Procedure Title: Device Research – Significant Risk (SR) versus Non-significant Risk (NSR) Determination

Associated Policy:	Human Research Protection Policy (OSA Policy 1.0)		
Responsible Unit:	Office of Scholarly Activity		
Created:	6/6/2018	**Executive Lead:**	Chief Research Officer
Effective:	6/6/2018	**Revision History:**	.01 – 10/08/2019; .02 – 3/22/2023
Approved by:	Institutional Review Board		
Procedure Number:	135.02		
Key Words:	Device, Significant Risk Device, Non-significant Risk Device, Device Determination, Investigational Device Exemption, IDE, Food and Drug Administration, FDA		
Purpose:	To meet the responsibilities for protecting human subjects as issued by the Office for Human Research Protections (OHRP) requirement for individuals involved in the conduct or review of human subjects research at institutions holding OHRP-approved Federal Wide Assurances (FWAs)		

Process:
This SOP serves to inform all agents, offices, departments, and affiliate sites of PNWU regarding the process for determination of significant risk/non-significant risk status for medical device studies submitted to the Pacific Northwest University of Health Sciences (PNWU) Institutional Review Board (IRB).

This SOP must be used as a guide in parallel with OSA Policy 1.0, to comply with human subject research protections. SOPs are not intended to supersede existing institutional policies, and local, state, and federal laws and regulations.

Responsible Parties

The Institutional Review Board (IRB) is responsible for:

- Reviewing applications in a timely fashion.
- Assessing risk and other considerations per federal regulations in the determination of exempt versus non-exempt studies.
- Communicating with the investigator as to the application status and modifications needed to ensure protection of human subjects.

The Office of Scholarly Activity (OSA) is responsible for:

- Monitoring compliance with this SOP.
- Posting this SOP for the PNWU community.
- Notifying the investigator, no earlier than 60 and no later than 30 days prior to the current IRB approval expiration date and providing them instructions for submitting a request for continuing review or a closure report.
- Ensuring all required information is received prior to forwarding a request for continuing review to the convened IRB and IRB Reviewer conducting the review.

The Investigator is responsible for:

- Completing all forms required by the IRB when conditions of approval are requested.
- Responding in a timely fashion to conditions of approval.

Definitions

Please reference the Glossary for complete definitions of the following terms and additional terms not listed.

- Exempt studies
- Federal Drug Administration (FDA)
- Full Board
- Health Information Portability and Accountability Act (HIPAA)
- Human Subject
- Investigational Device Exemption (IDE)
- Non-significant risk (NSR)
- Principal Investigator (PI)
- Quorum
- Significant risk (SR)
- Standard Operating Procedure

Procedure:

1. Clinical investigations undertaken to collect safety and effectiveness data for medical devices must be conducted according to the requirements of the IDE regulations found in 21 CFR 812. The Investigational Device Exemption (IDE) regulations describe three types of device studies: significant risk (SR), non-significant risk (NSR), and exempt studies. The major differences between SR and NSR status relate to the IDE approval process and the sponsor's recordkeeping and reporting requirements.

2. Under 21 CFR 812.3(m), 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.
   - Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

   a. If SR status is assigned to the use of a device in a particular study, then the sponsor must have an approved IDE application before the study can proceed. In addition, the sponsor must observe extensive requirements for reporting to the FDA on the progress of the research and report IRB approval to the FDA.
   b. All SR device studies are considered more than minimal risk and require full IRB review.
   c. If the IRB decides the study is significant risk, the IRB shall notify the investigator (in writing) that an IDE must be obtained from the FDA prior to IRB review of the study. Any amendments or corrections of deficiencies required by the FDA during the IDE process must be submitted for review and approval of the IRB. Once the IDE is obtained, the investigator may resubmit the study for IRB review.

d. If an IDE application is or has been submitted to the FDA, but final approval has not been granted, the IRB can proceed with the review of the study, but final approval will not be granted until documentation of the FDA approval is submitted.

