

Research Involving Medical Devices

1.0 Purpose:

The purpose of this policy is to ensure compliance with all Food and Drug Administration (FDA) investigational device regulations by defining investigator and institutional responsibilities and by establishing procedures for the proper review, control, storage, use and handling of these devices.

2.0 Scope:

At Wright State University (WSU), all human research studies involving medical devices must be reviewed by an IRB of record and conducted in compliance with Investigational Device Exemption (IDE) requirements (21 CFR 812) unless determined to be exempt via 21 CFR 812.2(c).

This policy also applies to research involving medical devices in which the WSU Institutional Review Board (IRB) acts as an IRB of Record for an external institution (e.g., Premier Hospitals, Dayton VA, etc....).

3.0 Definitions:

3.1 **Investigational Device** means a device, including a transitional device, that is the object of an investigation.

3.2 **Medical Device** means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them;
- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or;
- Intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

3.3 **Significant Risk (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 a use in 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.
- 3.4 **Non-Significant Risk (NSR) Device** means a device that does not meet the definition of a SR device. Note that “non-significant risk” and “minimal” risk is not synonymous.
- 3.5 **Category A Device** means an experimental/investigational device for which there is no Medicare coverage.
- 3.6 **Category B Device** means a non-experimental investigational device that is eligible for Medicare coverage.
- 3.7 **510(k) Device** means a new device that the FDA agrees is substantially equivalent to a device already on the market. 510(K) devices can be marketed without clinical testing. However, if clinical data are necessary to demonstrate substantial equivalence, any clinical studies must be conducted in compliance with the requirements of the IDE, IRB review and informed consent regulations.
- 3.8 **Investigational Device Exemption (IDE)** means a submission to the FDA that allows the investigational device to be used in a clinical trial in order to collect safety and effectiveness data required to support a Premarket Approval Application (PMA). All clinical evaluations of investigational devices must have an approved IDE before the study is initiated.
- 3.9 **IDE Number** means the FDA assigned special identifier that corresponds to each device granted an IDE.
- 3.10 **Sponsor** means a person who initiates, but who does not actually conduct, the investigation, that is, the investigational device is administered, dispensed, or used under the immediate direction of another individual. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.
- 3.11 **Sponsor-Investigator** means an individual who both initiates and actually conducts, alone or with others, an investigation, that is, under whose immediate direction the investigational device is administered, dispensed, or used. The term does not include

any person other than an individual. The obligations of a sponsor-investigator under this policy include those of an investigator and those of a sponsor. Sponsor-investigators responsibilities include the following:

- Maintaining the Investigational Device Exemption (IDE)
- Obtaining qualified investigators and monitors
- Providing necessary information and training for investigators
- Monitoring the investigation
- Controlling the investigational device
- Reporting significant adverse events to FDA/investigators
- Maintaining and retaining accurate records
- Implementing and maintain quality assurance with written standard operating procedures

At WSU, any investigator who wishes to assume the role of a sponsor-investigator must first consult with the Office of the Vice President for Research to assess the proposed research plan and expertise/resources available to comply with “sponsor” requirements above.

- 3.12 **Transitional Device** means a device subject to section 520(1) of the FD&C Act and which the FDA previously regulated as a new drug or an antibiotic drug before May 28, 1976.

4.0 Policy

This policy defines the applicability of federal regulations and the procedures the IRB follows to determine whether a:

- 4.1 Study meets one of the exemption criteria defined in Section 5.1
- 4.2 Study involves a non-significant risk (NSR) device and can be conducted under an Abbreviated IDE, or
- 4.3 Study involves a significant risk device and must be conducted under formal IDE submitted to and approved by FDA as defined by 21 CFR 812.

Research involving a marketed device that is only being used to 1) measure a clinical outcome for medical care or used to elicit a physiologic response unrelated to the device itself, and 2) collects no safety or effectiveness data about or on the marketed device is not subject to this policy or FDA IDE regulations. For example, when a study uses an MRI to measure tumor growth, but does not collect data on or assess how effective MRI is at making the measurement.

It is important to note that this policy does not cover activities involving Humanitarian Use Devices. Investigators must follow WSU’s “Humanitarian Use Device” policy in those cases.

5.0 Procedure

5.1 Exempt Determinations

There are five device exemption categories that may be applied to WSU clinical research studies. It is important to understand that these exemptions apply only so long as study investigators remain qualified to conduct the research (see 21 CFR 812.119 for more information regarding *Disqualification*). If the IRB grants an exemption, it means that the study does not require an Investigational Device Exemption (IDE). It does not mean that the study is “exempt” from IRB review per 45 CFR 46.101(b).

