federal Regulations 21 CFR 809: "In Vitro Diagnostic Products for Human Use": https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-809

7. APPENDICES

7.1 **Attachment A:** Type of Investigational Device Studies

8. REVISION HISTORY

8.1 DMID-RA-SOP-00004 revision 01 is the original version of this procedure within the eQMS.

9. ADDITIONAL INFORMATION

9.1 Document Lead: ORA Director

9.2 Posting externally: Yes

Attachment A: Type of Investigational Device Studies

TYPE	RISK OF THE DEVICE	IDE APPROVAL PROCESS	IRB REVIEW
Significant risk [SR] study	An SR device means an investigational device that: • Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; • Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; • Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or • Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.	• Must follow all the IDE regulations at 21 CFR 812; • Must have an IDE application approved by FDA before the study may proceed	Required
Non-significant risk [NSR] study	An NSR device study is one that does not meet the definition for an SR device study.	• Must follow the abbreviated requirements at 21 CFR 812.2(b); • Does not have to have an IDE application approved by FDA	Required
Exempted study	There are three possible device studies that are exempted from the FDA regulations on IDEs. These exemptions apply only so long as the investigator remains qualified to conduct the research (see http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=812.119 for Disqualification). iii. A diagnostic device (including in vitro diagnostic products in compliance with 21 CFR 809.10(c)if the testing: a. Is non-invasive b. Does not require an invasive sampling procedure that presents significant risk	• Not subject to the IDE regulations (21 CFR 812.2(C)). • IDE is not required.	Required

	c. Does not by design or intention introduce energy into a subject, and d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure. iv. Devices undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution , if the testing is not for the purpose of determining safety or effectiveness and does not put the subject at risk. v. Custom devices, as defined by FDA in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.		