3. Under 21 CFR 812.3(m), an NSR device study is one that does not meet the definition for an SR device study.
    a. If NSR status is assigned to a device study, then the sponsor may proceed without an approved IDE, must observe only abbreviated recordkeeping requirements, and is not required to inform the FDA about the conduct of the study or IRB approval.
    b. For NSR device studies, the IRB shall proceed to review the study per 21 CFR 56.111. If approved by the IRB, the investigator must comply with all abbreviated IDE requirements in 21 CFR 812.2(b), as well as informed consent and IRB regulations.

4. If a study is exempt from IDE regulations, then determination of risk status is not required.

5. Sponsors are responsible for making the initial risk determination and presenting it to the IRB. A sponsor letter of determination must be submitted with the protocol documenting the sponsor determination. Unless the FDA has already made a risk determination for the study, the IRB must review the sponsor's SR or NSR determination for the proposed study and modify the determination if the IRB disagrees with the sponsor. If the FDA has already made the SR/NSR determination for the study, the determination of the FDA is final and must be communicated by the sponsor to the IRB.

6. The PNWU IRB (or FDA) will determine whether the medical device is significant risk (SR) or non-significant risk (NSR) per 21 CFR 812 by use of any of the following:
    - A risk assessment report from the sponsor explaining the device classification.
    - The FDA letter approving the IDE (in which case the IRB will consider the investigation an SR device study.
    - Pre-market Approval letter, supplement letter or amendment letter from the FDA.
    - Information from the study application, master protocol, investigator's brochure (or package insert) and other risk evaluations presented by the sponsor or investigator.
    - Review of the FDA Information Sheet containing examples of SR and NSR devices located at http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf.
    - Reports of prior investigations conducted with the device.
    - Description of subject selection criteria.
    - Description of monitoring procedures.
    - Potential harm that may be caused by any surgical procedure used to place or implant the device.
    - The proposed use of the device and the nature of harm that may result from its use in the study.
7. When reviewing a device study, the IRB may make the following SR/NSR determination:
    - Approve as SR status; or
    - Approve as SR status with conditions (modifications); or
    - Approve as NSR status; or
    - Approve as NSR status with conditions (modifications); or
    - Require modifications to secure SR/NSR determination; or
    - Unable to make an SR/NSR determination.

8. The IRB will record its determination of SR/NSR status in the minutes of the meeting. This is a separate vote of determination from approval of the study. The minutes will describe the IRB's

reasons for its SR or NSR determination and may also include the documents used to establish the IDE status for the study.

a. For an SR determination, such documentation may include a copy of the IDE approval or conditional approval letter from the FDA.
b. For an NSR determination, the documentation may include FDA's NSR classification if the agency has made such a determination.

9. The IRB will review reports of unanticipated device effects occurring during an investigation. Investigators are required to report these effects to the sponsor and to the IRB as soon as possible. Please see OSA SOP 131 Reportable Events. Should the IRB determine that the information gained in these reports changes the risk assessment, the IRB can reconsider any NSR decision and/or require the modification of the informed consent to contain the new information.
    a. The IRB will re-review the NSR decision at the next full board meeting.

References:

1. Code of Federal Regulations, Title 45, Public Welfare, Department of Health and Human Services Part 46, Protection of Human Subjects, Revised January 15, 2009, Effective July 14, 2009.
2. Department of Health and Human Services, Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection, May 5, 2004.
3. Code of Federal Regulations, Title 42 Policies of General Applicability, Department of Health and Human Services, Part 50 Subpart F – Promoting Objectivity in Research.
4. Code of Federal Regulations, the Family Educational Rights and Privacy Act (FERPA), 20 U.S.C.§ 1232g; 34 CFR Part 99. https://www2.ed.gov/policy/gen/guid/fpco/ferpa/index.html.
5. FDA Guidance on Significant Risk and Non-significant Risk Medical Device Studies located at http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf.
6. FDA Guidance on Frequently Asked Questions About Medical Devices located at http://www.fda.gov/oc/ohrt/irbs/irbreview.pdf. Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.

Revision History:

Version/ Effective Date	Author	Section Changed & Reason for Revision
.00 / 06-06-2018	M. McCarroll	Original SOP
.01 / 10-08-2019	C. Case	Put into new PNWU SOP Format
.02 / 3-22-2023	C. Case	Removed reference to the L: Drive from the footer as all SOPs are now stored in the electronic IRB management system; minor punctuation corrections

Appendices:

None