As part of the initial IRB application process, the PI should indicate which of the following five exemption categories applies to the proposed study:

- 5.1.1 Devices, other than transitional devices, in commercial distribution prior to May 28, 1976 when used or investigated in accordance with labeling in effect at that time;
- 5.1.2 Devices, other than transitional devices, introduced into commercial distribution on or after May 28, 1976, that the FDA determines to be substantially equivalent to a device in commercial distribution prior to May 28, 1976, and which is used or investigated in accordance with approved labeling;
- 5.1.3 A diagnostic device (including in vitro diagnostic products in compliance with 21 CFR 809.10(c) if the testing:
 - 5.1.3.1 Is non-invasive
 - 5.1.3.2 Does not require an invasive sampling procedure that presents significant risk
 - 5.1.3.3 Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
- 5.1.4 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, or
- 5.1.5 Custom devices, as defined by 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

The IRB will consider the information provided by the PI, sponsor, or FDA which indicates that the device meets one of the categories above. If the IRB agrees that the study is exempt from IDE requirements, the IRB does not need to make a SR/NSR

determination and will evaluate the study in accordance with 21 CFR 50, 21 CFR 56, 45 CFR 46 and all applicable IRB policies and procedures. However, if unsure, the IRB may request that the PI consult with the FDA to verify that the study is exempt from IDE requirements.

5.2 Significant vs. Non-Significant Risk Determinations

Study sponsors are responsible for making the initial risk determination and presenting it to the IRB via the local PI. The IRB must review the sponsor's significant risk (SR) or non-significant risk (NSR) determination for every investigational medical device study and modify the determination if the IRB disagrees with the sponsor. **However, if the FDA has already made the determination for the study, the FDA's determination is final.**

To make a SR/NSR determination, the IRB will review information such as the sponsor's risk designation and justification, description of the device, reports of prior investigations, study protocol, and subject selection criteria at a convened meeting. If the PI requests a NSR determination, he/she will be required to provide additional information via the initial application questions regarding why the investigational device does not meet the definition of a SR device (see Definitions above).

If the IRB determines that a study involves a NSR device, the IRB may then approve the study using standard approval criteria at 21 CFR 56.111. Once the study receives IRB approval the PI must still follow the abbreviated IDE requirements including labeling, informed consent, monitoring, records, reports and prohibition on promotion. However, investigators are only required to submit study progress and final reports to the IRB.

The IRB's risk determination for the device must be recorded in the minutes of the convened meeting and in written correspondence (e.g., study approval letter) with the PI. If the IRB disagrees with the sponsor's NSR assessment and decides that the study is SR, the IRB will document this determination, and where appropriate, inform the sponsor per 21 CFR 812.66. The IRB may also vote to allow continuing review to be conducted using the expedited review procedure, if the research poses no more than minimal risk to subjects and no additional risks have been identified.

5.3 Significant Risk Device Requirements

Studies involving an investigational medical device determined to represent a SR may not proceed without submission of an Investigational Device Exemption (IDE) application to the FDA and subsequent receipt of confirmation of the FDA decision on the application. The term "exemption" in this case means exempt from laws prohibiting unapproved products to move in interstate commerce. It does not mean that the study is "exempt" from IRB review per 45 CFR 46.101(b).

The IDE allows the investigational medical device to be used in a clinical study to collect safety and efficacy data required to support a marketing application. An IDE may be held either by a commercial sponsor/institution (e.g., Medtronic or Johns Hopkins University) or by a sponsor-investigator.

For studies involving SR devices where the WSU PI is not the sponsor, the PI must provide the IRB at the time of his/her initial IRB submission with the IDE number and one of the following three documents to validate the IDE:

- 5.3.1 Written communication from the sponsor;
- 5.3.2 Written communication from the FDA (required for investigator-held IDE);
- 5.3.3 Sponsor protocol imprinted with IDE number.

5.4 Emergency Use

“Emergency use” means the use of an investigational medical device in an emergency situation. It is intended to provide patients and physicians with access to devices intended to treat life-threatening or serious diseases or conditions when there is no available alternative and no time to obtain FDA approval. “Emergency use” is not the same as “emergency research.” Emergency research is “planned research” conducted in emergent situations that is typically conducted without informed consent.

Emergency use may apply even if the investigational device is being studied in a clinical trial under an IDE at WSU/affiliated hospital. For example, if a WSU/affiliated hospital physician (who is not a member of the clinical study team) needs to use the device in a manner inconsistent with the approved investigational plan or wishes to use the device to treat a patient with a life-threatening or serious disease or condition, he/she may do so under this regulatory provision.

Emergency use of an investigational device may occur before an IDE is approved and when a device is not being studied under an IDE given the following criteria:

- 5.4.1 The patient has a life-threatening or serious disease or condition that needs immediate treatment;
- 5.4.2 No generally acceptable alternative treatment for the condition exists; and
- 5.4.3 Because of the immediate need to use the device, there is no time to use existing procedures to obtain FDA approval for the use.

The FDA expects a WSU/affiliated hospital physician to make the determination that the patient's circumstances meet the above criteria, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist. If a device is used in circumstances meeting the criteria listed above,

the WSU/affiliated hospital physician must follow as many patient protection procedures as possible. Such patient protection procedures include obtaining:

- 5.4.4 Informed consent from the patient or a legal representative;
- 5.4.5 Clearance from the institution via the Institutional Official (IO) or Designee;
- 5.4.6 Concurrence of the IRB chairperson;
- 5.4.7 An independent assessment from an uninvolved physician; and
- 5.4.8 Authorization from the device manufacturer.

If there is an IDE for the device, the IDE sponsor, utilizing information provided to sponsor by the WSU/affiliated hospital physician, must **notify the FDA of the emergency use within five days through submission of an IDE Report** (§812.35(a)(2)). This follow-up report should include a summary of the conditions constituting the emergency, the patient protection measures that were followed, and patient outcome information.

If no IDE exists, the WSU/affiliated hospital physician should submit a follow-up report on the use of the device (description of device used, details of the case, and the patient protection measures that were followed) to:

Food and Drug Administration
Center for Devices and Radiological Health
10903 New Hampshire Ave
Document Control Center
WO66 Rm G-609
Silver Spring, MD 20993

When possible, the WSU/affiliated hospital physician should submit Part I of the Emergency Use Notification form (<http://www.wright.edu/research/compliance/human-subjects#forms>) to the IRB office to receive review and approval from the IRB Chair/Designee prior to the use.

Within 5 working days of the emergency use, the WSU/affiliated hospital physician must also submit Part II of the Emergency Use Notification Form which requires the following information:

- A statement of who placed the device and why it was used.
- An evaluation of the likelihood of a similar need for the device occurring again.
- Copies of FDA correspondence as described above.
- Confirmation that the physician will refrain from further Emergency Use of the investigational product until any necessary approvals have been secured (e.g., opening of a new “high risk” arm on the trial), even if the conditions for an emergency use otherwise exist

- A copy of the unsigned consent form, if applicable
- If obtaining informed consent prior to use was NOT possible, include written certification from independent physician that:
 - It was not feasible to secure the recipient’s legally effective consent (for example because the recipient was unconscious or sedated or legally incompetent
 - Time was insufficient to secure consent from the recipient’s legally authorized representative
 - The patient was confronted by a life-threatening situation (including one involving risk of serious, irreversible morbidity), necessitating use of the product.
 - At the time of the procedure, there was no available alternative method of approved or generally recognized therapy that would have provided equal or greater likelihood of saving the subject’s life or avoiding serious, irreversible morbidity.

The notification form will be reviewed at the next convened meeting of the IRB, after which the WSU/affiliated hospital physician will receive written notification as to whether the IRB concurred with the emergency use and whether it requires any additional actions.

It is important to understand that the FDA allows for only one emergency use of a device without prospective IRB approval. Therefore, if subsequent use is anticipated it must occur under a fully-approved new IRB submission and IDE, if applicable.

5.5 Compassionate Use

The FDA provides procedures for the use of an investigational device outside the parameters of an approved protocol. In the case of a serious disease, a device may be made available after the completion of all the clinical trials. If an “immediately life-threatening disease” presents, an investigational device may be made available for treatment use prior to the completion of the research.

Investigators must contact the FDA to discuss “compassionate treatment” using an investigational device outside of an IRB-approved protocol and must obtain IRB approval for this use. The FDA will consider the use of an investigational device under a treatment IDE if:

- 5.5.1 The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
- 5.5.2 There is no comparable or satisfactory alternative device or other therapy available to treat or diagnose that stage of the disease or condition;

- 5.5.3 The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or such clinical trials have been completed;
- 5.5.4 The sponsor of the investigation is actively pursuing marketing approval/clearance of the investigational device with due diligence.

Written FDA approval of compassionate use of an investigational device must be included with an investigator's initial IRB submission (a.k.a., Initial Review Form) and IRB approval must precede any use of that device.

5.6 Unanticipated Adverse Device Effects (UADEs)

An Unanticipated Adverse Device Effect is defined by the FDA as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application. It also means any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

UADEs must be promptly reported to the IRB via the InfoED Reportable Events form in accordance with the WSU IRB's "Reportable Events Policy – P9."

6.0 Responsibilities and Authorities:

In accordance with FDA regulations 21 CFR 812 and WSU policies, the sponsors and/or investigators are responsible for ensuring that an investigation is conducted according to the signed agreement and the investigational plan; for protecting the rights, safety, and welfare of subjects under the investigator's care; ensuring that informed consent is obtained; and for the proper ordering, handling, storage, and disposition of investigational devices in clinical trials at WSU/affiliated hospital. If use of medical devices for research are not subject to site-specific hospital policies, investigators must ensure the following:

6.1 Ordering

Ordering of an investigational device must be done by the Principal Investigator (PI) or designated study personnel according to the terms of the executed agreement and only after the protocol has been approved by the IRB.

6.2 Receipt

Investigational devices may only be received by the PI or designated study personnel at a WSU/affiliated hospital business address.

6.3 Storage/Labeling

- 6.3.1 Investigational devices used in conjunction with a research protocol must be kept in a locked and secured area and must be labeled "Caution: Investigational Device-Limited by Federal Law (or United States Law) to Investigational Use."
- 6.3.2 Access to investigational devices must be limited to the PI or designated study personnel.
- 6.3.3 Study device supplies must be labeled as investigational by the manufacturer or PI (if not done by manufacturer) and maintained and stored separately in a secure location by research personnel.

6.4 Dispensing

- 6.4.1 The investigational device may not be given to anyone not enrolled in the study.
- 6.4.2 The PI must not supply the investigational device to any person not authorized.
- 6.4.3 For accountability purposes, an investigational device accountability log(s) must be kept for all investigational device studies. Documentation of the following elements should be recorded for each device used:
 - The type of device
 - Model number
 - Serial number
 - Lot number (if applicable)
 - Date received
 - Research subject Initials or ID number (for internal tracking purposes)
 - Date implanted or used
 - Device return, repair, or destruction information
- 6.4.4 Personnel may not remove any device(s) from a WSU/affiliated hospital floor or department stock and substitute them for an investigational device, even if the device, under study, is approved and used in practice.
- 6.4.5 If the sponsor provides an investigational device accountability log, study staff must review the log to determine if the required elements above are included. If the log provided by the sponsor does not include all the required elements, a separate log including those elements must be maintained.

6.5 Maintaining an Investigational Device Log(s):

- 6.5.1 Investigational device logs must be maintained by the study team and stored long term in the study's regulatory binder for the period required by the federal regulations or terms of the agreement, whichever is longer.
- 6.5.2 The full names, titles/positions, signatures and/or initials of all WSU/affiliated hospital personnel responsible for maintaining or documenting in the log(s) must be indicated on either the Delegation of Authority Log or in the investigational device log itself.
- 6.5.3 The PI or designated study personnel must regularly review the device logs to ensure that there is an adequate number of devices or the appropriate type of devices available (sizes, etc.) to conduct the scheduled clinical trial procedures.

6.6 Disposition

- 6.6.1 Upon conclusion or termination of the clinical investigation, or by the sponsor's request, the PI shall return to the sponsor any remaining supply of the device or otherwise dispose of the device(s) as the sponsor directs. Investigational device(s) should not be destroyed by the PI or study personnel without obtaining advanced written permission from the sponsor.
- 6.6.2 Study team must document the reason for disposition, timing of disposition and names of study personnel involved in disposition.
- 6.6.3 In the event of research software, WSU/affiliated hospital privacy/IT security officials must provide clearance for removal and disposition must include the date the software was deprogrammed or removed from the device(s).

6.7 Maintenance and Cleaning

All investigational devices must be properly maintained and cleaned.

7.0 Records:

All records related to this policy will be stored and maintained in accordance with any WSU policy, federal regulations and sponsor requirements associated with the human subject research under review by WSU IRB.

8.0 References:

- 8.1 21 CFR 812
- 8.2 21 CFR 50
- 8.3 21 CFR 56

- 8.4 45 CFR 46
- 8.5 21 CFR 807
- 8.6 21 CFR 809.10
- 8.7 VA Handbook 1108.04 and 1200.05
- 8.8 38 CFR 16
- 8.9 FDA IDE Guidance:
<https://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/investigationaldeviceexemptionide/ucm162453.htm>